"For some must watch, while some must sleep"

HAMLET - Act. III, Sc.ii
The Middle East Journal of Anesthesiology is a publication of the Department of Anesthesiology of the American University of Beirut, founded in 1966 by Dr. Bernard Brandstater who coined its famous motto: “For some must watch, while some must sleep” (Hamlet-Act. III, Sc. ii).

and gave it the symbol of the poppy flower (*Papaver somniferum*), it being the first cultivated flower in the Middle East which has given unique service to the suffering humanity for thousands of years. The Journal’s cover design depicts the Lebanese Cedar Tree, with’s Lebanon unique geographical location between East and West. Graphic designer Rabi Moukalled.

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(Hamlet-Act. III, Sc. ii)
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1 Train-of-four
2 Post tetanic counts
3 Second twitch


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## CONTENTS

### EDITORIAL

**«Routine» Preoxygenation**

.................................................................................................................. Anis Baraka

### REVIEW ARTICLE

**The Impact of Endotracheal Tube vs Laryngeal Mask Airway on the Incidence of Postoperative Nausea and Vomiting: A Systemic Review and Meta-Analysis**

.................................................................................................................. Jahan Porhomayon, Sina Davari Farid, Ali A. El-Solh, Ghazaleh Adlparvar, Nader D. Nader

### SCIENTIFIC ARTICLES

**Renal Protection in the Cardiac Surgery Patient: Peri-Operative Sodium Bicarbonate Infusion (Posbi) or Not?**

.................................................................................................................. Hassan H. Amhaz, Deepak Gupta, Larry Manders, George McKelvey, Marc S. Orlewicz, Romeo N. Kaddoum

**Effect of Ultrasound-Guided Subartorial Approach for Saphenous Nerve Block In Cases With Saphenous Nerve Entrapment In Adductor Canal For Controlling Chronic Knee Pain**

.................................................................................................................. Arman Taheri, Maryam Hatami, Majid Dashti, Alireza Khajehnasiri, Mahsa Ghajarzadeh

**Comparison of the Effects of Oral vs. Peritonsillar Infiltration of Ketamine in Pain Reduction After Tonsillectomy: A Randomized Clinical Trial**

.................................................................................................................. Afsaneh Norouzi, Abolfazl Jafari, Hamid Reza Khoddami Vishteh, Shahin Fateh

**The Impact of Anesthetic Techniques on Cognitive Functions After Urological Surgery**

.................................................................................................................. Mahtab Poor Zamany Nejat Kermany, Mohammad Hossein Soltani, Khazar Ahmadi, Hoora Motiee, Shermin Rubenzadeh, Vahid Nejati

**Comparison Between C-Mac® Video-Laryngoscope and Macintosh Direct Laryngoscope During Cervical Spine Immobilization**

.................................................................................................................. Shahir H.M. Akbar, Joanna SM Ooi

**Effects of Memantine on Pain in Patients With Complex Regional Pain Syndrome-A Retrospective Study**

.................................................................................................................. Mohammad-Hazem I. Ahmad-Sabry, Gholamreza Shareghi

**Effects of Dexamethasone and Pheniramine Maleate on Hemodynamic and Respiratory Parameters After Cementation in Cemented Partial Hip Prosthesis**

.................................................................................................................. Abdulkadir Yektaş

**Effect of Preoperative Oral Pregabalin on Postoperative Pain After Mastectomy**

.................................................................................................................. Mardhiah Sarah, Harnani Mansor, Choy Yin Choy
CONSUMPTION TRENDS OF RESCUE ANTI-PsYCHOTICS FOR DELIRIUM IN INTENSIVE CARE UNITS (ICU DELIRIUM) SHOW INFLUENCE OF CORRESPONDING LUNAR PHASE CYCLES: A RETROSPECTIVE AUDIT STUDY FROM ACADEMIC UNIVERSITY HOSPITAL IN THE UNITED STATES

Deepak Gupta, Vinay Pallekonda, Ronald Thomas, George Mckelvey, Farhad Ghoddoussi

ULTRASOUND-GUIDED SCIATICO-LITEAL NERVE BLOCK: A COMPARISON OF SEPARATE TIBIAL AND COMMON PERONEAL NERVE INJECTIONS VERSUS INJECTING PROXIMAL TO THE BIFURCATION

Alberto E. Ardon, Roy A. Greengrass, Upasna Bhuria, Steven B. Porter, Christopher B. Robards, Kurt Blasser

SUBTENON BUPIVACAINE INJECTION FOR POSTOPERATIVE PAIN RELIEF FOLLOWING PEDIATRIC STRABISMUS SURGERY: A RANDOMIZED CONTROLLED DOUBLE BLIND TRIAL

Radwa H Bakr and Hesham M Abdelaziz

CASE REPORTS

STRAIGHT TO VIDEO: TONSILLAR INJURY DURING ELECTIVE GLIDESCOPE-ASSISTED PEDIATRIC INTUBATION

Jason D. Rodney, Zulfiqar Ahmed, Deepak Gupta, Maria Markakis Zestos

PERCUTANEOUS BALLOON COMPRESSION OF GASSERIAN GANGLION FOR THE TREATMENT OF TRIGEMINAL NEURALGIA: AN EXPERIENCE FROM INDIA

Anurag Agarwal, Vipin Dhama, Yogesh K. Manik, M. K. Upadhyaya, C. S. Singh, V. Rastogi

BEDSIDE RETIANED RADIAL ARTERY CATHETER REMOVAL IN A HEMODYNAMICALLY UNSTABLE NEUROCRITICALLY-ILL PATIENT: A CASE REPORT

Christa O’Hana V. San Luis, Athir H. Morad

ESOPHAGEAL PERFORATION FOLLOWING OROGASTRIC SUCTION CATHETER INSERTION IN AN ELDERLY PATIENT

Roland N. Kaddoum, Fadi Farah, Rita W. Saroufim, Salah M. Zeineldine

LETTER TO THE EDITOR

PEDIATRIC ENDOTRACHEAL INTUBATION

Claude Abdallah
LIFE ON WHEELS

Triumph over the agony of pain and sadness; admission of the ways of the creator and “happy to be alive”; optimism with brilliant accomplishments from a wheelchair and “breathing happiness”, are but few of the accomplishments of faculties endowed on Alon P. Winnie, Professor and Chairman of the Department of Anesthesiology of the University of Illinois.

In his own words, Dr. Winnie writes

«Dear Anis⋆…

To fulfill my promise to you, the following… Let me preface it by telling you that it was written from the viewpoint of a rocking bed after I had been given my first wheelchair, for which I had waited for an eternity of months while physiotherapy tried to rid me of the rigidity left behind when the pain of the muscle spasms finally subsided… It was the middle of winter and I had a beautiful view of the slum section of the city just behind the hospital…The first half obviously representing the translation of my impression at night and the second during the day…

The sad white eye of this new night
Cries myriads of auto tears
That criss-cross over its many streeted face;
The freckles of which glow dimly

⋆ Dr. Anis Baraka, Department of Anesthesiology, American University of Beirut, Beirut, Lebanon. MEJA 3: 240, 1972.
And disappear
One by one
As an angry lock of cloud
Slips down
And covers sad eye rendered sadder
By the loss of legs,
Yet soon
The bright orange eye of the day
Combs back the clouds
Revealing life and lives
Breathing happiness
In little gray-blue puffs
From the cigarette chimneys
As the city yawns
As a sleepy but happy to be alive yawn
And readies itself
For this new day
Of life on wheels…”

Fig 2. Dr. Alon Winnie
“ROUTINE” PREOXYGENATION

It is a fact of great clinical importance that the body oxygen stores are so small, and if replenishment ceases, they are normally insufficient to sustain life for more than a few minutes. Breathing oxygen causes a substantial increase in the total oxygen stores; most of the additional oxygen is accommodated in the alveolar space (functional residual capacity) from which 80% may be withdrawn without the PaO2 falling below the normal vale. This concept is the basis of the preoxygenation technique.

In 1955, Hamilton and Eastwood demonstrated that denitrogenation of the functional residual capacity of the lung is 95% complete within 2-3 minutes, if a subject is breathing at a normal tidal volume form a circle anesthesia system using an oxygen flow of 5 l/min. These studies led to the recommendation of preoxygenation as a standard practice before rapid sequence induction of general anesthesia in patients with full stomach.

“Routine” preoxygenation has become a new “minimum standard” of care not only during induction of anesthesia and tracheal intubation, but also during emergence from anesthesia and tracheal extubation.

The original American Society of Anesthesiologists (ASA) difficult airway algorithm made no mention of preoxygenation. However, in an updated report of the ASA Task Force on “Management of the Difficult Airway” 2003, the topic of face mask preoxygenation before initiating management of the difficult airway was added.

Preoxygenation before induction of anesthesia was also recommended in patients with low functional residual capacity of the lung, associated with a high oxygen consumption. This category includes the neonates, the pregnant and the morbidly obese patients who rapidly decrease their oxygen saturation during apnea while breathing room air.

Preoxygenation is also recommended in patients with decreased oxygen delivery (Cardiac output x Hb conc x% saturation x 1.34) which include patients with low cardiac output or pulmonary disease, as well as patients with low or abnormal hemoglobin such as methemoglobin.

Before induction of general anesthesia, preoxygenation can be achieved either by tidal volume breathing of 100% oxygen for 3-5 minutes using an oxygen flow of 5 l/min as described by Hamilton and Eastwood, or by the 8 deep breaths technique for 60 seconds using an oxygen flow of 10 L/min as described by Baraka et al. The mean time to decrease of hemoglobin oxygen saturation from 100% to 99% is significantly longer during the subsequent apnea following the 8-deep breaths technique of preoxygenation than following the traditional tidal volume preoxygenation technique. As suggested by Benumof, the 8 deep breaths technique may be considered the best method of preoxygenation for both efficacy and efficiency. The high efficiency of preoxygenation by the deep breaths technique may be attributed to a relatively larger minute volume, and/or to
possible expansion of any collapsed alveoli by the deep breathing technique.

The beneficial effect of preoxygenation by tidal volume or deep breathing, can be further extended during subsequent apnea by the apneic diffusion oxygenation\textsuperscript{7-9}. The technique of ADO has been advantageous not only in patients with a difficult airway or pulmonary disease, but also in children, the pregnant and the morbidly obese patients who have a high oxygen consumption associated with a relatively low FRC\textsuperscript{4}. ADO has been also used to maintain oxygenation during bronchoscopy\textsuperscript{7}, and one-lung ventilation\textsuperscript{10}.

Apneic diffusion oxygenation (ADO) is achieved by preoxygenation by tidal volume\textsuperscript{2}, or deep breathing technique\textsuperscript{5}, to be followed by insufflations of high flow of 100% oxygen by a catheter into the pharynx via an open airway. During ADO, the increase in time to hemoglobin desaturation achieved by increasing the FIO2 from 0.9 to 1.0 is greater than that caused by increasing the FIO2 from 0.21 to 0.9\textsuperscript{9}. During ADO, CO2 is not exhaled because of the mass movement of oxygen down the trachea. The alveolar CO2 concentration (PACO2) shows an initial rise of 8-16 mmHg during the first minute, followed by a subsequent fairly linear increase of about 3 mmHg/ min. Thus, the ADO can maintain oxygenation for a prolonged period. However, the increase of PaCO2 will limit the period of apnea.

In conclusion, preoxygenation has been initially recommended for rapid-sequence induction of anesthesia in patients with full stomach, as well as in patients with predicted difficult airway. However, the technique is nowadays recommended as a routine during induction, as well as during recovery from general anesthesia, since difficult airway may be unpredicted.

Preoxygenation, followed by apneic diffusion oxygenation is indicated in patients who desaturate rapidly during apnea such as the neonate, the obese and the pregnant patients who have a relatively low FRC associated with a high oxygen consumption. ADO is also advantageous in patients with decreased oxygen delivery such as the elderly, cardiac and pulmonary diseased patients. The technique is also used to maintain oxygenation during certain procedures such as bronchoscopy, and one-lung ventilation.

“Routine” preoxygenation with 100% oxygen is considered a “safety” measure during anesthetic induction and emergence from anesthesia, and is advantageous in critically-ill patients requiring airway management. However, it must be used as an adjunct rather than an alternative to a sequence of fundamental precautions that minimize adverse sequelae\textsuperscript{1}.

Anis Baraka, MD, FRCA (Hon)
Emeritus Professor of Anesthesiology
American University of Beirut
References

REVIEW ARTICLE

THE IMPACT OF ENDOTRACHEAL TUBE VS. LARYNGEAL MASK AIRWAY ON THE INCIDENCE OF POSTOPERATIVE NAUSEA AND VOMITING: A SYSTEMIC REVIEW AND META-ANALYSIS

JAHAN PORHOMAYON*, SINA DAVARI FARID**, ALI A. EL-SOLH***, GHAZALEH ADLPARVAR**** AND NADER D. NADER*****

Abstract

Objective: To investigate the impact of Endotracheal tube (ETT) vs. Laryngeal Mask Airway (LMA) on postoperative nausea and vomiting (PONV) in patients undergoing surgery with general anesthesia.

Methods: Key words searching from databases such as Medline, Embase, and Cochrane library provided 14 studies focusing on the use of ETT vs. LMA for general anesthesia. Pooled estimate of relative risk with 95% confidence interval using random effect model was conducted.

Results: 14 studies were selected for meta-analysis with a total of 1866 patients. 9 studies focused on the outcome of PONV in adult patients. It showed incidence of PONV with of LMA and ETT in adult of about 204/690 (30%) and 145/725 (20%) respectively with [Odds Ratio (OR) = 1.69, 95% CI, 0.76-3.75, P = 0.20]. Heterogeneity was high (I² = 87%). Five studies focused on the outcome of PONV in pediatric patients with PONV in LMA and ETT group of 85/229 (37%) and 72/222 (32%) respectively with (OR = 1.30, 95% CI, 0.61-2.76, P = 0.50). Heterogeneity was moderate at (I² = 53%). When all patients were combined heterogeneity was high at 81% with OR = 1.56, 95% CI, 0.87-2.79, P = 0.14.

Conclusion: Risk of PONV shows an increase trend toward the use of LMA. Larger randomized trials are needed to assess the impact of airway devices on PONV.

Keywords: Postoperative, Nausea and Vomiting, Endotracheal Tube, Laryngeal Mask Airway.

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Introduction

PONV remain a common problem occurring in 20-30% of surgical population, and can be as high as 70-80% in the high risk population. It increases cost, and delays discharge, and decreases patient satisfaction. In this analysis, nausea is defined as an uncomfortable feeling of stomach which might lead to the eagerness to vomit, while vomiting refers the actual motion of throwing up.

PONV could lead to pulmonary aspiration of gastric content and may lead to aspiration pneumonia with potentially fatal consequences. Our current knowledge outlines several well-established risk factors for the occurrence of PONV. These risk factors include: patient, anesthesia and surgical risk specific risk factors. The patient specific risk factors include, female gender, history of PONV or motion sickness, non-smoking status, age greater than or equal to three, and family history of PONV in children. Anesthesia related risk factors include volatile anesthetics, use of Nitrous oxide, and opioid use. There is also a dose relation between volatile anesthetics and opioids. Surgical risk factors include duration of surgery and type of procedure, in particular strabismus correction in children and laparoscopic procedures.

In addition to these well-established risk factors, there are other etiologies for development of PONV such as, the lower American society of anesthesiology (ASA) classification, the use of large doses of neostigmine (>2.5mg), restrictive vs. liberal intraoperative fluid strategy, ventilation mode, starvation nausea, heartburn, anxiety, depression, Hepatitis C, P450 inducers/suppressors (medications and food), migraines, and ethnicity. However, the role of airway devices and its impact on the incidence of PONV remains controversial. Therefore, the following systematic review was conducted to study the influence of airway devices on the incidence of PONV.

Materials and Methods

We conducted databases searches from Embase, Cochrane, Medline with the term “Laryngeal mask AND Endotracheal tube AND Post-operative AND Nausea AND Vomiting”. Abstracts were reviewed and only prospective RCTs included. A total of 6568 articles were identified. 5967 were excluded because it was not related to risk factors or airway device. 601 relevant articles related to PONV risk factors and airway device were screened. 584 were excluded because they were either review, duplicate and non-relevant duplications. 17 articles were assessed for eligibility with additional 3 articles excluded due to its retrospective nature and low quality. Finally, 14 articles included for final analysis [Figure 1].

Compared to Yu, we included newer studies published since, as well as pediatric studies. We also included RCTs with the use of non-depolarizers muscle relaxant and Neostigmine usage in the ETT group. RCTs with regional techniques were also excluded.

Data Extraction

Timing of PONV reporting varied among studies. Some studies reported PONV in the post-anesthesia
recovery unit (PACU) while others reported PONV on the first postoperative day. When confronted with multiple data points, data extracted for analysis with earliest time for PONV was reported. This was an effort to reduce confounding factors such as, rescue anti-emetics given after surgery. Furthermore, PACU treatment for PONV was not always standardized and was often based on individual patient variables and anesthesiologist preference. Characteristics of each study was extracted, which included last name of first author, publication year, patient age range, procedure type, usage of anesthetics and prophylactic anti-emetics. The following outcomes were also extracted including the incidence of PONV for both ETT and LMA group. After data searching and study selection, 14 studies were included in our meta-analysis. Study characteristics and demographics were shown in Table 1. 12 studies reported postoperative vomiting as the primary outcome and 10 reported postoperative nausea as the primary outcome. One study did not differentiate between nausea and vomiting. Results were shown in Table 2.

<table>
<thead>
<tr>
<th>Studies Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joshi 1997†</td>
</tr>
<tr>
<td>Adult ASA 1or 2; Succinylcholine or non-depolarizer + Neostigmine sometimes used in ET group; Higher overall fentanyl dose in intra-op ETT group; post-op pain management unstated</td>
</tr>
<tr>
<td>Patel 2010‡</td>
</tr>
<tr>
<td>Age 3-10; ProSeal LMA vs ETT; lower abdominal procedures; no opioids given intraop; caudal injection with GA with Sevo + N2O; universal OG tube use</td>
</tr>
<tr>
<td>Klockgether 1996§</td>
</tr>
<tr>
<td>Age 4-14, strabismus surgery, identical induction (Propofol, Vecuronium, Alfentanil), identical maintenance (67% N2O, Propofol, Alfentanil). PONV incidence by 24 hours reported</td>
</tr>
<tr>
<td>Dokserod 2010~</td>
</tr>
<tr>
<td>Age 3-16 tonsillectomy &amp; adenoidectomy; prophylactic Dexamethasone used; nausea and vomiting not reported separately</td>
</tr>
<tr>
<td>Gulati 2004β</td>
</tr>
<tr>
<td>Age 1-12 ophthalmologic procedures; greater duration of surgery and more strabismus procedures in LMA group</td>
</tr>
<tr>
<td>Hohlrieder 2007a</td>
</tr>
<tr>
<td>Adult 18-75, standardized induction and maintenance with oral midazolam, propofol, fentanyl, and Neostigmine in both groups. ProSeal LMA used along with ETT; Universal use OG tube placement and decompression; No prophylactic anti-emetics</td>
</tr>
<tr>
<td>Cork 1994γ</td>
</tr>
<tr>
<td>Adult outpatient peripheral orthopedic procedures; Non-depolarizers and Neostigmine used in both groups; no sig differences in patient population or duration or opioids intra-op; greater morphine post-op in ET group</td>
</tr>
<tr>
<td>Hohlrieder 2007b</td>
</tr>
<tr>
<td>Adult female 18-75 for laparoscopic gynecological surgery; iv induction after oral midazolam, ProSeal LMA used along with ETT; Universal OG placement + Dexamethasone 4mg + Tropisetron 2mg prophylactic dose administered</td>
</tr>
<tr>
<td>Quinn 1996†</td>
</tr>
<tr>
<td>Adult 18-64; Nasal ET with Mivacurium vs. none for LMA group; no prophylactic anti-emetics</td>
</tr>
<tr>
<td>Swann 1993λ</td>
</tr>
<tr>
<td>Adult laparoscopic gynecological surgeries; ASA 1-2 single blinded RCT LMA vs ET. Atracurium and Neostigmine 2.5mg given in ET group only; controlled ventilation with ETT vs intermittent manual assistance to maintain ETCO2 in LMA group</td>
</tr>
<tr>
<td>Griffiths 2013α</td>
</tr>
<tr>
<td>Adult ASA 1-2 Laparoscopic gynecological procedures. Single blinded RCT ProSeal LMA vs ET: same induction; Dexamethasone prophylaxis; universal reversal with Neostigmine 2.5mg</td>
</tr>
<tr>
<td>Idrees 2000µ</td>
</tr>
<tr>
<td>Adult ASA 1-2 Limb surgery. Single blinded RCT ProSeal LMA vs ETT; Standardized induction + maintenance; Dexamethasone prophylaxis;</td>
</tr>
<tr>
<td>Gul 2012ν</td>
</tr>
<tr>
<td>Age 1-12 strabismus surgery; ProSeal LMA vs. ETT; inhaled induction, 50% N2O, Atracurium in both groups. Universal OG tube and gastric decompression</td>
</tr>
<tr>
<td>Porhomayon 2012χ</td>
</tr>
<tr>
<td>Adult, mostly male, undergoing general anesthesia with N2O in knee surgery</td>
</tr>
</tbody>
</table>
Meta-analysis of subgroups

In terms of PONV in subgroups of adults and pediatric patients, the incidence of PONV was higher in adults’ patients. PONV in adult with the use of LMA and ETT was about 204/690 (30%) and 145/725 (20%) respectively with (OR = 1.69, 95% CI, 0.76-3.75, P = 0.20). In pediatric population PONV in the LMA and the ETT group was 85/229 (37%) and 72/222 (32%) respectively with (OR = 1.30, 95% CI, 0.61-2.76, P = 0.50). Overall, LMA was associated with higher incidence of PONV. Statistical heterogeneity for adult and pediatric patients was 87% and % 53 respectively. Test for subgroup difference was not statistically significant with p value of 0.64 and I² = 0.

Discussion

The impact of the airway device on PONV remains unresolved. Previous models included the influence of airway devices on development of PONV,

### Table 2

<table>
<thead>
<tr>
<th>Author</th>
<th>Postoperative Vomiting</th>
<th>Postoperative Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ETT</td>
<td>LMA</td>
</tr>
<tr>
<td>Joshi 1997</td>
<td>8/174 (4.6%)</td>
<td>15/207 (7.2%)</td>
</tr>
<tr>
<td>Patel 2010</td>
<td>1/30 (3.3%)</td>
<td>0/30 (0)</td>
</tr>
<tr>
<td>Klockgether 1996</td>
<td>24/50 (48%)</td>
<td>16/50 (32%)</td>
</tr>
<tr>
<td>Doksrod 2010</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gul 2012</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gulati 2004</td>
<td>2/30 (6.7%)</td>
<td>5/30 (16.7%)</td>
</tr>
<tr>
<td>Hohlrieder 2007a</td>
<td>18/100 (18%)</td>
<td>4/100 (4%)</td>
</tr>
<tr>
<td>Cork1994</td>
<td>1/22 (4.5%)</td>
<td>1/22 (4.5%)</td>
</tr>
<tr>
<td>Hohlrieder 2007b</td>
<td>6/50 (12%)</td>
<td>1/50 (2%)</td>
</tr>
<tr>
<td>Quinn 1996</td>
<td>3/50 (6%)</td>
<td>2/50 (4%)</td>
</tr>
<tr>
<td>Swann 1993</td>
<td>4/30 (13.3%)</td>
<td>8/30 (26.7%)</td>
</tr>
<tr>
<td>Griffiths 2013</td>
<td>27/57 (47.4%)</td>
<td>28/59 (47.5%)</td>
</tr>
<tr>
<td>Porhomayon</td>
<td>25/157 (15%)</td>
<td>12/157 (7%)</td>
</tr>
<tr>
<td>Idrees</td>
<td>50/3 (1.6%)</td>
<td>50/12(4%)</td>
</tr>
</tbody>
</table>

**Statistical Analysis**

RevMan 5.2 was used to calculate the odds ratio for the incidence of PONV. Subgroup analysis including only adult or pediatric patients was also performed. I² was used to assess heterogeneity with a value below 30% standing for low heterogeneity, a value between 30% and 50% standing for moderate heterogeneity and a value above 50% standing for high heterogeneity. Random effect model was used in all analyses. A p value of <0.1 was significant.

**Results**

A total of 1899 patients were included. The incidence of PONV with of LMA and ETT was 289/919 (31%) and 217/947 (22%) respectively. In all patients heterogeneity was high at 81% with OR = 1.56, 95% CI, 0.87-2.79, P = 0.14 [Figure 2, 3].
and children. This systematic review and meta-analysis includes 14 total studies focusing on the incidence of PONV comparing the different airway devices including ETT and LMA. Overall, no statistically significant difference was noted between airway devices, although a trend towards higher incidence was noted with the use of LMA group. Subgroup analysis included only children and adult, showed similar trend with stronger association in adult patients.

Compared with previously meta-analysis by Yu, we included 3 newer studies and 5 pediatric RCTs. Therefore, our final analysis was more reliable. Of the studies included, only the four by Holhreider, Quinn, Idrees and Klockgether-Radke showed a significant reduction of PONV with the use of Pro-Seal LMA. A recent meta-analysis of RCTs in 2010 by Yu looked at the risk of airway complications between the LMA and ETT. Since the primary goal of Yu study was to look at the airway complications, he failed to show statistical significance in the incidence of PONV between the two devices. Additionally, pediatric studies were excluded due to differences in airway anatomy between adult

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LMA Events</th>
<th>Total</th>
<th>ETT Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio (M-H, Random, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 Adult</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cork</td>
<td>4</td>
<td>22</td>
<td>6</td>
<td>22</td>
<td>6.1%</td>
<td>0.59 [0.14, 2.48]</td>
</tr>
<tr>
<td>Griffiths</td>
<td>27</td>
<td>57</td>
<td>28</td>
<td>59</td>
<td>8.4%</td>
<td>1.00 [0.48, 2.07]</td>
</tr>
<tr>
<td>Hohlrieder</td>
<td>63</td>
<td>100</td>
<td>17</td>
<td>100</td>
<td>8.6%</td>
<td>8.31 [4.29, 16.10]</td>
</tr>
<tr>
<td>Hohlrieder1</td>
<td>16</td>
<td>50</td>
<td>2</td>
<td>50</td>
<td>5.8%</td>
<td>11.29 [4.44, 32.38]</td>
</tr>
<tr>
<td>Idrees</td>
<td>12</td>
<td>50</td>
<td>3</td>
<td>50</td>
<td>6.4%</td>
<td>4.95 [1.30, 18.81]</td>
</tr>
<tr>
<td>Joshi</td>
<td>31</td>
<td>174</td>
<td>43</td>
<td>207</td>
<td>9.0%</td>
<td>0.83 [0.49, 1.38]</td>
</tr>
<tr>
<td>Porhomayon</td>
<td>25</td>
<td>157</td>
<td>12</td>
<td>157</td>
<td>8.4%</td>
<td>2.29 [1.11, 4.74]</td>
</tr>
<tr>
<td>Quinn</td>
<td>16</td>
<td>50</td>
<td>11</td>
<td>50</td>
<td>7.9%</td>
<td>1.67 [0.68, 4.08]</td>
</tr>
<tr>
<td>Swann</td>
<td>10</td>
<td>30</td>
<td>23</td>
<td>30</td>
<td>7.1%</td>
<td>0.15 [0.05, 0.47]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>690</td>
<td>725</td>
<td>68.0%</td>
<td></td>
<td>1.69   [0.76, 3.75]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>204</td>
<td>145</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 1.22$; $\chi^2 = 60.13$, df = 8 ($P < 0.00001$); $I^2 = 87$
Test for overall effect: $Z = 1.29$ ($P = 0.20$)

| 1.1.2 Pediatric   |            |       |            |       |        |                                |
| Dokrood           | 36         | 69    | 37         | 62    | 8.5%   | 0.74 [0.37, 1.47]              |
| Gul               | 4          | 40    | 4          | 40    | 6.0%   | 1.00 [0.23, 4.31]              |
| Gulati            | 6          | 40    | 7          | 40    | 6.9%   | 0.83 [0.25, 2.74]              |
| Klockgether       | 38         | 50    | 24         | 50    | 8.0%   | 3.43 [1.46, 8.06]              |
| Patel             | 1          | 30    | 0          | 30    | 2.4%   | 3.10 [0.12, 79.23]             |
| Subtotal (95% CI) | 229        | 222   | 32.0%      |       | 1.30   [0.61, 2.76]            |
| Total events      | 85         | 72    |            |       |        |                                |

Heterogeneity: $\tau^2 = 0.36$; $\chi^2 = 8.45$, df = 4 ($P = 0.08$); $I^2 = 53$
Test for overall effect: $Z = 0.67$ ($P = 0.50$)

Total (95% CI) 919 947 100.0% 1.56 [0.87, 2.79]
Total events 289 217
Heterogeneity: $\tau^2 = 0.92$; $\chi^2 = 69.58$, df = 13 ($P < 0.00001$); $I^2 = 81$
Test for overall effect: $Z = 1.48$ ($P = 0.14$)
Test for subgroup differences: $\chi^2 = 0.22$, df = 1 ($P = 0.64$), $I^2 = 0$

The graph favors ETT with less PONV.

but failed to show sufficient independent significance to be included in the final models. But we continue to see investigators including PONV as a variable outcome difference between LMA and ETT. Two prospective randomized control trials (RCT) by Holhreidner reported statistically significant reduction of PONV with the use of Pro-Seal LMA. A recent meta-analysis of RCTs in 2010 by Yu looked at the risk of airway complications between the LMA and ETT. Since the primary goal of Yu study was to look at the airway complications, he failed to show statistical significance in the incidence of PONV between the two devices. Additionally, pediatric studies were excluded due to differences in airway anatomy between adult
statistically significant reduction in PONV with LMA. Of note, the studies by Hollreider\textsuperscript{7} were conducted with Pro-Seal LMA and universal oro-pharyngeal tube placement with gastric decompression. Therefore gastric decompression may have a role in preventing PONV.

The study by Joshi, Swann, Doksröd and Cork\textsuperscript{15,20,21} indicated higher PONV with the use of ETT. One hypothesis leading to the difference in the incidence of PONV between the airway devices may be related to greater stimulation with the use of ETT requiring higher doses of anesthetics and opioids\textsuperscript{3} when compared to the LMA group\textsuperscript{6}. Opioids and volatile anesthetics have also a role in the development of PONV with a dose dependent effect on the development of PONV. Alteration in barometric pressure was demonstrated by Nader et al\textsuperscript{22} when LMA was used in comparison to ETT. Although the authors of that article did not demonstrate a statistically significant difference in PONV between the ETT and LMA, they showed a higher trend of PONV in the LMA group. This study was underpowered and additional trials are necessary to address this hypothesis.

**Limitations**

Due to nature of meta-analysis, results were analyzed from wide variety of RCTs with differing anesthetic techniques, types of surgery, anesthesiologist experience, various types of LMA, and time when outcome was measurement. Heterogeneity was high due to different anesthetic techniques\textsuperscript{23}, type of surgeries and heterogeneous population. However, with RCT there was standardization of anesthetic techniques between two groups to minimize confounding factors. Those without standardization between two groups were excluded from the trial. Despite standardization of anesthetic techniques, there were differences in duration of anesthesia and intra-operative opioid usage. There were statistically significant differences
in patient selection as well as type of procedure within some of the RCTs. Additionally, patient characteristics relevant to the risk of PONV was not always reported.

Consistent with previously performed meta-analysis\(^9\) studying the same outcome, we were able to identify only a limited number of studies addressing the influence of airway device on PONV. Furthermore, many of the RCTs had small sample sizes limiting reliability in concluding the incidence PONV between the two groups. Furthermore, two large retrospective studies\(^{24,25}\) were identified, but were not included in the final analysis due to high degree of variability in anesthetic techniques.

**Conclusion**

Further research and additional randomized controlled trials are needed to precisely identify the influence of airway device on PONV. These trials should provide essential information for the design, conduct, and presentation of these studies. When comparing group, comparability should be based on well-proven risk factors. And lastly, interpretation of results should take into account the study hypothesis, sources of potential bias or imprecision, and the difficulties associated with multiplicity of analysis and outcome.
References

Abstract

Background: Acute renal failure following cardiac surgery is not uncommon and carries a high level of morbidity and mortality. The aim of our study was to determine whether peri-operative sodium bicarbonate infusion (PoSBi) would decrease acute kidney injury in cardiac surgery patients and improve post-operative outcomes.

Methods: A retrospective analysis of 318 cardiac surgery patients from 2008-2011 was performed. Clinical parameters were compared in patients receiving PoSBi versus sodium chloride. Serum creatinine levels were measured in the first five post-operative days. The primary outcome measured was the number of patients developing post-operative renal injury. Secondary outcomes included three-month mortality, intensive care unit and hospital length of stay.

Results: Patients given PoSBi showed no significant differences compared to the normal saline cohort in regards to increases in serum creatinine [<25% rise in Cr: 93% vs 94%; >25% rise in Cr: 6% vs 6%; >50% rise in Cr: 1% vs 1%; >100% rise in Cr: 1% vs 0%, all with p-value >0.99]. There were fewer patients with AKIN stage 1 renal failure receiving PoSBi [8% vs 28%, p = 0.02] however there was no difference between PoSBi and sodium chloride cohorts in AKIN stages 2 and 3 renal failure. Mortality, duration of hospitalization and ICU stay were not statistically significant.

Conclusions: PoSBi resulted in fewer patients developing AKIN stage 1 renal failure. Despite this, there appears to be little benefit in the prevention of acute kidney injury after 48 hours or mortality reduction in cardiac surgery patients.
Introduction

Acute kidney injury (AKI) in patients undergoing cardiac surgery is a common and serious occurrence with an incidence ranging between 3% and 50% of patients and is associated with significant morbidity and mortality rates as high as 38%-50%. Of these patients, 1% will require dialysis, with associated mortality rates in this group as high as 60%-70%. There are numerous factors that contribute to postoperative renal failure, including ischemia, drugs, generation of reactive oxygen free radicals, hemolysis and activation of inflammatory and complement pathways. Additionally, numerous independent risk factors have been found to be predictive of post-operative AKI following cardiac surgery. Although some studies have shown sodium bicarbonate to ameliorate post-operative kidney injury, its use in cardiac surgery remains controversial. We present a retrospective multi-centered study of 318 patients undergoing cardiac surgery to evaluate whether peri-operative sodium bicarbonate infusion (POSBI) would reduce post-operative AKI.

Material and Methods

After institutional review board approval (Wayne State University IRB committee, IRB#065611M1E), a retrospective analysis of 318 post-cardiac surgery patients, from two institutions within our medical center over a four-year period (2008-2011) was performed. Biochemical and clinical parameters were compared in patients receiving POSBI versus sodium chloride. Inclusion and exclusion criteria of the study are listed in Table 1. Serum creatinine levels were measured in the first five post-operative days in patients who received sodium bicarbonate and those receiving sodium chloride.

Starting in 2009, our medical center instituted a sodium bicarbonate infusion protocol for patients undergoing cardiac surgery due to new literature showing possible benefit from POSBI. Previously, patients received normal saline at a rate of 1-1.5 cc/kg/hr from the start of surgery for a total of 24 hours. The sodium bicarbonate infusion protocol simply added 3 Amps (150mEq) of sodium bicarbonate in 1 liter of D5W. The protocol was to infuse the sodium bicarbonate at a rate of 1-1.5 cc/kg/hr starting from the beginning of surgery for a total of 24 hours as normal saline was previously done.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18-80</td>
<td>End Stage Renal Disease (ESRD)</td>
</tr>
<tr>
<td>CABG +/- valve surgery, intracardiac surgery</td>
<td>Emergency cardiac surgery</td>
</tr>
<tr>
<td>Redo cardiac surgery</td>
<td>Use of intra-aortic balloon pump (IABP)</td>
</tr>
<tr>
<td>Pre-operative plasma creatinine concentration &gt;1.3 mg/dL</td>
<td>Currently enrolled in another study</td>
</tr>
<tr>
<td>NYHA class III/IV</td>
<td>Known blood-borne Infectious disease</td>
</tr>
<tr>
<td>Left Ventricle EF &lt;35%</td>
<td>Chronic corticosteroid therapy</td>
</tr>
</tbody>
</table>

* Cardiac surgery patients having one or more of the listed criteria

To determine a sample size for the study a Chi-squared power analysis was chosen to obtain an alpha error probability of 0.05 and a power of 0.95. A sample size of 300 patients (at least 150 in each group; effect size d=0.2 small-medium) was deemed to give the study sufficient power. Repeated Measures Analysis of Variance (ANOVA) and T-tests (Unpaired; two sided) were used where appropriate to measure continuous variables between the 2 patient groups with post hoc differences measured using the Student-Neuman-Keuls test. Comparisons between study groups on proportional differences were examined using a non-parametric Fisher’s Exact Chi-square test, when applied to 2X2 tables. A p-value of <0.05 was considered significant.

Of note, the 318 patients that were included in our study were patients of only two cardiothoracic surgeons who used sodium bicarbonate consistently following the protocol implementation in 2009. Hence, when data before 2009 was obtained for patients not receiving POSBI we used the patients from only these two surgeons. For this reason, the 318 cardiac surgery patients only represent a smaller fraction of total cardiac surgery patients at our institution. This was done to minimize surgeon bias and to exclude surgeons
who did not consistently use POSBI.

The primary outcome measured was the number of patients who developed post-operative renal injury following cardiac surgery. Kidney injury was defined into four categories which were based on baseline serum creatinine levels to those on the fifth postoperative day: serum creatinine increases <25%, an increase greater than 25%, greater than 50%, and greater than 100% from baseline. The proportion of kidney injury between these groups as defined by the AKIN criteria was also compared, Table 2. Other secondary outcomes that were measured included intensive care unit (ICU) and hospital length of stay, and three-month mortality rates.

### Table 2

**Acute Kidney Injury Network (AKIN) Classification Criteria**

<table>
<thead>
<tr>
<th>Classes</th>
<th>Serum Cr (sCr) Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>sCr increase x 1.5 - 2 (50%-100%) or sCr increase &gt;0.3 mg/dL from baseline</td>
</tr>
<tr>
<td>2</td>
<td>sCr increase x 2 - 3 (101%-200%) from baseline</td>
</tr>
<tr>
<td>3</td>
<td>sCr increase x 3 (&gt;201%) or sCr &gt;4 mg/dL with increase &gt;0.5 mg/dL</td>
</tr>
</tbody>
</table>

### Table 3

**Patient pre-operative characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sodium Bicarbonate</th>
<th>Sodium Chloride</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr, mean (SD)</td>
<td>62 (11)</td>
<td>63 (12)</td>
<td>0.56</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>119 (68)</td>
<td>77 (54)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>56 (32)</td>
<td>66 (46)</td>
<td>0.39</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African Americans, n (%)</td>
<td>118 (67)</td>
<td>103 (72)</td>
<td>0.17</td>
</tr>
<tr>
<td>Non - African Americans, n (%)</td>
<td>57 (33)</td>
<td>40 (28)</td>
<td></td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>158 (90)</td>
<td>133 (93)</td>
<td>0.42</td>
</tr>
<tr>
<td>Chronic kidney disease, n (%)</td>
<td>47 (27)</td>
<td>38 (27)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peripheral vascular disease, n (%)</td>
<td>28 (16)</td>
<td>40 (28)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>146 (83)</td>
<td>114 (80)</td>
<td>0.47</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease, n (%)</td>
<td>57 (33)</td>
<td>39 (27)</td>
<td>0.33</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>77 (44)</td>
<td>65 (45)</td>
<td>0.82</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, percent (SD)</td>
<td>49 (15)</td>
<td>49 (15)</td>
<td>0.83</td>
</tr>
<tr>
<td>Hemodialysis, n (%)</td>
<td>13 (7)</td>
<td>17 (12)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blockers, n (%)</td>
<td>137 (78)</td>
<td>86 (60)</td>
<td>0.0005</td>
</tr>
<tr>
<td>ACE inhibitors or angiotensin blockers, n (%)</td>
<td>86 (49)</td>
<td>83 (58)</td>
<td>0.12</td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitor, n (%)</td>
<td>144 (82)</td>
<td>96 (67)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Pre-operative creatinine levels</strong></td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Cr &lt;1.0, n (%)</td>
<td>60 (34)</td>
<td>56 (38)</td>
<td></td>
</tr>
<tr>
<td>1.0 &lt;Cr &lt;1.6, n (%)</td>
<td>68 (39)</td>
<td>48 (33)</td>
<td></td>
</tr>
<tr>
<td>1.4 &lt;Cr &lt;1.6, n (%)</td>
<td>22 (13)</td>
<td>11 (8)</td>
<td></td>
</tr>
<tr>
<td>1.7 &lt;Cr &lt;1.9, n (%)</td>
<td>3 (2)</td>
<td>7 (5)</td>
<td></td>
</tr>
<tr>
<td>Cr &gt;2, n (%)</td>
<td>21 (12)</td>
<td>23 (16)</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-operative Ejection Fraction (EF)</strong></td>
<td></td>
<td></td>
<td>0.47</td>
</tr>
<tr>
<td>EF &lt;15%, n (%)</td>
<td>0 (0)</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>15% &lt;EF &lt;25%, n (%)</td>
<td>16 (9)</td>
<td>11 (7)</td>
<td></td>
</tr>
<tr>
<td>25% &lt;EF &lt;35%, n (%)</td>
<td>16 (9)</td>
<td>15 (10)</td>
<td></td>
</tr>
<tr>
<td>35% &lt;EF &lt;45%, n (%)</td>
<td>21 (13)</td>
<td>21 (15)</td>
<td></td>
</tr>
<tr>
<td>45% &lt;EF &lt;55%, n (%)</td>
<td>34 (20)</td>
<td>29 (20)</td>
<td></td>
</tr>
<tr>
<td>EF &gt;55%, n (%)</td>
<td>90 (49)</td>
<td>73 (48)</td>
<td></td>
</tr>
</tbody>
</table>
Results

Three hundred and eighteen patients underwent cardiac surgery at our institutions from 2008 thru 2011. There were 175 patients who received POSBI and 143 patients received only sodium chloride. Preoperative patient characteristics of the study are listed in Table 3. Patient characteristics were fairly matched between POSBI and normal saline groups with the exception that recipients of POSBI were more likely to be male and be on β-blockers and statins. However, more peripheral vascular disease was seen in patients receiving normal saline. New institutional mandates regarding patients receiving preoperative β-blockers, around the same time the sodium bicarbonate infusion protocol was instituted, is a likely reason for why the sodium bicarbonate group received more β-blockers. Regarding the surgery type, no significant differences were seen between groups with the exception that more patients who underwent mitral valve repair received POSBI. However, when considering all valve surgeries combined, there was no significant difference seen between the POSBI and normal saline groups. Although aortic clamp times did not differ between the groups, cardiopulmonary bypass (CPB) time was slightly lower in the sodium bicarbonate group, Table 4.

Serum creatinine levels measured on the fifth post-operative compared to baseline were divided into four categories: <25%, >25%, >50%, and >100%. There were no significant differences between patients receiving POSBI versus normal saline, Table 5. When renal dysfunction was defined using the AKIN criteria, creatinine levels 48 hours post-operatively compared to baseline, patients receiving POSBI had fewer patients with AKIN stage 1 renal failure. However, no significant differences were observed between the two groups in regards to AKIN stage 2 and 3, Table 6.

<p>| Table 4 |
| Type of surgery and patient intra-operative characteristics |</p>
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sodium Bicarbonate</th>
<th>Sodium Chloride</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac surgery</td>
<td></td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Valve surgery only, n (%)</td>
<td>58 (33)</td>
<td>41 (27)</td>
<td>0.29</td>
</tr>
<tr>
<td>Aortic valve replacement, n (%)</td>
<td>25 (14)</td>
<td>18 (12)</td>
<td>0.57</td>
</tr>
<tr>
<td>Mitral valve replacement, n (%)</td>
<td>14 (8)</td>
<td>16 (10)</td>
<td>0.39</td>
</tr>
<tr>
<td>Mitral valve repair, n (%)</td>
<td>12 (7)</td>
<td>3 (2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Double valve surgery, n (%)</td>
<td>7 (4)</td>
<td>4 (3)</td>
<td>0.52</td>
</tr>
<tr>
<td>CABG only, n (%)</td>
<td>100 (57)</td>
<td>80 (54)</td>
<td>0.56</td>
</tr>
<tr>
<td>Valve and CABG surgery, n (%)</td>
<td>17 (9)</td>
<td>22 (14)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time, mins (SD)</td>
<td>106 (38)</td>
<td>119 (57)</td>
<td>0.02</td>
</tr>
<tr>
<td>Aortic clamp time, mins (SD)</td>
<td>86 (32)</td>
<td>93 (52)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

<p>| Table 5 |
| Post-operative sCr changes in patients receiving POSBI vs Normal Saline |</p>
<table>
<thead>
<tr>
<th>Post-operative sCr change</th>
<th>Sodium Bicarbonate</th>
<th>Normal Saline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25% sCr Rise</td>
<td>163 (93%)</td>
<td>134 (94%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>&gt;25% sCr Rise</td>
<td>10 (6%)</td>
<td>8 (6%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>&gt;50% sCr Rise</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>&gt;100% sCr Rise</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Total</td>
<td>175</td>
<td>143</td>
<td></td>
</tr>
</tbody>
</table>
secondary outcomes that were measured in the study included 30-day mortality, length of hospitalization and ICU stay, Table 7. Our average ICU length of stay was higher than other studies secondary to several patients in each cohort with ICU stays longer than one month. However, total hospital length of stay was consistent with other published studies. No significant differences were seen between groups in regards to 30-day mortality, length of hospitalization or ICU stay.

Discussion

Acute kidney injury (AKI) is a common and serious complication following cardiac surgery with an incidence ranging from 3% to 50%\(^1,7\). AKI following cardiac surgery carries a significant cost burden and is an independent predictor of mortality. Pre-operative serum creatinine levels are the most important predictive factor for post-operative AKI\(^7,10\). Approximately 10% to 20% of patients with baseline creatinine levels between 2mg/dL and 4mg/dL will require dialysis and those with creatinine levels greater than 4mg/dL will require dialysis 30% of the time\(^7\). Patients requiring post-operative dialysis have a mortality rate of 60-70%. To date, no treatment including peri-operative sodium bicarbonate infusion has been shown to be effective in preventing renal failure after cardiac surgery\(^1,7,9\).

Only a few prospective randomized control trials have been done to evaluate the role of sodium bicarbonate or other adjuvant therapies (N-acetylcysteine and fenoldopam) in the prevention of acute kidney injury following cardiac surgery. Haase et al\(^1\), conducted a pilot double-blinded, randomized control trial of 100 cardiac surgery patients. The patients underwent treatment to see if POSBI can attenuate postoperative increases in serum creatinine. Their primary outcome was reaching a serum creatinine of >25% above baseline within the first five postoperative days. They found a statistical significance using bicarbonate in patients with creatinine increases >25% however there was no difference in patients with creatinine increases of either >50% and >100%. There was no statistical significance found when acute kidney injury was defined by the AKIN criteria. No mortality benefit was seen in patients receiving POSBI. Furthermore, other large RCT studies looking at N-acetylcysteine, fenoldopam and statins failed to show a clear benefit in postoperative renal protection.

Post-operative renal failure is multifactorial: ischemia-reperfusion injury seen from hemodynamic instability and aortic cross clamping, low cardiac output states, loss of pulsatile flow while on bypass, nephrotoxic drugs, generation of reactive oxygen free radicals, and the activation of neutrophils, inflammatory and complement pathways\(^7,10,11\). Furthermore, mechanical and shear forces on red blood cells seen in cardiopulmonary bypass is associated with levels of free hemoglobin which exceeds the capacity of haptoglobin. Thus, longer bypass times are

| Table 6 | Post-operative AKIN stage in patients receiving POSBI vs Normal Saline |
|---------|-----------------|-----------------|-----------|
| Post-operative AKIN stage | Sodium Bicarbonate | Normal Saline | p-value |
| Normal | 148 (85%) | 110 (62%) | 0.09 |
| AKIN Stage 1 | 14 (8%) | 24 (28%) | 0.02 |
| AKIN Stage 2 | 7 (4%) | 5 (3%) | >0.99 |
| AKIN Stage 3 | 6 (3%) | 4 (3%) | >0.99 |
| Total | 175 | 143 | |

| Table 7 | Secondary outcomes measured |
|---------|-----------------|-----------------|-----------|
| Secondary outcomes | Sodium Bicarbonate | Normal Saline | p-value |
| Mortality, n (%) | 27 (15) | 25 (16) | 0.76 |
| Intensive Care Unit stay, days (SD) | 9.2 (8.6) | 10 (9.2) | 0.39 |
| Duration of hospitalization, days (SD) | 10.7 (9.9) | 12 (8.7) | 0.22 |
associated with increased free hemoglobin exposure and can theoretically worsen kidney injury. Under acidic conditions increased free iron release from hemoglobin occurs which catalyzes the Haber-Weiss reaction promoting hydroxyl radical formation. The alkanilizing effects of sodium bicarbonate on the urine are thought to provide some degree of renal protection due to the reduction in hydroxyl radical formation from free iron and tubular cast formation.

Classification of renal injury, as with AKIN, does not provide insight into the nature of the injury. Typically, the window for therapeutic intervention has passed once serum creatinine levels begin to rise. As a result, biomarkers for the early detection of renal injury have been sought after. Neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, IL-18, kidney injury molecule-1 (Kim-1) and many more have all been studied. Urinary NGAL levels are virtually undetectable in patients with normal kidney function and serve as a marker of oxidative stress. Urinary NGAL levels greater than 100ng/mL two hours following cardiopulmonary bypass predict acute kidney injury (sensitivity, 82%; specificity, 90%) much higher than other studied biomarkers. In a study by Haase et al., the use of sodium bicarbonate does not appear enough to thwart the acute kidney injury seen following cardiac surgery despite a significant attenuation in urinary NGAL.

Several risk factors have been identified that are associated with AKI in cardiac surgery patients, Table 8. Chertow et al. conducted a large cohort study of 42,273 patients undergoing coronary artery bypass graft (CABG) or valvular heart surgery. This study showed that 1.1% of these patients had AKI after surgery, and the mortality in this group was 63.7%. The end result of the study was that cardiac surgery was an independent risk factor for developing AKI, and was associated with a high mortality rate. The rate of AKI and AKI-related mortality could not be explained by comorbidities alone. In addition to cardiac surgery, cardiopulmonary bypass itself was found to be an independent risk factor for the development of AKI.

Although there appears to be a beneficial effect of POSBI within the literature there are several important factors that must be considered. First, the definition of “AKI”, an increase in serum creatinine >25%, is quite liberal. This equates to less than a 0.1mg/dL/day increase in serum creatinine over the first five post-operative days. Mehta and colleagues convened in an international meeting to develop a uniform system for the diagnosis and classification of acute kidney injury, which is formally known as the AKIN criteria. When AKI is defined as an increase in serum creatinine >50%, no difference is found between POSBI and normal saline groups seen in the prospective pilot study. Regardless of stage, no significance was found when the AKIN criteria were used. Although we found a lower incidence of AKI stage 1 renal failure in patients receiving POSBI, it appears that by the fifth post-operative day these benefits are no longer seen.

The use of sodium bicarbonate and its resulting alkalemia is not benign. Mortality, CO₂ retention and associated hypoxia from impaired oxygen delivery are all potential complications of POSBI. Haase et al. showed considerable group differences from baseline...
Renal Protection in the Cardiac Surgery Patient

to 24 hours post-operatively in plasma bicarbonate concentration, base excess, and pH levels. Therefore, careful monitoring of plasma pH and bicarbonate levels would be warranted in instances where large amounts of sodium bicarbonate are being administered.

Our study has several limitations that should be noted. Although retrospective, pre-operative patient characteristics between cohorts were fairly matched however if we were to match for every characteristic the overall numbers would be low and the study underpowered. Additionally, we did not include patients with new-onset hemodialysis requirements following cardiac surgery. Numerous patients have multiple uncontrolled comorbidities with baseline renal dysfunction that may have contributed to the extended ICU length of stay compared to other studies however overall length of hospitalization remained consistent.

Conclusion

We present a retrospective multicenter study comparing the use of POSBI to that of sodium chloride in patients undergoing cardiac surgery to prevent post-operative renal failure. Despite a lower incidence of patients developing AKIN stage 1 renal failure in the POSBI cohort, the benefit does not persist through the fifth post-operative day. With no reduction in mortality, hospital or ICU length of stay, there currently appears to be no benefit with the use of POSBI in cardiac surgery patients.

Acknowledgments

Dimitrios Apostolou, MD - cardiothoracic surgeon of patients in study
Ali Kafi, MD - cardiothoracic surgeon of patients in study
References


EFFECT OF ULTRASOUND-GUIDED SUBSARTORIAL APPROACH FOR SAPPHENOUS NERVE BLOCK IN CASES WITH SAPPHENOUS NERVE ENTRAPMENT IN ADDUCTOR CANAL FOR CONTROLLING CHRONIC KNEE PAIN.

Arman Taheri*, Maryam Hatami**, Majid Dashti***, Alireza Khajehnasiri**** and Mahsa Ghajarzadeh*****

Abstract

**Background:** Saphenous nerve neuropathy is one of the causes of chronic pain of the knee.

Blockade of saphenous nerve under sonographich guide has been used for controlling pain in recent years. The goal of this study was to evaluate the effect of saphenous nerve block for controlling pain in patients with chronic knee pain.

**Method:** Thirty five patients with chronic knee pain referred to Amir Alam hospital during June 2012-June 2013 were enrolled in this study. Under sonographic approach, subsartorial blockade of saphenous nerve conducted and patients were followed up for 3 months after treatment. Demographic data, ASA (American Society of Anesthesiologists) category, weight, height, complications of intervention and pain scores were recorded.

**Results:** In 54%, the NRS was zero 30 minutes after intervention. In one patient (2.8%) all NRSs were 0 after intervention. We observed no sensory dysfunction in enrolled cases.

**Conclusion:** the result of current study showed that ultrasound guided subsartorial approach is moderately effective in blockade of saphenous nerve in cases with saphenous nerve entrapment in adductor canal for controlling chronic knee pain.

**Keywords:** ultrasound-guided block, knee pain, pain management.

Introduction

Saphenous nerve is a terminal branch of the femoral nerve which innervates medial, anteromedial, and posteromedial aspects of the lower extremity. Saphenous nerve entrapment is one of the causes of chronic knee pain (especially at medial site) which could mimic orthopedic disorders of the knee or L4 radiculopathy.
Blockage of saphenous nerve could be applied for procedures on the medial aspect of the distal leg. Different approaches could be applied for blockage of saphenous nerve such as perifemoral, trans-sartorial, block at the medial femoral condyle, below-the-knee field block, and blockade at the level of the medial malleolus. Benzon et al found that trans-sartorial approach was the best approach for complete sensory blockade.

In recent years, blockade of the saphenous nerve under the guidance of ultrasound has been considered as an acceptable approach. Tsai et al reviewed the medical records of 39 cases who underwent subsartorial saphenous nerve block for lower extremity surgery and found that this technique was successful in 77% of cases.

The aim of the study is to evaluate effect of saphenous nerve block in cases with saphenous nerve entrapment in adductor canal for controlling chronic knee pain.

**Method and material**

In this cross-sectional study which conducted between June 2012-June 2013 in Amir Alam hospital (affiliated hospital of Tehran university of medical sciences), patients with chronic knee pain (pain more than 3 months), Numeric rating scale ≥7 and tenderness in adductor canal were enrolled. Patients with previous surgery of lower extremities, recent trauma to the knee, consumption of anti-coagulant agents, drug abuse, severe osteoarthritis (according to radiologic findings), allergy to local anesthetic agents, psychologic disorders, and active infection were excluded.

For blockade, patients were placed in supine position, with the lower extremity rotated externally at the hip, and the knee slightly flexed. The mid-thigh area was prepped and 8-12 MHz linear probe was placed at the proximal aspect of the leg (10 cm proximal to medial condyle) to obtain a cross-sectional view of the femoral artery in short-axis. The saphenous nerve was defined as a highly hyperechoic structure medial to femoral artery. The needle was inserted lateral to femoral artery then proceeded to the medial aspect of the artery where the saphenous nerve was located. After negative aspiration, 10 cc Bupivacaine 25% and 40 mg methyl prednisolone sulphate under the sonography guidance were injected. Maximal NRS was recorded after 30 minutes, one week, one month and three months after intervention. The Numeric Rating Scale (NRS) is a 10-point scale for patient self-reporting of pain. Zero means ‘No pain’ and 10 means ‘Worst possible pain’.

Official approval from ethics committee of TUMS was obtained for the study and all the patients gave informed consent.

Demographic data, ASA, weight, height, and complication of intervention were recorded.

Statistical analyses were performed with SPSS software version 18.0 (Statistical Product and Service Solutions, SPSS Inc., Chicago). Results are presented as mean ± SDs, and frequencies. The Student’s t test was used for continuous variables, and the Pearson x² test with Fisher’s exact test was applied for categorical variables. Repeated measure ANOVA was used to compare mean NRS during study period. P value <0.05 was considered statistically significant.

**Results**

Thirty five cases enrolled in this study. Mean age of all cases was 54.6 ± 12.8 years. Twenty four cases (68.6%) were female and 11 (31.4%) were male. Twenty there (65.7%), 9 (25.7%), and 3 (8.6%) patients were ASA class I, II, and III respectively. Only the left knew was affected in 9 patients (25.7%), only the right knee was affected in 11 patients (31.4%) while both knees were affected in 15 patients (42.9%).

Mean BMI, and pre-intervention NRS were 25.1 ± 2.3 (kg/m²) and 8 ± 0.8 (7-10) respectively.

Repeated measure ANOVA showed that mean NRS significantly decreased throughout the evaluation time (p < 0.001) (Table 1).

In nineteen patients (54%), the NRS was zero at 30 minutes after intervention (Table 2).

Only one patient (2.8%) had a NRS of 0 throughout the study period. We observed no sensory dysfunction in in all enrolled cases.
Discussion

The result of this study showed that ultrasound-guided sub-sartorial blockade of saphenous nerve in cases with saphenous nerve entrapment in adductor canal is a successful method for controlling pain during post intervention period in patients with chronic knee pain.

We observed that pain NRS became zero 30 minutes after intervention in 54% of cases and pain eradicated in 2.8% of patients who suffer from chronic knee pain. However, this success rate is lower that the rates in previous studies.

Romanoff et al evaluated 30 patients with saphenous nerve entrapment in adductor canal who underwent series of nerve blockade (mean 1.9 of blockade). They reported VAS score of 6.4 at baseline and 2.8 at the end of the study. Eighty seven of cases had improved at the final stage of the study⁶.

Their findings along with our results show that saphenous nerve blockade in cases with saphenous nerve entrapment in adductor canal is effective for controlling pain.

In another study by Manickam, et al, blockade of the saphenous nerve at the distal part of adductor canal for patients who underwent ankle or foot surgery resulted in 100% success rate⁷.

The lower success rate in the current study could be attributed due to our first experiment in doing sub-sartorial blockade of saphenous nerve.

During follow up we found that NRS decreased significantly and then increased but the mean score at the end of follow up was lower than pre intervention score. It could show that this approach is useful for reducing pain for a short time and it is not applicable for eradicating pain. May be continuous blockades or other methods such as radio frequency (RF) is necessary for eradicating pain in cases with chronic knee pain.

Chronic knee pain is a disabling condition which affects quality of life of the patients and limits daily activity⁸. Different underlying diseases such as osteoarthritis, rheumatoid arthritis, bursitis, chondromalacia patella, baker’s cyst and jumper’s knee are among common causes of chronic knee pain.

This study has some limitations. First, the sample size was low and the follow up period was short. Larger studies with long follow up periods are recommended.

Conclusion: The results of the current study showed that ultrasound guided subsartorial approach is moderately effective in blockade of saphenous nerve in cases with saphenous nerve entrapment in adductor canal for controlling chronic knee pain.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>(mean ± SD) NRS during evaluation time</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS before intervention</td>
<td>NRS after 30 minutes</td>
</tr>
<tr>
<td>8 ± 0.8</td>
<td>0.7 ± 0.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Success rates during follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success rate</td>
<td></td>
</tr>
<tr>
<td>Reduction of NRS scores to 0 after 30 minutes</td>
<td>19 (54.3%)</td>
</tr>
<tr>
<td>Reduction of NRS scores to 0 after one week</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>Reduction of NRS scores to 0 after one month</td>
<td>4 (11.4%)</td>
</tr>
<tr>
<td>Reduction of NRS scores to 0 after 3 months</td>
<td>3 (8.6%)</td>
</tr>
</tbody>
</table>
References


Abstract

**Background:** Although oral ketamine has been used in some cases to reduce pain in children, the use of this drug to reduce pain after tonsillectomy has not been studied yet.

**Methods:** This double-blind clinical trial was conducted in 2009 in 92 children who were aged three to nine years old, met ASA I or II criteria, and were candidate for tonsillectomy. Patients were divided randomly into two groups. Half an hour before general anesthesia, 5 mg/kg ketamine mixed in 2 cc/kg apple juice was given to the children in oral ketamine group and 2 cc/kg of apple juice alone was given to the children in the peritonsillar group. After general anesthesia and three minutes before surgery 1 cc of 0.9% normal saline in the oral group and 1 cc of ketamine (0.5 mg/kg) in the peritonsillar group was injected to the tonsil bed of patients.

**Results:** There was no difference between the two groups in terms of sex, age, and weight. Duration of surgery was significantly shorter in the peritonsillar group (P <0.001) and the severity of postoperative bleeding was significantly higher in peritonsillar group (P = 0.022). However, postoperative bleeding recurred in 25 patients (27%) and there was no statistically significant difference between the two groups. The level of pain in children six hours after surgery according to CHEOPS criteria was significantly lower in the peritonsillar group (0.9 ± 0.8) than in the oral group (2.6 ± 1) (P <0.001).

**Conclusions:** The finding of this study showed that, compared with the peritonsillar infiltration of ketamine, the use of oral ketamine before general anesthesia was less effective in reducing postoperative pain of tonsillectomy in children.

**Keywords:** tonsillectomy, adenotonsillectomy, postoperative pain, ketamine.
Introduction

Adenotonsillectomy is one of the most common ear, nose, and throat surgeries in children and postoperative pain is one of its important complications. Inadequate control of postoperative pain leads to different complications such as poor nutrition, dehydration, sleep disorders, behavioral changes, nausea, and vomiting; moreover, it can increase the length of hospitalization and consequently increase healthcare costs. Despite the high prevalence of pain after tonsillectomy and adenotonsillectomy and the presence of different analgesics and assessment tools for measuring age-related pain, the choice of appropriate analgesic to be used after tonsillectomy operation is still controversial.

To reduce pain after tonsillectomy in children, different groups of drugs (oral paracetamol, opioids, NSAIDs, and local anesthetics) have been studied. Although paracetamol is a safe and effective analgesic, when it is used alone it cannot achieve an appropriate analgesic effect after tonsillectomy. Opiates may reduce upper airway tone, suppress the cough reflex, cause sedation and respiratory depression (especially in unintended outpatient surgery), and also lead to postoperative nausea and vomiting. Although NSAIDs are an alternative to opioids, they may increase the risk of postoperative bleeding and reoperation. In addition, local anesthetics are associated with vasoconstriction.

N-methyl-D-aspartate (NMDA) receptors in the dorsal horn of the spinal cord are involved in central sensitization to painful stimuli. Ketamine is a non-competitive antagonist of NMDA receptors which has analgesic effects at sub-anesthetic doses. Safari et al showed that the use of ketamine reduced the need for postoperative opioids and other analgesics in children undergoing tonsillectomy. Intravenous injection, peritonsillar infiltration, rectal, spray at the site of surgery, continuous infusion and subcutaneous injection of ketamine have been investigated for pain reduction after tonsillectomy. To our knowledge, no previous studies have evaluated the role of oral ketamine for pain reduction after tonsillectomy.

The aim of the current study is to compare oral ketamine to peritonsillar ketamine infiltration for pain relief after tonsillectomy.

Materials and Methods

This double-blind clinical trial was conducted in 2009 on 92 children aged three to nine years old who were referred to Amir Kabir hospital in Arak City. Inclusion criteria were: being aged three to nine years old, meeting ASA I or II criteria, and candidate for tonsillectomy surgery. Exclusion criteria were: the presence of an underlying disease, and the presence of contraindications to the use of ketamine including upper airway active infection, increased intracranial pressure, open eyes surgery, and seizures. The study was approved by the Ethics Committee of the Arak University of Medical Sciences.

After explaining the procedures of the study to parents and obtaining their informed consent, patients who met inclusion criteria were divided randomly into two groups. In order to double-blind study, injectable medications were tagged using similar labels and oral ketamine was also given to patients mixed in apple juice by a medical student. Anesthesiologist and ENT specialists were unaware of the patient group and used apple juices and injectable medications for patients, respectively. Anesthesia was started using fentanyl and atropine as premedication and then anesthesia was induced using sodium thiopental 6 mg/kg and atracurium 0.5-1 mg/kg and it was sustained with isoflurane 1%, NO2 and O2 with a ratio of 50%. All patients were intubated and to prevent entering blood to the throat, which is of the factors causing nausea, gauze was placed in the throat.

Half an hour before general anesthesia, 5 mg/kg ketamine mixed in 2 cc/kg apple juice was given to the children in oral ketamine group and 2 cc/kg of apple juice alone was given to the children in the peritonsillar group. After the induction of general anesthesia and three minutes before surgery 1 cc of normal saline in the oral group and 1cc of ketamine (0.5 mg/kg) in the peritonsillar group was injected to the each tonsil bed of patients (a total of 2 cc injections for each child). Injection was performed by an ENT specialist.

Age, sex, weight, duration of surgery, intraoperative blood loss, postoperative bleeding (in the recovery room), nausea, vomiting, and postoperative bleeding recurrence six hours after surgery were recorded by the medical student who was unaware of
patient group. In order to measure the pain six hours after surgery, Modified Scoring CHEOPS criterion was used (Table 1). The range for this criterion is from 0 to 10 where a higher score indicates greater pain.\(^7\)

Power calculations had indicated that 46 children would be required per group to detect a difference of 30% in facial CHEOPS pain scoring with a power of 85% and \(\alpha = 0.05\). SPSS 13 software was used for data analysis. Qualitative variables were described using frequencies and percentages and quantitative variables were described using mean and standard deviation. In order to compare the two groups, chi-square test and Mann-Whitney U test were used. P-value less than 0.05 was considered as a significant level.

### Results

There were no differences between the two groups in terms of sex, age, and weight (Table 2). Table 3 shows the comparison of the characteristics of surgeries and postoperative complications between the two groups. Duration of surgery was \(\leq 20\) minutes in

### Table 1

**Modified CHEOPS scoring**

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cry</td>
<td>No cry</td>
<td>Crying, moaning</td>
<td>Scream</td>
</tr>
<tr>
<td>Facial</td>
<td>Smiling</td>
<td>Neutral</td>
<td>Grimace</td>
</tr>
<tr>
<td>Verbal</td>
<td>Positive statement</td>
<td>Negative statement</td>
<td>Suffering from pain, another complaint</td>
</tr>
<tr>
<td>Torso</td>
<td>Neutral</td>
<td>Variable, taut, upright</td>
<td>Stretched</td>
</tr>
<tr>
<td>Legs</td>
<td>Neutral</td>
<td>Kicking</td>
<td>Stretched, continuous move</td>
</tr>
</tbody>
</table>

### Table 2

**Comparison of demographic characteristics between groups**

<table>
<thead>
<tr>
<th></th>
<th>Oral group (N = 46)</th>
<th>Peritonsillar group (N = 46)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37 (80%)</td>
<td>9 (20%)</td>
<td>0.101</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 (65%)</td>
<td>16 (35%)</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td>≤5 yr</td>
<td>9 (20%)</td>
<td>12 (26%)</td>
</tr>
<tr>
<td></td>
<td>6-7 yr</td>
<td>18 (39%)</td>
<td>11 (24%)</td>
</tr>
<tr>
<td></td>
<td>≥8 yr</td>
<td>19 (41%)</td>
<td>23 (50%)</td>
</tr>
<tr>
<td>Weight</td>
<td>≤20 Kg</td>
<td>18 (39%)</td>
<td>18 (39%)</td>
</tr>
<tr>
<td></td>
<td>21-24 Kg</td>
<td>18 (39%)</td>
<td>12 (26%)</td>
</tr>
<tr>
<td></td>
<td>≥25 Kg</td>
<td>10 (22%)</td>
<td>16 (35%)</td>
</tr>
</tbody>
</table>

### Table 3

**Comparison of surgery time and side effects between groups**

<table>
<thead>
<tr>
<th></th>
<th>Oral group (N = 46)</th>
<th>Peritonsillar group (N = 46)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery time</td>
<td>≤20 min</td>
<td>0 (0%)</td>
<td>19 (41%)</td>
</tr>
<tr>
<td></td>
<td>21-29 min</td>
<td>18 (39%)</td>
<td>7 (15%)</td>
</tr>
<tr>
<td></td>
<td>≥30 min</td>
<td>28 (61%)</td>
<td>20 (44%)</td>
</tr>
<tr>
<td>Post-op bleeding</td>
<td>Mild</td>
<td>9 (20%)</td>
<td>14 (30%)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>37 (80%)</td>
<td>27 (59%)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>0 (0%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td>Post-op bleeding recurrence</td>
<td>9 (20%)</td>
<td>16 (35%)</td>
<td>0.101</td>
</tr>
<tr>
<td>Nausea &amp; Vomiting</td>
<td>0 (0%)</td>
<td>2 (4%)</td>
<td>0.153</td>
</tr>
</tbody>
</table>
19 patients (21%), 21-29 minutes in 25 patients (27%), and ≥30 minutes in 48 patients (52%). The durations of surgeries were significantly shorter in the peritonsillar group than in the oral group (P <0.001). The severity of postoperative bleeding was mild in 23 patients (25%), moderate in 64 patients (70%), and severe in five patients (5%); overall, the incidence of postoperative bleeding was significantly higher in peritonsillar group than in the oral group (P = 0.022). Postoperative bleeding recurred in 25 patients (27%) and there was no statistically significant difference between the two groups. Only two patients had postoperative nausea and vomiting, and there was no significant difference between the two groups.

The level of pain in children six hours after surgery according to CHEOPS criteria was significantly lower in the peritonsillar group (0.9 ± 0.8) than in the oral group (2.6 ± 1) (P <0.001). Table 4 shows the characteristics of pain in each item. All the children in the peritonsillar group had neutral facial expression; however in the oral group only half the children had neutral facial expression (P <0.001). In the peritonsillar group, 39% of children were suffering from pain, whereas 76% of patients in the oral group were suffering from pain (P <0.001). The leg condition was neutral in all children in the peritonsillar group, while only 30% of children in the oral group had neutral condition (P <0.001). There was no significant difference between the two groups in terms of children cry and their body shape (Torso).

**Discussion**

The findings of this study showed that, compared with oral ketamine, the peritonsillar infiltration of ketamine after general anesthesia and immediately before tonsillectomy shortened the duration of operation and reduced the severity of postoperative pain. Although postoperative bleeding was more in the ketamine peritonsillar group, the recurrent bleeding, nausea, and vomiting after surgery was not significantly different between the two groups. Thus, it seems that, compared to peritonsillar infiltration, the use of oral ketamine 5 mg/kg is less effective in reducing pain in children after tonsillectomy.

Ketamine is a noncompetitive antagonist of the NMDA receptor. These receptors are located in the dorsal horn of the spinal cord and play an important role in the development of central sensitization to painful peripheral stimuli. Seemingly, hyperexcitability of the central nervous system appears to be the cause of the

**Table 4**

<table>
<thead>
<tr>
<th></th>
<th>Oral group (N = 46)</th>
<th>Peritonsillar group (N = 46)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cry</td>
<td>28 (61%)</td>
<td>36 (78%)</td>
<td>0.070</td>
</tr>
<tr>
<td>Crying, moaning</td>
<td>18 (39%)</td>
<td>10 (22%)</td>
<td></td>
</tr>
<tr>
<td>Scream</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Facial</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smiling</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td>23 (50%)</td>
<td>46 (100%)</td>
<td></td>
</tr>
<tr>
<td>Grimace</td>
<td>23 (50%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Verbal</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Positive statement</td>
<td>0 (0%)</td>
<td>16 (35%)</td>
<td></td>
</tr>
<tr>
<td>Negative statement</td>
<td>11 (24%)</td>
<td>12 (26%)</td>
<td></td>
</tr>
<tr>
<td>Suffering from pain, another complaint</td>
<td>35 (76%)</td>
<td>18 (39%)</td>
<td></td>
</tr>
<tr>
<td><strong>Torso</strong></td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Neutral</td>
<td>46 (100%)</td>
<td>46 (100%)</td>
<td></td>
</tr>
<tr>
<td>Variable, taut, upright</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Stretched</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Legs</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neutral</td>
<td>14 (30%)</td>
<td>46 (100%)</td>
<td></td>
</tr>
<tr>
<td>Kicking</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Stretched, continuous move</td>
<td>32 (70%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>
oral ketamine Vs. peritonsillar infiltration in tonsillectomy
wind-up phenomenon and subsequent hyperalgesia in the place of injury. The goal of preemptive analgesia is to prevent the afferent impulses to the spinal cord that is causing such a phenomenon. Hence, preemptive analgesia may prevent pain memory in the central nervous system and reduce the need for analgesics in the postoperative period. It has been shown that ketamine’s effects on these receptors can reduce pain in humans.

Ketamine has been used in different ways, at different doses and different times as an analgesic after tonsillectomy surgery, but the reported results were not consistent have been various. Some studies failed to show the effect of ketamine on reducing pain after tonsillectomy. O’Flaherty et al.’s study which compared the effects of the administration of intravenous ketamine with that of placebo and Van Elstraet et al’s study which examined the effect of ketamine on pain after tonsillectomy in adults did not show a positive effect in reducing pain after tonsillectomy. However, other studies reported that using ketamine was effective in reducing pain following tonsillectomy. Murray et al showed that a low-dose of intravenous ketamine may be effective in reducing pain after tonsillectomy. Marcus et al and Elhakim et al stated that the intramuscular ketamine can be used as an alternative analgesic for tonsillectomy. Erhan et al. reported that ketamine injection in the tonsillar area was more effective than placebo in reducing pain without inducing sedation or nausea. Dal et al. reported that intravenous or peritonsillar infiltration of ketamine before adenotonsillectomy surgery could reduce postoperative pain and reduce the need for analgesics without causing any adverse effects. More recent studies have also suggested the effect of ketamine on reducing pain after tonsillectomy. Sizer et al showed that intravenous ketamine was effective in reducing pain following tonsillectomy. According to a study by Siddiqui et al. peritonsillar infiltration of ketamine with doses of 0.5 or 1 mg/kg reduced pain after tonsillectomy, compared to control. Our study also showed that peritonsillar infiltration of ketamine could be a useful method for reducing pain following tonsillectomy in children.

Although ketamine has been used via different methods to reduce pain after tonsillectomy, oral method, however, has not been used yet for this purpose. Filatov et al. have compared oral ketamine as premedication with rectal diazepam/diclofenac in adenoidectomy surgery and reported that oral ketamine group had slightly higher pain scores than other group. However, they conclude that oral ketamine is not suitable for premedication in upper airway surgeries. Oral ketamine has been effective in children for controlling pain in different cases such as abdominal malignancy surgery, sickle cell crisis, and chronic pains. It has also been used for anesthetic premedication in children in surgeries such as dental, ophthalmic and minor surgeries. In addition, oral ketamine is effective in postoperative agitation in children. In the present study we examined the effects of oral ketamine in reducing pain after tonsillectomy and compared it with peritonsillar ketamine. Although Ketamine reduced postoperative bleeding, overall it was associated with more pain in children than peritonsillar infiltration. Thus, it seems that oral ketamine with a dose of 5 mg/kg is less effective in reducing pain in children after tonsillectomy compared to peritonsillar infiltration.

Conclusions

The finding of this study indicated that, compared with the use of oral ketamine before tonsillectomy, the peritonsillar infiltration of ketamine after general anesthesia and immediately before tonsillectomy was more effective in reducing postoperative pain in children.
References


THE IMPACT OF ANESTHETIC TECHNIQUES ON COGNITIVE FUNCTIONS AFTER UROLOGICAL SURGERY

Mahtab Poor zamany Nejat kermany*, Mohammad Hossein Soltani**, Khazar Ahmadi***, Hoora Motiee***, Shermin Rubenzadeh*** and Vahid Nejati***

Abstract

Background: Postoperative cognitive dysfunction (POCD) is a well-recognized complication of cardiac and noncardiac surgery. However, contradictory results concerning postoperative mental function have been reported. The aim is to determine the effect of anesthetic techniques (general or spinal) on cognitive functions using more sensitive neuropsychological tests in patients undergoing urological surgery.

Material and Methods: A total of thirty patients were enrolled in the study and assigned to receive either general (n=15) or spinal (n=15) anesthesia. A battery of neuropsychological tests including Wisconsin Card Sorting Test, Iowa Gambling Task, Stroop Color-Word Test, N-back Task and Continuous Performance Test was performed preoperatively and three days later.

Results: The two experimental groups were similar at baseline assessment of cognitive function. Although there were no statistically significant differences between general and spinal anesthetic groups with respect to Wisconsin Card Sorting Test and Iowa Gambling Task, a significant intergroup difference between pre-and postoperative N-back scores was detected in the general anesthesia group (p=0.001 & p=0.004). In addition, patients within this group had significantly higher error rates on the Stroop Color-Word (p=0.019) and Continuous Performance Tests (p=0.045). In contrast, patients receiving spinal anesthesia exhibited little change or marginal improvement on all subscales of the battery.

Conclusions: Our findings indicate significant decline in specific aspects of mental function among patients who were administered general anesthesia compared with the other technique. It seems that spinal anesthesia contributes to lower disturbance after surgery.

Key word: Anesthesia - Cognitive function - Urology.

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Introduction

Postoperative cognitive dysfunction (POCD) is a common complication in adult patients undergoing surgical procedures which refers to decline in variety of neuropsychological domains such as verbal or visual memory, executive functioning, language comprehension, attention and concentration. Although primarily observed after cardiac surgery, it has also been detected following major noncardiac surgeries. While POCD is presumed to be transient and the long-term effects are considered uncertain, recent studies suggest that the symptoms of neurocognitive change may persist long after the operation and diminish quality of life. Patients with POCD are more likely to withdraw from employment and social activities that will lead to premature dependency. The ISPOCD 1 study (International Study of Post-Operative Cognitive Dysfunction) of 1,218 elderly patients (60 yr or older) scheduled for major noncardiac surgery showed that cognitive impairment was present in 25.8% patients one week after the operation and in 9.9% of them after 3 months. Furthermore, postoperative cognitive decline has been associated with significantly higher risks of postoperative morbidity and mortality, particularly in elderly. A similar study revealed that patients with POCD at hospital discharge were more likely to die within 3 months of the discharge. In general, the rate of cognitive dysfunction has been positively correlated with mortality risk. Several studies show an increased risk of early mortality in elderly individuals with cognitive deterioration.

The etiology of POCD is likely multifactorial with type of surgical procedure (due to differences in duration) metabolic/endocrine stress response, imbalance of neurotransmitter system (particularly acetylcholine and serotonin), hypoxia and hospitalization, all potentially playing a role. Advanced age, history of cerebral vascular accident with no residual impairment, lower educational level, evidence of cognitive dysfunction at hospital discharge and alcohol abuse also contribute to the pathogenesis of POCD. With further identification of preoperative risk factors for POCD, patients and healthcare providers can be better informed before making a decision to proceed with major surgery.

It has been speculated that POCD risk could be reduced by performing certain surgical procedures under regional anesthesia. Results of a study indicated that the maintenance of mental function in an elderly population was better following spinal anesthesia when compared with general anesthetic technique. Similarly, another report showed that the incidence of cognitive deterioration was lower after epidural anesthesia. A recent study found that general anesthesia posed a significant risk for the occurrence of early POCD in elderly patients that could persist for 3 days after surgery. However, review of the existing literature has not revealed a significant difference between the two intraoperative anesthetic techniques. The heterogeneity of procedures used to measure cognitive deficits and methodological inconsistencies make the limited literature on POCD difficult to interpret. Most of these tests are subsets of test banks used to assess the memory and intelligence of adults. The use of more sensitive neuropsychological tests may elucidate more prolonged damage to cognitive performance. In addition, the majority of previous investigations have primarily focused on elderly patients, a population with an increased vulnerability to neurological deterioration after exposure to anaesthesia. As a result, the cognitive effects of anesthesia and surgery in young and middle-aged adults are poorly understood. The objective of this study was to evaluate post-operative mental function of patients who had undergone general or spinal anesthesia for a urologic surgery, and to compare the effect of these two anesthetic techniques on mental function.

Material and Methods

From July to September 2011, 30 patients undergoing urological surgery following either general or spinal anesthesia were participated in the study at Shahid Labbafinezhad Hospital. Written informed consent was taken from all patients and university ethics committee approved the study structure. Entry criteria included age (24+ yr), normal mental status, speaking and reading fluency in the Persian language and the absence of any serious vision or hearing impairment that would preclude neuropsychological testing. Participants were excluded if they had any
prior history of dementia, central nervous system disease, psychiatric disorders, alcoholism and drug abuse. In addition, any patients with history of allergy to anesthetic drugs were also excluded. Information about the demographic status, medical history, education and occupational history of the subjects were documented.

Anesthetic techniques and agents

All patients received 5cc/kg normal saline serum before anesthesia. In the group of patients who underwent general anesthesia, the following agents were used for the induction of anesthesia: Fentanyl (2µ/kg), Midazolam (1mg), Lidocain (1.5mg/kg), Propofol (2mg/kg) and Atracurium (0.5mg/kg). For maintenance phase of general anesthesia, Propofol (100-200µ/kg) and Remifentanil (0.1 µ/kg/min) were used. Spinal Anesthesia was done by injection of 2.5 to 3 cc bupivacaine 0.5% (Marcaine®) in the subarachnoid space. For post-operative pain control, intravenous pethidine (25-50 mg) was administrated in the recovery room and Diclofenac 100mg suppository was given in the ward as needed.

Neuropsychological Assessment

The cognitive function evaluation was performed in an undisturbed room with only the patient and the psychometrician present. Patients completed the tests one day prior to surgery and at hospital discharge (three days after the operation). The psychological measures included Wisconsin Card Sorting Test, Stroop Color-Word Task, Continuous Performance Test, N-Back Task and Iowa Gambling Test that were administered in about 30 minutes. These measures primarily focus on executive functions and memory, elaborated as follows:

Wisconsin Card Sorting Test is commonly regarded as “the gold standard executive function task”26,27. Patients were asked to match response cards to reference cards according to three dimensions of sorting principle (color, form and number)28. Stroop Color-Word Test estimates the patient’s ability to concentrate and ignore distracting stimuli29. Continuous Performance Test (CPT) requires subjects to maintain vigilance and react to the presence or absence of specific stimuli within a continuously presented set of distracters30,31. N-Back Task is one of the most popular experimental paradigms for studies of working memory, in which subjects are asked to monitor the identity or location of a set of verbal or nonverbal stimuli and to indicate when the currently presented stimulus is the same as the one presented in trials previously32,33. Iowa Gambling Task evaluates decision-making under initially ambiguous conditions. It simulates real-life decision making by testing the ability of subjects to learn to sacrifice immediate rewards in favor of long-term gains34,35.

Statistical Analysis

Given the large number of dependant variables, comparison of the cognitive function between the two anesthesia groups was performed with multivariate analysis of covariance (MANCOVA) using SPSS (version 18). Follow-up tests were conducted when warranted by multivariate results with ANOVA and paired t-tests. Pre-test scores were considered to be covariate variables in order to control for the practice effect. The customary two-tailed α level of significance was set at 0.05.

Results

Thirty patients (13 women and 17 men) were recruited. The subjects had a mean age of 44.6 (±12.66). 36.6% subjects were classified as young (24-39yr), 53.33% were middle-aged (40-59) and 10% were elderly (60-65). General anesthesia was used in 15 patients (50%), and the remaining subjects received spinal anesthesia.

The baseline characteristics of the patients included in the study are listed in table 1. Data analysis revealed that the two groups did not differ in preoperative scores. However, statistically significant differences were observed when postoperative scores were compared with the baseline levels. Results indicated significant association between general anesthetic technique and damage to particular domains of cognitive functions. Although subtests of the Wisconsin Card Sorting Test and Iowa Gambling Task did not change significantly
between the two groups, separate univariate analysis and paired t-test showed that patients were more likely to have worse 1-and 2-back test performance after general anesthesia (p=0.001 & p=0.004). These patients also had significantly higher omission error score on the Continuous Performance Task (p=0.045) and considerable error rates on the 3rd part of the Stroop Color-Word Test (p=0.019). It is worth noting that patients receiving spinal anesthesia showed little change or slight improvement on all subscales of the battery. The mean pre-and postoperative neuropsychological test scores are exhibited in Table 2.

**Discussion**

This study is one of the few investigations of postoperative cognitive function that includes younger population. In the current study, we used some of the most popular neuropsychological tasks to assess executive functions. Comparison of the two arms of the study was based on MANCOVA which provided more statistical power. Our data revealed that general anesthesia was associated with weaker performance in the memory and concentration domains. These results are in accordance with the findings of Chung et al, who found that patients receiving general anesthesia performed worse on digit-symbol substitution for 2-3 days after surgery. Herbert and colleagues also noted that choice reaction time was impaired for 36 hours after administration of general anesthesia. Findings of another study indicated that general anesthesia patients perceived residual impairment of their cognitive faculties after 3 days.

Previous research addressing the role of anesthesia on cognitive deterioration has yielded conflicting results. The absence of a consistency regarding the operational definition of POCD may contribute to this issue. Our findings are inconsistent with the vast majority of existing evidence demonstrating no significant difference between intraoperative regional and general anesthesia in preserving postoperative cognitive function.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>General characteristics of the patients, compared in two groups (general vs. spinal anesthesia.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Age</td>
</tr>
<tr>
<td>Age Groups</td>
<td></td>
</tr>
<tr>
<td>24-39 (Young)</td>
<td>22.7</td>
</tr>
<tr>
<td>40-59 (Middle-aged)</td>
<td>28.9</td>
</tr>
<tr>
<td>60 and above (Elderly)</td>
<td>26.7</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22.7</td>
</tr>
<tr>
<td>Female</td>
<td>22.7</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Less than High school</td>
<td>22.7</td>
</tr>
<tr>
<td>High School</td>
<td>22.7</td>
</tr>
<tr>
<td>More than High school</td>
<td>22.7</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
</tr>
<tr>
<td>Lithotripsy</td>
<td>22.7</td>
</tr>
<tr>
<td>Intravesical injection</td>
<td>22.7</td>
</tr>
<tr>
<td>Radical Nephrectomy</td>
<td>22.7</td>
</tr>
<tr>
<td>Varicocelectomy</td>
<td>22.7</td>
</tr>
<tr>
<td>Bladder Stone Removal</td>
<td>22.7</td>
</tr>
<tr>
<td>TUL</td>
<td>22.7</td>
</tr>
<tr>
<td>TURT</td>
<td>22.7</td>
</tr>
</tbody>
</table>
ImpacT of anesThesIa on cognITIve funcTIon. For instance, in a prospective, randomized study, Williams-Russo et al. compared the effect of epidural versus general anesthesia on the incidence of POCD in patients undergoing elective unilateral total knee replacement and found no significant difference postoperatively. In another randomized trial, no significant differences were found in the postoperative mental abilities between patients who received general, regional or combined anesthetic techniques. O’Hara et al. observed no clinically important impacts on major outcomes in patients who were administered general or spinal anesthetic techniques after the hip surgery. In a systematic review, Wu et al. found that intraoperative neuraxial anesthesia does not decrease the incidence of POCD when compared with general anaesthesia.

Detection of POCD requires two crucial elements: a sensitive battery of tests and controlling for the practice effect. We used some of the well-known psychological measurements to determine more subtle defects. The enhancement observed in this trial cannot be attributed to practice effect. In as much as, pretest scores were considered as covariate variables.

There may be several factors that might have a negative impact on cognitive function after general anesthesia. Some agents that are used to induce and maintain anesthesia may deteriorate cognition and memory. In addition, there may be a possibility of hemodynamic instability, hypoxia and stress induced response due to prolonged intubation; the factors that are not commonly related to regional anesthesia.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Pre-and postoperative (at hospital discharge) test results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative</td>
</tr>
<tr>
<td></td>
<td>General</td>
</tr>
<tr>
<td></td>
<td>(n-15)</td>
</tr>
<tr>
<td>Wisconsin Card Sorting Test</td>
<td></td>
</tr>
<tr>
<td>Achieved Clusters</td>
<td>1.66±0.61</td>
</tr>
<tr>
<td>Number of Total Errors</td>
<td>37.93±6.39</td>
</tr>
<tr>
<td>Perseverative Errors</td>
<td>15.46±3.62</td>
</tr>
<tr>
<td>Iowa Gambling Task</td>
<td>25.20±2.48</td>
</tr>
<tr>
<td>N-Back Task</td>
<td></td>
</tr>
<tr>
<td>1-back</td>
<td>19.93±6.71</td>
</tr>
<tr>
<td>2-back</td>
<td>8.13±3.29</td>
</tr>
<tr>
<td>Continuous Performance Test</td>
<td></td>
</tr>
<tr>
<td>Omission Error</td>
<td>16.06±8.67</td>
</tr>
<tr>
<td>Commission Error</td>
<td>1.064±0.51</td>
</tr>
<tr>
<td>Hit Reaction Time</td>
<td>0.548±0.06</td>
</tr>
<tr>
<td>Stroop Color-Word Task</td>
<td></td>
</tr>
<tr>
<td>Error Rates 1</td>
<td>1.33±0.97</td>
</tr>
<tr>
<td>Reaction Time 1</td>
<td>0.46±0.45</td>
</tr>
<tr>
<td>Error Rates 2</td>
<td>0.53±0.74</td>
</tr>
<tr>
<td>Reaction Time 2</td>
<td>0.34±0.55</td>
</tr>
<tr>
<td>Error Rates 3</td>
<td>17.40±7.91</td>
</tr>
<tr>
<td>Reaction Time 3</td>
<td>1.85±0.93</td>
</tr>
</tbody>
</table>

Values are given as mean±SE. "*" mark indicates significant difference in the assigned group before and after the operation.
This study was limited by two major factors. Firstly, patients were not allocated randomly to the general or spinal anesthesia groups. Secondly, we were unable to include a control group of healthy volunteers matched with the experimental groups in the present study. Hospitalized patients not undergoing surgery or any other intervention were also considered as a better control group, but a sufficient sample size for comparison could not be attained due to lack of participation. Our findings should therefore be interpreted with caution. A more extensive study with follow-up testing is required to determine the precise profile of the postoperative cognitive impairment.

In conclusion, our results suggest a linkage between general anesthesia and weaker postoperative mental function. Local anesthesia might have an advantage over general anesthesia in terms of neuropsychological functioning.

Acknowledgments

The authors thank the hospital staff and patients for taking part in this study. Their assistance was essential for data collection and the coordination of the research protocol.

Conflict of interest:

The authors have no conflict of interest.
References


Comparison between C-MAC® video-laryngoscope and Macintosh direct laryngoscope during cervical spine immobilization

Shahir HM Akbar* and Joanna SM Ooi**

Abstract

Background: Video-laryngoscopes have gained popularity in the recent years and have shown definite advantages over the conventional Macintosh direct laryngoscopes. However, there is still insufficient evidence comparing the C-MAC® with the Macintosh for patients during manual inline stabilization (MILS).

Methods: This prospective, randomized, single blind study was carried out to compare tracheal intubation using the C-MAC® video-laryngoscope and Macintosh laryngoscope in patients during MILS. Ninety consented patients, without features of difficult airway, who required general anesthesia and tracheal intubation were recruited. Intubation was performed with either the C-MAC® video-laryngoscope or the Macintosh laryngoscope by one single investigator experienced with both devices. Various parameters which included Cormack and Lehane score, time to intubate, intubation attempts, optimization maneuvers, complications and hemodynamic changes were recorded over the initial period of 5 minutes.

Results: C-MAC® video-laryngoscope performed significantly better with lower Cormack and Lehane grades, shorter time to intubate of 32.7 ± 6.8 vs. 38.8 ± 8.9 seconds (p=0.001) and needed less optimization maneuvers. There were no significant differences seen in the intubation attempts, complications or hemodynamic status of the patients with either device.

Conclusion: The C-MAC® video-laryngoscope was superior to the Macintosh laryngoscope for patients requiring intubation when manual inline neck stabilization was applied.

Keywords: C-MAC® laryngoscope, Macintosh laryngoscope, intubation, neck immobilization, manual inline stabilization.

Introduction

Securing the airway with tracheal intubation in a patient suspected or known to have a cervical spine injury has always been a challenge regardless of whether it is conducted in a controlled operating room environment, in a busy critical zone of the emergency department or in an out-of-hospital setting. This has been recognized since the early 1950’s and by the early 1980’s the standard of care to overcome this scenario was to use the time tested formulae of direct laryngoscopy with tracheal intubation using manual inline stabilization (MILS)1 with a Macintosh laryngoscope. MILS is a maneuver that ensures a neutral alignment and motionless cervical spine

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during the intubation process and is carried out by a healthcare personnel who places a hand on each side of the patient's neck with fingers pressed on each mastoid process and the hands then pressed firmly into the operating table. While the practice of MILS was considered to be the standard care with regards to prevention or worsening of any neurological morbidity, it has been found that MILS produced significantly worse laryngoscopy view upon direct laryngoscopy for tracheal intubation. The delay in or a failed tracheal intubation could potentially result in hypoxia leading to worse outcomes and is a leading cause of morbidity and mortality for patients in both the operative setting and in an emergency situation.

With due consideration to the above, advances in technology have provided alternatives to the conventional Macintosh laryngoscope to perform direct laryngoscopy during a MILS scenario. Considerable development has occurred especially in the field of indirect laryngoscopy using video-assisted techniques producing devices such as the Glidescope® (Saturn Biomedical System Inc., Burnaby, Canada) and the Airwayscope® laryngoscope (Pentax Corporation, Tokyo, Japan). These new devices have been shown to have definite advantages over the conventional Macintosh direct laryngoscopy in scenarios where MILS was applied. These included better glottic visualization, less optimizing maneuvers needed for a successful intubation and more favorable hemodynamic profiles during the intubation itself.

The C-MAC® (Karl Storz, Tuttingen, Germany), a portable video-laryngoscope is unique as it offers an original Macintosh blade shape with an approximately 80° angle of view and practically eliminated fogging of the camera. Owing to its similar design to the Macintosh blade, there would not be very much of a learning curve to using it by most anesthetic doctors. An initial study showed great promises in it being able to obtain good view of the glottis on the first attempt in all patients. At this point of time the question of whether any video-laryngoscope is definitely better in MILS is yet to be answered convincingly.

The aim of this study was to compare laryngoscopic views (based on Cormack and Lehane grading) during tracheal intubation when using either the C-MAC® video-laryngoscope or the Macintosh laryngoscope during MILS. The time taken to intubate (seconds), number of intubation attempts, optimization maneuvers required, complications encountered and the changes in hemodynamic parameters of the patients being intubated were also compared.

Methods

This study design was based on a prospective, randomised, single-blinded clinical trial that was done following approval of the Dissertation Committee of the Department of Anesthesiology and Intensive Care, Universiti Kebangsaan Malaysia Medical Center (UKMMC) and the Research Ethics Committee of UKMMC (Research No. FF-024-2011).

After obtaining written informed consent, ninety patients between 18 and 60 years of age with American Society of Anesthesiology (ASA) physical status I or II, scheduled for elective surgery under general anesthesia that required tracheal intubation were enrolled in the study. Those patients who had features of difficult airway (e.g. Mallampati grade >III, thyromental distance <6cm or a Body Mass Index >35kg/m²), pregnant or had other conditions associated with an increased risk of pulmonary aspiration were excluded from the study. Likewise patients who had pre-existing cervical neck pathologies, hypertensive individuals and those with allergies or contraindications to medications used for general anesthesia were excluded as well.

The selected patients were then randomised into two arms. Group 1 patients were intubated with the C-MAC® video-laryngoscope whereas patients in Group 2 were intubated with the Macintosh (MAC) laryngoscope. This randomisation process was done using ‘Random Numbers Tables’ that were computer generated.

In the operating room, all patients received a standardized general anesthetic. Both groups of patients were started on IV fluid of Lactated Ringer’s solution. Induction of anesthesia with the administration of 100% oxygen at 6 liters/min, IV fentanyl (2 mcg/kg) and IV propofol (up to 2 mg/kg) was carried out to induce unconsciousness defined as loss of eyelash reflex. Subsequently manual
ventilation was initiated with sevoflurane (2.0%) in oxygen as test ventilation, before administration of IV vecuronium (0.6 mg/kg) as a muscle relaxant. Standard anesthetic monitoring which included ECG, non-invasive blood pressure (NIBP), oxygen saturation (SpO₂), end tidal carbon dioxide (EtCO₂) and a multi-gas analyzer were provided to both groups of patients. After full muscle relaxation was confirmed with a nerve stimulator, the patient’s neck was immobilized utilizing MILS technique. The MILS was performed by another medical officer who stood at the right side of the patient caudal to the intubator and the patient’s airway. The assistant placed a hand on each side of the patient’s neck with fingers pressed on each mastoid process and the hands were then pressed firmly into the operating table ensuring neutral alignment and a motionless cervical spine as described in Advanced Trauma Life Support².

Intubation was then performed with one of the two devices (both with blade #3) as per the group that the patient was in. A tracheal tube size #7.5 - 8 for males and #7 - 7.5 for females was used. Once the vocal cords were visualized they were graded using the Cormack and Lehane (CL) grading. After successful tracheal intubation in all patients, mechanical ventilation was commenced for the duration of the procedure with anesthesia being maintained with sevoflurane (1.0 MAC) and air-oxygen mixture (FiO₂ 0.5).

In each group, tracheal intubation was considered a failure if it could not be established with three attempts, within three minutes or desaturation of SpO₂ <92%. In the event of such an incident, MILS was abandoned and intubation was performed using the Macintosh blade with optimal patient head and neck positioning. Any additional instruments to aid intubation were used if deemed necessary. All intubations were performed by the investigator SH, an anesthetic trainee whose previous experience includes >30 intubations with the C-MAC® video-laryngoscope.

Data collected included CL score, time to intubate in seconds (defined as when either of the blades was inserted beyond the lip until first appearance of the capnograph waveform) and number of intubation attempts. In addition, the nature of optimisation maneuvers done such as the use of a gum elastic bougie (GEB), external laryngeal manipulation (ELM) or presence of a second assistant were also recorded. Complications including fogging of lens, local trauma (mucosal/lip/dental), hypoxia (SpO₂ <92%) and failed intubation were recorded. Recording of the patient’s baseline mean arterial pressure (MAP) and heart rate (HR) along with repeat recordings at fixed one minute time intervals for 5 minutes were done. No other medications were administered, or procedures performed during the 5-minute data collection period after tracheal intubation. Subsequent management was left to the discretion of the anesthetist providing care for the patient.

The sample size was obtained using the computer software: “Power and Sample Size Calculations Version 3.0.14, January 2009” otherwise known as PS2. (http://bisotat.mc.vanderbilt.edu/powersamplesize ). The alpha error was set at 5% (p<0.05) and a beta error of 20% (power = 0.8). The p0 was set at 0.2 from a previous study with the Macintosh laryngoscope using MILS where 20% of patients obtained CL grade 1 views⁹. Since the C-MAC® video-laryngoscope has not been studied previously in this manner, the probability of obtaining a CL grade 1 view was estimated as 50% from a preliminary study¹². Thus the p1 was set at 0.5 and the results calculated using the sample size software as discussed previously. The sample size required was found to be 38 patients, which was rounded up to 40 patients on each arm. A dropout rate of 10% was factored in to give a sample size of 45 patients in each arm and thus a total sample size of 90 patients.

Data analysis was done using Chi-square test for non-parametric data and Student’s t-test for parametric data. A p value of less than 0.05 was considered as statistically significant. All analysis was performed using SPSS for Windows (version 12.0, Chicago, IL).

Results

A total of 90 patients were enrolled into the study with 45 patients in each group. There were no significant differences in the patient characteristics such as age, gender, ASA physical status, BMI and Mallampati grades between the two groups as shown in Table 1.
The CL grade was significantly better in Group 1 using the C-MAC® producing a CL Grade I for 67% of the study population compared to Group 2 with only 38% of the sample having CL Grade I as shown in FIGURE 1 (p <0.05). None of the patients in Group 1 had CL Grade IV whereas there was one patient in Group 2 with CL grading of IV. The majority of patients intubated with the MAC (56%) were found to have a CL Grade of II. The CL grading correlated well with the time to intubate (TTI) which was found to be significantly shorter in Group 1 with a mean time of 32.7 ± 6.8 vs. 38.8 ± 8.9 seconds for Group 2 (p = 0.001) as shown in Table 2.

The number of intubation attempts required in the two groups however was found to be not significantly different. The majority of patients in both

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**Table 1**

Demographic and patient characteristics. Values expressed as Mean ± SD or number (%)

<table>
<thead>
<tr>
<th></th>
<th>C-MAC® (n = 45)</th>
<th>MAC (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.8 ± 15.1</td>
<td>41.6 ± 14.8</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22 (48.9)</td>
<td>24 (53.3)</td>
</tr>
<tr>
<td>Male</td>
<td>23 (51.1)</td>
<td>21 (46.7)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 ± 4.7</td>
<td>26.9 ± 3.7</td>
</tr>
<tr>
<td>ASA I</td>
<td>30 (66.7)</td>
<td>32 (71.1)</td>
</tr>
<tr>
<td>ASA II</td>
<td>15 (33.3)</td>
<td>13 (28.9)</td>
</tr>
<tr>
<td>Mallampati I</td>
<td>25 (55.6)</td>
<td>22 (48.9)</td>
</tr>
<tr>
<td>Mallampati II</td>
<td>20 (44.4)</td>
<td>23 (51.1)</td>
</tr>
</tbody>
</table>

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**Table 2**

Intubation characteristics. Values are expressed as Mean ± SD or numbers (%)

<table>
<thead>
<tr>
<th></th>
<th>C-MAC® (n=45)</th>
<th>MAC (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTI (seconds)</td>
<td>32.7 ± 6.8*</td>
<td>38.8 ± 8.9</td>
</tr>
<tr>
<td>Intubation attempts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>44 (97.8)</td>
<td>39 (86.7)</td>
</tr>
<tr>
<td>2</td>
<td>1 (2.2)</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Optimization maneuvers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>38 (84.4)**</td>
<td>27 (60.0)</td>
</tr>
<tr>
<td>GEB</td>
<td>3 (6.7)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>ELM</td>
<td>3 (6.7)</td>
<td>14 (31.1)</td>
</tr>
<tr>
<td>ELM + GEB</td>
<td>1 (2.2)</td>
<td>3 (6.7)</td>
</tr>
<tr>
<td>Second assistant</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blade size change</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Failed intubation</td>
<td>0</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Lip trauma</td>
<td>0</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Esophageal intubation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dental trauma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SpO₂&lt;92%</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* p = 0.01, ** p <0.05.

---

**Fig. 1**

Cormack and Lehane grades obtained in the two groups

* p <0.05
due to the presence of a built in software system that initiates pre-warming of the optical system by the camera light\(^\text{12}\).

Both groups had similar trends of MAP and HR over the 5-minute data collection period as shown in Figures 2 and 3. There were no recorded increases of more than 20% of their respective baseline values of these two parameters. However at one point of time (T+1: one minute post intubation) Group 2 had a higher MAP of 93.5 ± 16.0 vs. 86.9 ± 10.4 mmHg for Group 1\((p<0.05)\). The rest of the data points were not statistically different between the groups.

**Discussion**

From this study, we found that using the C-MAC® video-laryngoscope would be of benefit in patients with
MILS due to its superiority in various aspects compared to the Macintosh laryngoscope. The C-MAC® was able to obtain better CL scores with a majority of them being CL Grade I without requiring additional optimization maneuvers. The Macintosh laryngoscope on the other hand had majority of CL II grades. Poor laryngoscope views in the setting of MILS is a known factor that will complicate intubation in this group of patients. The limited neck movement from the MILS made direct laryngoscopy become more challenging mainly due to difficulties in aligning the oral, pharyngeal and laryngeal axis which was required for a successful tracheal intubation. In order to overcome this situation, having an indirect laryngoscope such as the C-MAC® with a camera mounted on the blade capturing live images and projecting them onto a video screen dramatically reduces the line of sight required which in turn resulted in the much improved CL scores as seen occurring in our study. This advantage was also noted by McElwain and Laffey where 35% of patients intubated with the C-MAC® had a CL Grade 1 vs. the Macintosh which produced CL Grade 1 in 19% of their study sample.

The mean difference of 18 seconds reduction in TTI for the C-MAC® obtained in our study may initially seem unremarkable at its face value especially since the lengthened period of apnea for the macintosh group was not associated with desaturation or other hemodynamic changes. However, in an emergency airway management situation where the patient is at risk of hypoxia, any reduction in the TTI could be a very crucial factor. In a similar study the TTI recorded however was longer although insignificantly for the C-MAC® [TTI of 27secs IQR 18, 47] vs. Macintosh [TTI of 23 sec IQR 14, 47]. A point to note in that study was that the measurement of TTI was not standardized. The investigators measured the TTI from the time the laryngoscope blade passed the lips up till they visualized the ETT passing the vocal cords and in cases where the ETT was not visualized, the appearance of capnograph tracing was taken as the end point. In our study the TTI was standardized and recorded for all intubations from the time the laryngoscope blade passed the lips till the appearance of the capnograph.

Using the C-MAC® also resulted in less need for additional optimization maneuvers compared to the Macintosh Group. In our study we found that the Macintosh group required the use of ELM in 61% of patients which was similarly seen in other studies as well. The main reason behind this was because of the need for the intubator to obtain a best line of sight by aligning the intubation axis as has been discussed earlier. This however is not needed when using the C-MAC® as the vocal cords are readily visualized due to the blade mounted camera and 80° angle of view. During the course of our intubations, we did not require a change in blade size or use of second assistant for either of the groups and blade size #3 was used for both devices.

Patients from both groups had no significant complications. Oxygenation was well maintained despite the variation in intubation times due to the process of preoxygenation that was conducted in our study. There may possibly have been hypoxemia if this crucial step was omitted highlighting once again its importance especially in emergency airway management. The lack of significant airway trauma in both groups as observed in our study arise possibly because of the similar shape and structure of the two laryngoscope blades that results in similar mechanical forces and movements during intubation when using either of the devices. These similarities in the low occurrence of airway trauma was also observed in other studies as well.

There are a few limitations that can be identified in our study. Firstly, it is not possible to blind the investigator about the device being used. The performance of the device is highly dependent on the capabilities of the operator. However due to the overall similar design of the two blades this would be quite unlikely to affect performance markedly. Nevertheless all the intubations were carried out by a single investigator (SH) so that the variability in technique and operator bias could be minimized. The other issue lies with the subjectivity of the CL scoring. Once again by utilizing a single operator we hope that this can be overcome as well.

One important factor to keep in mind is that this study was conducted on adequately fasted, pre-oxygenated patients with no difficult airway
management anticipated. These patients underwent elective surgery exclusively. Thus the situation would be expected to be very different in the post-trauma patients presenting to the emergency department or operating room for emergency airway management. Further well planned studies will be required to assess how the C-MAC® performs in these situations.

Conclusion

In conclusion, our study demonstrated that the C-MAC® video-laryngoscope was superior for patients being intubated during manual inline neck stabilization when compared to the standard Macintosh laryngoscope.
References


Abstract

Introduction: Memantine was discovered in 1968 and is used as a treatment for Alzheimer’s disease. We evaluated the use of memantine to treat complex regional pain syndrome in this retrospective study.

Patients and methods: 56 patients with CRPS, who were treated with trial of memantine for at least two months with 40mg QHS from 2007 until 2009.

Results: 34 females and 22 male patients. Age-46.0±/9.7 years. Number of years with CRPS-9.24 ± 5.7 years. Memantine was started at 5 or 10mg QHS, before being increased by 5 or 10mg every 4-7 days, as tolerated, to a maximum dose of 40mg-60mg, as tolerated. In all, 13 patients showed complete remission from CRPS withVAS 0 and the disappearance of allodynea for at least nine months after the use of memantine. In addition, 18 patients showed partial improvement of VAS and allodynea. Eight patients showed no improvement even after continuous use of memantine at a dose of 40mg QHS for two months. Seven patients could not take more than 5mg of memantine per day and had to stop it due to side effects. In terms of subjective improvement in short-term memory, nine patients showed much improvement, 14 patients showed some improvement, three patients showed no changes and one patient did not answer the questionnaire. Regarding subjective feelings of having a better quality of life, 17 patient answered yes, three did not feel any changes, six could not give an answer and two did not fill out the questionnaire.

Conclusions: Memantine is a promising option for the treatment of CRPS. A randomised controlled study is needed to evaluate its efficacy.

Introduction

Bowsher (1991) found that neuropathic pain affected 25-50% of chronic pain patients in most pain clinics. Richards (1967) reported the history of CRPS and its terminology. Although previous descriptions were of single cases, Weir Mitchell, Morehouse and Keen (1864) first described the condition in full in the book “Gunshot Wounds and other Injuries of Nerves”. The
authors described the condition as a burning pain, which Weir Mitchell later described as causalgia in 1872 in the Merck Manual for Health Professionals. Thomas and Grossberg explained the multimodal therapies and treatments used for Alzheimer’s disease, including memantine which was discovered in 1968.

Sinet et al. (2007) published his preliminary report on the use of memantine in complex regional pain syndrome with promising results. Schleley et al.’s (2007) experiment with memantine in patients with phantom limb pain, in combination with continuous brachial plexus blocks, showed a decrease in phantom pain up for to six months. However, treating CRPS remains an off-label use for memantine. In this study, we evaluated the use of memantine in patients with complex regional pain syndrome.

Patients and methods

We reviewed the charts of patients with diagnosed with CRPS that were treated in our clinic from 2007 until 2009. In all, 56 CRPS patients (52 CRPS I, four CRPS II) were treated with memantine, including 34 females and 22 males. Retrospective, open label data and results were gathered from treating our patients during at least two years of follow-up after beginning memantine. All patients consented to the off label use of memantine for the treatment of CRPS.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>Frequency</td>
</tr>
<tr>
<td>42.9</td>
<td>21</td>
</tr>
<tr>
<td>57.1</td>
<td>28</td>
</tr>
<tr>
<td>100.0</td>
<td>49</td>
</tr>
</tbody>
</table>

Patients received a minimum dose of 40mg/day-60mg/day, as long as a better response was achieved with no side effects. Seven patients were excluded from the study because they did not tolerate a memantine dose of even 5 mg a day. Five of the seven patients had already been diagnosed with bipolar affective disorder at least two years prior to their CRPS diagnosis and were on antipsychotic medications and mood stabilisers prior to receiving the memantine. Severe hallucinations, wild dreams, and psychotic ideations were the frequent complaints while on memantine.

The mean age of the participants was 46.0 ± 9.7 years. The average number of years since the participants’ diagnoses of CRPS was 9.24 ± 5.7 years. Memantine was started at 5 or 10mg QHS, before being increased by 5 or 10mg every 4-7 days, as tolerated, up to a maximum level of 40mg, or 60mg if a better response was achieved with no side effects. No changes were made in any of the patients’ current poly-pharmacy treatment plans for CRPS during the experiment until the patients asked for to stop or decrease their non-experimental medications.

Before the starting memantine, all of our patients had been taking a large variety of CRPS treatments including:

- Several diagnostic/therapeutic sympathetic blocks (all patients), and/or continuous sympathetic blocks (if possible, some patients).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Paired Samples Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Std. Error</td>
<td>Std. Deviation</td>
</tr>
<tr>
<td>.20065</td>
<td>1.40456</td>
</tr>
<tr>
<td>0.44134</td>
<td>3.08937</td>
</tr>
<tr>
<td>.29776</td>
<td>2.08432</td>
</tr>
<tr>
<td>.41853</td>
<td>2.92973</td>
</tr>
</tbody>
</table>

A number of months of proper physical therapy.

Psychological therapy, if needed.

Extensive poly-pharmacy therapy: membrane stabilisers, NSAIDS, anti-depressants, muscle relaxants, alpha-2 agonists, alpha-1 antagonists, steroids, opioids and/or biphosphonats.

A few had intrathecal delivery systems ([opioids/baclofen/clonidine/local anaesthetic] combinations).

A few had epidural Dorsal Column Stimulation for pain modulation.

A few had a combination of treatments five and six.

Each patient was encouraged to maximise participation in daily living activities.
All patients received a monthly evaluation for signs of changes in:

- Allodynia
- Burning pain
- Short-term memory loss
- Anger level
- Normalcy in everyday life

To assess for burning pain, the following assessments were used:

1) Quantitative Visual Analog Scale (VAS) before and after six months on the full dose of memantine.
2) Quantifying the number of exaggerated burning attacks per month on the primary CRPs extremity (patients voted to call these “a 10/10 Fire Storm”).

Allodynia was assessed according to the following:

1) Percentage of decrease of the disgusting unpleasing feelings related to soft touch of the skin of the area affected by CRPS.
2) For the patients that enjoyed taking a shower prior to the development of CRPS, the time spent in the shower from before and after six months on memantine.

To assess for CRPs-related migraine headaches, a quantitative decrease in the number of migraine attacks/month before and after six months on memantine was examined.

We followed the patients for at least two years after the start of the memantine.

Results

In all, 56 patients were enrolled in the study, and ultimately, seven were excluded, as they did not tolerate the memantine. Of the patients that were excluded, six were females and one was male. Five of the seven patients had been already diagnosed with bipolar affective disorder at least two years prior to the CRPS diagnosis, and were on antipsychotic medications and mood stabilisers prior to beginning memantine. Severe hallucinations, wild dreams, and psychotic ideations were the frequent complaints related to side effects while on memantine. Out of the 49 patients that continued to use memantine, 21 were male (42.9%) and 27 were female (57.1%).

The mean VAS was 8.1633 (SD: 1.40456) before the use of memantine and 3.5510 (SD: 3.08937) after the use of memantine, which was statistically significant at $p < 0.001$. Those that responded positively to the memantine did not ask for any increase in other pain medications, and instead, asked for the dosages of the other medications to be decreased. The mean burning pain was 7.7755 (SD: 2.08432) before the use of memantine and 3.7143 (SD: 2.92973) after the use of memantine, which was statistically significant at $p < 0.000$. Out of 49 patients, 13 (26.5%) showed a complete disappearance of the pain, burning and allodynea.

Discussion

Memantine is a drug with the ability to block NMDA receptors in the brain. Juliato Piovesan et al. (2008) suggested that memantine was much more potent inhibitor of central and peripheral sensitisation than were non-NMDA antagonists. Park et al. (2012) tested the drug on trigeminal pain in rats. Belozertseva and Bespalov (1998), as well as Popik and Kozela (1999), showed that memantine could attenuate the tolerance to morphine in animal models. Davidson and Carlton’s (1998) experiment demonstrated that the local use of memantine in attenuating pain in animal models was comparable to the use of dexmethylorphan and ketamine. Eisenberg et al. (1998) failed to find clinical benefits of using memantine for post-herpetic neuralgia when using doses of 10-20mg/day. Nikolajsen et al. (2000), in a randomised cross-over study, could not find any difference when using 20mg/day of memantine after amputation or nerve injury surgery. Siniset al. (2007) published preliminary results in human patients with CRPS that had good response to the medication when using 20 mg/day. Scheley et al. (2007) found a decrease in the medication requirements, as well as in the phantom limb pain, when using memantine at doses of 20-30mg/day compared to those people that did not use the drug. Grande et al. reported the use of memantine with small doses of ketamine for opioid tolerant oncology patients, demonstrating less opioid consumption at memantine doses of 20mg a day, and recommended more studies be done in this area. Thomas and Grossberg (2009)
recommended the use of memantine for Alzheimer’s disease and other neuropsychiatric diseases due to its level of safety.\(^4\) Oliván-Blázquez et al. (2014) found promising results for memantine use at doses of 20g/day when used for fibromyalgia\(^15\).

We used the memantine in our practice for resistant cases of CRPS and used larger doses than what was recommended for use in patients with Alzheimer’s disease (40mg/day), which could be why other studies results did not show the same benefits. Also, in our study, the pathology was different than in the other studies, which might also contribute to the conflicting results. Our study was limited in the lack of randomisation with a controlled group that used a placebo. However, in our study, we compared the same patient before and after the use of memantine, using the patients’ data before the treatment as the control. We concluded that memantine is effective and is a promising option for the treatment of CRPS. More studies are needed using blinding, randomisation and possibly placebo procedures.

**References**

- Partially published as an abstract presentation in the 8\(^{th}\) Congress of European Federation of IASP Chapter (EFIC) October 9-12, 2013 in Florence, Italy.

EFFECTS OF DEXAMETHASONE AND PHENIRAMINE MALEATE ON HEMODYNAMIC AND RESPIRATORY PARAMETERS AFTER CEMENTATION IN CEMENTED PARTIAL HIP PROSTHESIS

Abdulkadir Yektaş*, Funda Gümüş*, Tolga Totoz*, Nurten Gül*, Kerem Erkalp* and Aysin Alagöl*

Summary

Purpose: To prevent hemodynamic and respiratory changes that are likely to occur during cementation in partial hip prosthesis by prophylactic use of pheniramine maleate and dexamethasone.

Methods and Materials: The study included 40 patients aged between 60 and 85 years with an American Society of Anesthesiologists (ASA) grade of II-III who underwent partial hip prosthesis. Just after spinal anesthesia, 4 mL normal saline was pushed in patients in Group S, whereas 45.5 mg pheniramine maleate and 8 mg dexamethasone mixture was pushed intravenously in a total volume of 4mL in patients in Group PD.

Results: Amounts of atropine and adrenaline administered after cementation were significantly higher in Group S than in Group PD (P <0.05). There was a significant difference between SpO₂ values before and after cementation in Group S; SpO₂ value was lower after cementation (P <0.05) except for 1. min after cementation. SpO₂ value increased 1 min after cementation (P = 0.031)

Conclusion: Prophylactic use of pheniramine maleate and dexamethasone in partial hip prosthesis led to an increase in SpO₂ value and a decrease in the utilization of adrenaline and atropine after cementation.

Keywords: Methylmethacrylate, partial hip prosthesis, bone cement implantation syndrome, pheniramine maleate, dexamethasone.

Introduction

Partial hip arthroplasty is usually performed in elderly population in whom concomitant diseases may enhance the likelihood of a more progressive BCIS (Bone Cement Implantation Syndrome). BCIS is the most important cause of intraoperative morbidity and mortality in patients undergoing cemented hip arthroplasty, and rarely, hypoxia and confusion may be encountered in the postoperative period. Intraoperative mortality rate is 0.43 % for cemented partial hip prosthesis in patients with or without femur fracture¹. Although the etiology and pathophysiology of BCIS have not been understood clearly, few mechanisms including monomer-mediated model, embolic model, histamine release and hypersensitivity, complement activation, and multimodal model

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have been suggested. In a study, blockade of histamine receptors by clemastine and cimetidine (H₁ and H₂ antagonists) was reported to have protective effects. Pheniramine maleate is an H₁ receptor antagonist. H₁ receptor antagonists have been successfully used before drug infusion to prevent and for acute treatment of type I hypersensitivity. Dexamethasone is a synthetic glucocorticosteroid. In animal studies, this glucocorticosteroid has been demonstrated to inhibit airway eosinophilia in the presence of antigen by inhibiting interleukin-5 synthesis and to be successfully used for the prophylaxis of type I hypersensitivity reaction.

The aim of the present study is to assess the effect of pheniramine maleate and dexamethasone on incidence of hypotension, bradycardia and hypercarbia associated with BCIS.

Methods and Materials

After obtaining approval from the Ethical Committee of Bağcılar Training and Research Hospital and written informed consents of the patients, 40 patients aged between 60 and 85 years with an American Society of Anesthesiologists (ASA) grade of II-III who underwent partial hip prosthesis with cement due to femur neck fracture under spinal anesthesia were included in the study. The present study was designed as a prospective, randomized and double-blinded study.

Data of the patients regarding age, height, weight, gender, concomitant diseases, medications, smoking status, ASA classification and surgery duration of surgery were recorded.

Patients with allergic diseases, those using anti-allergic medications or corticosteroids, who have deep venous thrombosis and lower extremity venous insufficiency, those with cardiac disease likely to cause atrial fibrillation or thromboembolism, or paraplegia-hemiplegia, who were immobile before fracture (i.e., bedridden patients), those with previous cardiac surgery, and those having a contraindication for regional anesthesia were excluded from the study.

The patients did not receive any premedication. The patients were positioned with the hip that would be operated being on top, and an 18 G intravenous canula was placed into a peripherial vein in the dorsal aspect of the hand opposite to the surgery side and 0.9% NaCl was administrated at a rate of 10 mL kg⁻¹ h⁻¹ for first hour and than 5 mL kg⁻¹ h⁻¹. In order to obtain blood sample for blood gas analysis, an intra-arterial catheter was inserted into the radial artery of the arm on the surgery side via a 20-gauge intravenous catheter, and it was washed with heparinized fluid and closed using a three-way tap. The patients were administrated oxygen at a rate of 2 L/min through a free oxygen mask which was fixed hole in any side of the free oxygen mask in which the free end of end-tidal CO₂ (ET-CO₂) line. All patients underwent electrocardiography, non-invasive arterial blood pressure measurement, peripheral pulse oximetry and end-tidal CO₂ monitoring. All patients underwent spinal anesthesia. Patients in both groups were positioned laterally with the leg that would be operated being on top, and spinal anesthesia was performed via a 27-gauge Quincke-type needle after performing cutaneous-subcutaneous infiltration anesthesia using 2 mL of 2% lidocaine through L4-L5 space. After observing cerebrospinal fluid (CSF) outflow, 1 mL (5 mg) isobaric bupivacaine and 25 µg (0.5 mL) fentanyl were administered in a total volume of 1.5 mL. Spinal anesthesia was performed by a specialist in both groups. The patients in whom spinal anesthesia was unsuccessful three times were excluded from the study. Then the patient were randomly divided into the following two groups using sealed envelopes: 1) Group S (n = 20) patients were administrated 4 mL of normal saline, 2) Group PD (n = 20) patients were administrated 45.5 mg pheniramine maleate and 8 mg dexamethasone. Prior to spinal anesthesia, basal values of arterial blood pressure, heart rate, oxygen saturation by pulse oximeter (SpO₂), end-tidal CO₂ (ETCO₂), and blood gases were recorded. Pre-prepared syringes were used; thus, both the anesthesiologist and the patient were blinded to the content.

Cephalazoline sodium 1 g was administered iv approximately 30 to 60 min prior to surgery for prophylaxis.

Values of arterial blood pressure, heart rate, SpO₂, end-tidal CO₂, and blood gases were recorded for all patients prior to surgical procedure and at 10-min intervals until the first minute before cementation.
Amount of bleeding, amount of crystalloid administered by IV route, and, if used, doses of atropine and adrenaline were also recorded until the first minute before cementation. Those parameters were recorded at 1-min intervals in the first 5 min after cementation and then every 5 minutes. Measurements were discontinued at the 25th min after cementation. Amount of administered crystalloid throughout the surgical procedure and amount of bleeding were recorded. Arterial blood gases were analyzed before spinal anesthesia, just before cementation, and at the 10th and 25th min after cementation. Measurements were discontinued at the 25th min after cementation.

A 5 µg adrenalin was pushed via venous route in the following conditions: 1) a decrease in mean blood pressure more than 30% of the initial value until cementation, 2) after cementation, a more than 30% decrease in the blood pressure value measured before cementation. In case of a decrease in heart rate below 50 beats/min, 0.5 mg atropine was injected. Patients in whom amount of bleeding before cementation exceeded 400 mL were excluded from the study (bleeding before cementation exceeded 400 mL in any of the patients), and blood loss was replaced by normal saline.

When the surgical procedure was completed and following postoperative observation, patients with a modified Aldrete score of ≥9 were transferred to the clinic.

**Statistical Analysis**

Based on a preliminary study performed in 10 patients, we estimated that a sample size of 20 patients in each group would be sufficient with a 5% error and a statistical power of 80% assuming that the mean arterial pressure on the 25th min would be 92 ± 15 mmHg in Group PD and 85 ± 15 mmHg in Group S.

Descriptive statistics of data were expressed as mean ± standard deviation. Normal distribution of variables was tested by Kolmogorov Smirnov test. Comparison of data regarding age, height, weight, gender, type of surgery, duration of surgery, time elapsed from spinal anesthesia to cementation, and ASA grades were performed using the Chi square test. Heart rate, arterial blood pressure values, SpO₂, end-tidal CO₂ and blood gas measurements, amount of bleeding throughout surgery before and after cementation, amount of crystalloid, amount of atropine and adrenaline were compared between the groups by an independent-t test. Data analyses were performed using the Statistical Package for the Social Sciences (SPSS, Inc. Chicago, IL, USA) version 11.5. A P value <0.05 was considered statistically significant.

**Results**

Distributions of age, weight, height, type of surgery, duration of surgery, duration of cementation, ASA grades and gender in the study groups are presented in Table 1. There were no statistically significant differences between the groups in terms of age, weight, height, type of surgery, duration of surgery, duration of cementation, ASA grade and gender.

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 20)</th>
<th>Group PD (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>80.50 ± 7.05</td>
<td>76.85 ± 9.31</td>
<td>0.198</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.75 ± 11.14</td>
<td>70.60 ± 10.45</td>
<td>0.989</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168.45 ± 8.40</td>
<td>166.35 ± 5.65</td>
<td>0.462</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>79.30 ± 27.29</td>
<td>84.55 ± 18.01</td>
<td>0.579</td>
</tr>
<tr>
<td>Duration of cementation (min)</td>
<td>61.60 ± 22.87</td>
<td>64.35 ± 10.55</td>
<td>0.968</td>
</tr>
<tr>
<td>ASA (II/III)</td>
<td>14/6</td>
<td>13/7</td>
<td>0.708</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>11/9</td>
<td>12/8</td>
<td>0.061</td>
</tr>
</tbody>
</table>

SD: standard deviation; ASA: the American Society of Anesthesiologists; F: female; M: male

Doses of atropine and adrenaline and the amounts of intravenous fluid and bleeding in the study groups are presented in Table 2. The dose of adrenaline used...
after cementation was significantly higher in Group S than in Group PD (P = 0.022). The dose of atropine used after cementation was significantly higher in Group S than in Group PD (P = 0.014).

Comparison of the study groups in terms of systolic diastolic and mean arterial pressures, heart rate and SpO₂ before and after cementation are presented in Table 3. There were no statistically significant differences between the groups in terms of systolic/diastolic and mean arterial pressure, heart rate and SpO₂. Heart rate increased significantly 2 min after cementation in Group PD when compared to before (p = 0.008) (Table 3).

In Group S, SpO₂ increased 1 min after cementation (P = 0.031), and were significantly lower at the rest of all times when compared to the value before cementation (P = 0.003, P = 0.003, P <0.001, P = 0.003, P = 0.001, P = 0.001, P = 0.001, P = 0.004, respectively) (Table 3).

There were no significant differences between Group S and Group PD in terms of P₉₉ (P = 0.168), partial arterial carbon dioxide pressure (PₐCO₂) (P = 0.067), partial arterial oxygen pressure (PₐO₂) (P = 0.056) and end-tidal CO₂ values before cementation and at the 10th (P = 0.067) and 25th (P = 0.152) min after cementation.

In addition, there were no significant differences in both groups in terms of pH, PₐCO₂, PₐO₂ and end-tidal CO₂ values before cementation, and at the 10th min pH (P = 0.102), PₐCO₂ (P = 0.063), PₐO₂ (P = 0.175) and end-tidal CO₂ values (P = 0.448) and 25th min pH (P = 0.193), PₐCO₂ (P = 0.186), PₐO₂ (P = 0.084) and end-tidal CO₂ values (P = 0.054) min after cementation.

One patient in Group S developed cardiopulmonary arrest at the 1st min after cementation and accepted as dead after performing cardiopulmonary resuscitation (CPR) for 45 min. Blood gas values and end-tidal CO₂ values of this case was not consistent with pulmonary embolus.

All patients were transferred to the clinic after observing postoperatively in recovery room for 2 hours and then all patients were discharged. None of the patients developed postoperative hypoxia or confusion.

### Discussion

Respiratory and cardiovascular changes during partial hip replacement seriously affect the prognosis of patients. These changes exist in a wide spectrum of disorders ranging from temporary hypoxia to cardiac rhythm disorders and even cardiac arrest\(^{12,13}\).

Several mechanisms have been suggested in the etiology and pathophysiology of BCIS including monomer-mediated model, embolic model, histamine release and hypersensitivity, complement activation, and multimodal model\(^7\). A study has shown that implantation of methacrylic bone cement into the femur may increase plasma histamine level by more than 1 ng/mL. Temperate histamine release may cause severe,

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**Table 2**

Distribution of amounts of atropine, adrenaline, and intravenous fluid, and the amount of bleeding in the study groups. Numbers are presented as mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 20)</th>
<th>Group PD (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline after cementation (µg)</td>
<td>4.50 ± 11.34</td>
<td>0.75 ± 1.83</td>
<td>0.022</td>
</tr>
<tr>
<td>Atropine after cementation (mg)</td>
<td>0.25 ± 0.91</td>
<td>0.00 ± 0.00</td>
<td>0.014</td>
</tr>
<tr>
<td>Intravenous crystalloid before cementation (mL)</td>
<td>560.50 ± 206.33</td>
<td>480.00 ± 176.51</td>
<td>0.345</td>
</tr>
<tr>
<td>Intravenous crystalloid administered throughout surgical procedure (mL)</td>
<td>890.00 ± 282.65</td>
<td>827.50 ± 181.71</td>
<td>0.274</td>
</tr>
<tr>
<td>Amount of bleeding before cementation (mL)</td>
<td>184.25 ± 96.99</td>
<td>158.75 ± 77.01</td>
<td>0.243</td>
</tr>
<tr>
<td>Total amount of bleeding (mL)</td>
<td>228.75 ± 118.73</td>
<td>211.00 ± 77.50</td>
<td>0.059</td>
</tr>
</tbody>
</table>

SD: standard deviation
Table 3
Systolic, Diastolic and Mean Arterial Pressure, Heart Rate and Peripheral Oxygen Saturation (Mean ± SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>Before C</th>
<th>1.min</th>
<th>2.min</th>
<th>3.min</th>
<th>4.min</th>
<th>5.min</th>
<th>10.min</th>
<th>15.min</th>
<th>20.min</th>
<th>25.min</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAP</td>
<td>S</td>
<td>137.4 ± 27.0</td>
<td>127.2 ± 28.3</td>
<td>128.2 ± 24.4</td>
<td>127.2 ± 25.9</td>
<td>130.3 ± 28.3</td>
<td>131.5 ± 25.5</td>
<td>135.3 ± 24.3</td>
<td>130.2 ± 28.4</td>
<td>135.1 ± 24.1</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>125.6 ± 22.1</td>
<td>124.0 ± 26.0</td>
<td>118.8 ± 27.6</td>
<td>121.1 ± 22.9</td>
<td>122.1 ± 22.7</td>
<td>119.9 ± 34.1</td>
<td>132.8 ± 20.3</td>
<td>134.6 ± 23.5</td>
<td>131.6 ± 23.9</td>
</tr>
<tr>
<td>DAP</td>
<td>S</td>
<td>76.4 ± 21.0</td>
<td>69.9 ± 17.7</td>
<td>73.6 ± 17.4</td>
<td>74.3 ± 21.8</td>
<td>74.3 ± 23.1</td>
<td>74.0 ± 20.1</td>
<td>74.2 ± 21.4</td>
<td>72.9 ± 21.4</td>
<td>72.2 ± 19.01</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>71.8 ± 16.5</td>
<td>69.8 ± 15.6</td>
<td>67.0 ± 14.3</td>
<td>67.8 ± 13.6</td>
<td>67.9 ± 15.4</td>
<td>68.0 ± 13.6</td>
<td>70.9 ± 12.4</td>
<td>70.7 ± 11.8</td>
<td>69.1 ± 11.6</td>
</tr>
<tr>
<td>MAP</td>
<td>S</td>
<td>93.8 ± 20.7</td>
<td>83.1 ± 22.1</td>
<td>88.3 ± 20.7</td>
<td>87.9 ± 25.3</td>
<td>91.6 ± 27.2</td>
<td>89.5 ± 20.6</td>
<td>91.8 ± 26.3</td>
<td>93.2 ± 26.1</td>
<td>89.9 ± 18.5</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>85.4 ± 21.8</td>
<td>81.7 ± 16.9</td>
<td>81.7 ± 16.9</td>
<td>78.9 ± 17.4</td>
<td>79.5 ± 16.2</td>
<td>81.9 ± 15.8</td>
<td>87.7 ± 15.8</td>
<td>90.8 ± 14.9</td>
<td>84.4 ± 13.9</td>
</tr>
<tr>
<td>HR</td>
<td>S</td>
<td>76.4 ± 13.0</td>
<td>79.4 ± 18.9</td>
<td>76.1 ± 23.9</td>
<td>75.7 ± 24.0</td>
<td>74.7 ± 24.6</td>
<td>74.4 ± 23.1</td>
<td>75.1 ± 25.7</td>
<td>79.7 ± 25.1</td>
<td>81.2 ± 27.2</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>84.4 ± 18.7</td>
<td>87.1 ± 21.8</td>
<td>95.1 ± 24.5*</td>
<td>86.9 ± 22.2</td>
<td>88.3 ± 18.7</td>
<td>87.6 ± 19.3</td>
<td>87.3 ± 17.9</td>
<td>88.4 ± 20.3</td>
<td>87.41 ± 7.9</td>
</tr>
<tr>
<td>SpO2</td>
<td>S</td>
<td>97.5 ± 2.8</td>
<td>97.8 ± 2.8</td>
<td>92.6 ± 21.9*</td>
<td>92.1 ± 21.9*</td>
<td>92.2 ± 21.9*</td>
<td>92.7 ± 21.9*</td>
<td>92.7 ± 21.9*</td>
<td>92.2 ± 21.9*</td>
<td>92.5 ± 21.9*</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>97.2 ± 2.4</td>
<td>96.3 ± 2.9</td>
<td>95.9 ± 3.2</td>
<td>96.0 ± 3.0</td>
<td>95.8 ± 2.8</td>
<td>95.9 ± 2.8</td>
<td>95.6 ± 2.9</td>
<td>93.4 ± 9.8</td>
<td>95.5 ± 3.3</td>
</tr>
</tbody>
</table>

SAP: Systolic Arterial Pressure; DAP: Diastolic Arterial Pressure; MAP: Mean Arterial Pressure; HR: Heart Rate; SpO2: Peripheral Oxygen Saturation; Group; S: Saline; Group; PD: pheniramine maleate-dexamethasone; Before C: Before cementation.
There is no statistical difference between groups (P >0.05)
* P <0.05 when compared with Before Cementation.
sometimes fatal, cardiovascular complications in very old patients in case they have signs of hypovolemia or cardiac diseases.

Cardiac problems defined to date have been mostly about wall motion and rhythm disorders, with no remarkable changes in heart rate. We also found no significant difference between heart rates before and after cementation; heart rate at the 2nd min after cementation was higher than before cementation only in Group PD. In Group S, as compared with before cementation, heart rate decreased by 0.40% at the 2nd min, 1% at the 3rd min, 2.5% at the 4th min and 3.1% at the 5th min, but thereafter returned to the normal values. The dose of atropine administered was significantly higher in Group S than in Group PD. However, as heart rate was recorded with 5-min intervals, such decrements in HR were not reflected in the statistical analysis. In Group PD, an increase in the heart rate was observed by 12.73% at the 2nd min (P <0.05), 3% at the 3rd min, 4.62% at the 4th min and 3.79% at the 5th min.

Potential causes of hypotension, one of the parameters of BCIS, include histamine release and type I hypersensitivity reaction, or hemodynamic impairment caused by pulmonary air or by fat embolism and reflex mechanisms responsive to this. An experimental study has demonstrated that methylmethacrylate monomers influence intracellular and extracellular calcium mobilization, resulting in direct relaxation in venous and arterial smooth muscles. Nevertheless, this hypothesis has not been verified by in vivo animal experiments and it has been determined that plasma methylmethacrylate concentration after cemented hip arthroplasty is lower than the concentration that is likely to cause pulmonary or cardiovascular effects. A clinical study evaluating plasma concentrations revealed that maximum levels of serum methylmethacrylate were measured 30 s after cementation and this was thought to cause a decrease in arterial blood pressure. Another study compared non-cemented hip arthroplasty with cemented hip arthroplasty using transesophageal echocardiography and demonstrated a higher embolic load in the cemented hip arthroplasty group. The authors concluded that, embolism might also cause hypotension due to increase in pulmonary arterial pressure together with decrease in right ventricular function. In the present study, there were no significant differences between the groups in terms of the amounts of crystalloid and bleeding before cementation and throughout the surgical procedure.

The amount of adrenaline administered in Group S was significantly higher than that administered in Group PD; however, as blood pressure was measured at specific time intervals, such variations in blood pressure had no impact on the statistical outcomes.

A patient in Group S developed hypotensive bradycardic arrest at the 1st min after cementation, which was not responsive to CPR. There were no significant differences in Pao2, pH, Paco2 and end-tidal CO2 values of this patient before cementation and during CPR performed after cementation; this ruled out the possibility of massive embolism.

In the present study, despite oxygen provided through a free oxygen mask at a rate of 2 L/min in both groups, there was a significant difference between SpO2 values before and after cementation in Group S. An increase by 0.25% at the 1st min and a decrease by 7.1% at the 2nd min after cementation were observed, and this decrease continued until the end of surgery in the same manner. Various studies have demonstrated hypoxia development during hip and knee arthroplasty. This has been thought to result from pulmonary embolism or pulmonary vasoconstriction due to cement toxicity. In the present study, there was no significant difference between SpO2 values before and after cementation in Group PD; this suggests that dexamethasone and pheniramine maleate prevented bronchospasm resulted from pulmonary vasoconstriction caused by cement toxicity and pulmonary embolism. Studies performed after observation of intraoperative deaths occurred during cemented arthroplasty have demonstrated the presence of bone marrow embolism, fat embolism and bone embolism and methylmethacrylate particles in the lungs. Medulla residue may cause embolism in the lungs, heart or paradoxically in the brain and coronary arteries. This suggests that hypotension occurs due to characteristic hypoxia and right ventricular dysfunction as the consequence of pulmonary embolism. However, a definite correlation could not be established in the literature between the degree of embolism detected by performing transesophageal
It has been reported that blood cement monomer levels do not reach high concentrations that likely can cause toxicity in human\textsuperscript{32}, in which both mechanisms are considered to play a role. Among anaphylatoxins, C3a and C5a are potent mediators that lead to vasoconstriction and bronchoconstriction\textsuperscript{33}. The levels of C3a and C5a have been observed to increase in cemented hemiarthoplasties by complement activation\textsuperscript{33}. In human studies, high dose (2g) methylprednisolone have been demonstrated to reduce hypoxia and complement activation. The decreases in anaphylatoxin release and oxygen saturation are reduced by methylprednisolone\textsuperscript{33}. However, whether methylmethacrylate particles or embolus material causes complement activation is not clear. Complement levels were not studied in the present study. We thought that complement activation might have been prevented by dexamethasone, due to the less decrease in hemodynamic values-although no statistically difference was found, but clinically important-1 min after cementation and lack of desaturation in Group PD.

In conclusion, the dose of adrenaline and atropine used after cementation was significantly lower and, SpO\textsubscript{2} values were stable after cementation in Group PD; on the other hand, in Group S, SpO\textsubscript{2} values decreased after cementation, except for 1. min after cementation. SpO\textsubscript{2} value increased 1 min after cementation. This suggests that prophylactic administration of pheniramine maleate and dexamethasone may minimize the clinical symptoms of BCIS.
References

Abstract

**Background:** This was a randomized, double-blinded clinical trial to study the effects of a single oral dose of pregabalin 150 mg in postoperative pain management after mastectomy.

**Methods: Design:** forty nine patients ASA I or II, aged between 20-60 years, scheduled for mastectomy with or without axillary lymph nodes dissection (ALND) were recruited into this study. They were randomized into two groups, placebo (n = 24) or pregabalin (n = 25) receiving either oral pregabalin 150 mg or placebo when called to operation theatre (OT). The assessment of pain score were performed at recovery, 2, 4, 6 and 24 hours postoperatively at rest and on movement, using the verbal numeral rating score (VNRS).

**Results:** VNRS scores for pain at rest were lower in the pregabalin group at 2 (p = 0.024), 4 (p = 0.006) and 6 (p = 0.003) hours postoperatively, and also at 4 (p = 0.005) and 6 (p = 0.016) hours postoperatively on movement compared to the placebo group. Incidences of dizziness were common, however, side effects such as nausea and vomiting, headache, somnolence and visual disturbance were low and comparable in both groups.

**Conclusion:** a single dose of 150 mg pregabalin given preoperatively compared to placebo significantly reduced postoperative pain scores after mastectomy.

**Keywords:** pregabalin, postoperative pain, mastectomy, opioid.

Introduction

Preventive analgesia is a treatment approach that aims to reduce the development of central sensitization in the postoperative period by reducing peripheral nociceptive input into the central nervous system, thus reducing postoperative pain and analgesics consumption. The concept of preventive analgesia includes multimodal antinociceptive techniques with analgesics that exceed the expected duration of action and also attenuate peripheral or central hypersensitivity. Effective methods include systemic NSAIDs, single dose epidural analgesia, systemic NMDA receptor antagonists, systemic opioids and local anaesthetic infiltration. Gabapentin and pregabalin have been proven to be effective medications in serving these purposes.

Pregabalin was originally developed as an antiepileptic drug with an improved pharmacological profile when compared to that of its predecessor gabapentin. Although gabapentin and pregabalin were first identified as useful in the treatment for neuropathic pain, recent reviews showed that they reduced postoperative acute pain and analgesic consumption as well. Gabapentin has been shown to be an effective analgesic for tonsillectomy, mastectomy and knee arthroplasty.
however pregabalin appears to be a better option when compared with gabapentin as it has better analgesic efficacy and an improved pharmacokinetic profile\(^9\). Pregabalin and gabapentin bind to the \(\alpha_\delta\) sub-unit of pre-synaptic voltage-gated calcium channels in the spinal cord and brain\(^{12,3,4,5}\). By altering calcium currents, it reduces or modulates the release of several excitatory neurotransmitters including glutamate, norepinephrine, substance P and calcitonin gene-related peptide, producing inhibitory modulation of ‘over-excited’ neurons and returning them to a normal state.

One advantage of pregabalin in clinical use is that it has higher bioavailability when giving orally with linear pharmacokinetics property compared to gabapentin. It is rapidly and extensively absorbed after oral dosing in the fasting state with maximal plasma concentration occurring within 1 hour after single or multiple doses\(^9\). Absorption of gabapentin is limited by saturable, active and dose dependent transport in gastrointestinal tract but absorption of pregabalin is not saturable, resulting in a linear pharmacokinetic profile with bioavailability exceeding 90% and independent of dose\(^3,5\). In recent years, pregabalin has been introduced as an adjunct in multimodal management of postoperative analgesia in many studies because of its favourable pharmacokinetics\(^{10-15}\).

The aim of this study was to compare the effect of single-dose 150 mg oral pregabalin to placebo on postoperative pain after mastectomy for breast cancer.

**Methods**

This randomized, double-blinded clinical trial was done following approval of the Dissertation Committee of the Department of Anaesthesiology and Intensive Care, Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and the Research Ethics Committee of UKMMC (Research No. FF–444-2012).

Forty nine, ASA I or II patients, aged 20 to 60 years who were scheduled for elective mastectomy with or without axillary lymph nodes dissection (ALND) were included in the study. Informed and written consent was obtained from all patients during preoperative anaesthetic assessment a day before surgery. Exclusion criteria included, known contraindication to medication use in the study, patients with chronic pain or on daily intake of analgesic and impaired kidney function (creatinine level >80 \(\mu\)mol/L). Patients were randomized using computer-generated randomized numbers to receive either pregabalin (Lyrica\(^a\)) or placebo (vitamin B complex). Information regarding the study and the verbal numerical rating scale (VNRS) range from 0 – 10 was explained to the patients. On the day of surgery, all patients were given premedication of oral midazolam 7.5 mg with either oral pregabalin 150 mg (in 2 tablets) or oral vitamin B complex (in 2 tablets) one hour before being sent to operating room. Patients were instructed to close their eyes before given the test drug to swallow.

In the operation theatre, basic monitoring included electrocardiogram (ECG), oxygen saturation (SpO\(_2\)) and non invasive blood pressure (NIBP). General anesthesia was induced with IV propofol 1.5 – 2.5 mg/kg and IV fentanyl. After the patient was adequately anaesthetized, a supraglottic airway device was inserted. Anaesthesia was maintained with sevoflurane in 50% O\(_2\)/50% air mixture maintaining minimum alveolar concentration (MAC) of 0.8–1.0. Intraoperatively, patients were given IV morphine 0.1–0.2 mg/kg as an analgesic. Additional IV parecoxib 40 mg was given at the time of skin suturing. Adequate local anesthetic infiltration of levobupivacaine up to 2 mg/kg was given by the surgeon at the incision site.

Pain was assessed by independent observer in the recovery area, 2, 4, 6 and 24 hours postoperatively using the VNRS at rest and on movement. In the ward, all patients received oral etoricoxib 120 mg daily with oral paracetamol 1g every 6 hours as a standard analgesic. If the pain score was rated 5 or more, intravenous tramadol 50 mg was given as a rescue medication. Any incidence of side effects such as nausea, vomiting, headache, somnolence, dizziness and visual disturbance were documented.

Based on previous study\(^{13}\), with the power of 0.8, alpha value of 0.05 and dropout rate of 10%, the sample size calculated was 60. Statistical analysis and calculations was performed using SPSS for Windows Version 12.0. VNRS pain score and amount of intraoperative morphine used were analysed using Mann-Whitney U-test. Categorical variables such as number of patients needed rescue analgesic and
incidence of side effects were evaluated with $X^2$ test or Fischer’s exact test. A $p$ value of <0.05 was considered statistically significant.

Results

Forty nine patients were recruited in this study in which 24 patients were in the placebo group and 25 patients were in the pregabalin group. There were no statistical differences with regards to age, weight, height, race, ASA and type of operation (Table 1).

Figure 1 showed VNRS at rest in pregabalin group compared to placebo. There were statistically significant differences at 2, 4 and 6 hours postoperatively.

Figure 2 showed VNRS on movement in

Table 1
Demographic data values are expressed as mean± SD or number(percentage)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=24)</th>
<th>Pregabalin (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52.0 ± 8.4</td>
<td>51.5 ± 9.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.4 ± 8.0</td>
<td>60.2 ± 5.0</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.9 ± 3.0</td>
<td>156.2 ± 2.8</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>12 (50)</td>
<td>17 (68)</td>
</tr>
<tr>
<td>Chinese</td>
<td>8 (33.3)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>Indian</td>
<td>4 (16.7)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>12 (50)</td>
<td>15 (60)</td>
</tr>
<tr>
<td>II</td>
<td>12 (50)</td>
<td>10 (40)</td>
</tr>
<tr>
<td>Type of operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mastectomy</td>
<td>6 (25)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Mastectomy with ALND</td>
<td>18 (75)</td>
<td>19 (76)</td>
</tr>
</tbody>
</table>

*p value = 0.024. “p value = 0.006. ′ p value = 0.003.
pregabalin group compared to placebo. There were statistically significant differences at 4 and 6 hours postoperatively.

There was no statistically significant difference in the mean intraoperative morphine consumption in both placebo group and pregabalin group.

Six patients from the placebo group and three patients in the pregabalin group needed tramadol as a rescue drug postoperatively, however the difference was statistically not significant. There was no difference in postoperative oral analgesic consumption for both groups.

Adverse effects postoperatively in both groups, which was statistically not significant are presented in table 2.

There was no documented incidence of somnolence or visual disturbances in any of the patients.

<table>
<thead>
<tr>
<th>Incidence of side effects</th>
<th>Placebo (n = 24)</th>
<th>Pregabalin (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Headache</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9</td>
<td>16</td>
</tr>
</tbody>
</table>

Discussion

In this current study, we found that preoperative single dose of oral pregabalin 150 mg was effective in reducing both the resting and on movement postoperative pain in patients undergoing mastectomy with or without ALND. Spreng et al, showed a reduction of postoperative pain at rest and morphine consumption from 4 up to 24 hours postoperatively after lumbar discectomy with a single dose of oral pregabalin 150 mg10. In another study, Agarwal et al used a single dose of oral pregabalin 150 mg and effectively reduced postoperative pain and fentanyl consumption in patients undergoing laparoscopic cholecystectomy up to 24 hours11. Jokela et al used oral pregabalin 150 mg preoperative for day-case gynecological laparoscopic surgery and had better analgesia during the early recovery but not sustained up to 24 hours12. A study by Kim et al where mastectomy patients received oral pregabalin 75 mg twice a day showed that there was reduced postoperative pain and analgesic consumption respectively13. That study also showed the ability of divided doses of pregabalin to reduced pain after 48 hours up to 1 week after surgery.

Itticaikulthol et al used a higher dose of oral pregabalin 300 mg preoperatively and showed reduction of pain scores and morphine consumption.
for abdominal hysterectomy with or without salphingo-oophorectomy up to 24 hours post operatively. However a study by Paech et al using a lower dose of oral pregabalin 100 mg preoperatively was unable to reduce acute pain or improve recovery after minor gynecological surgery. Most of these studies also showed comparable rescue analgesic needed similar with the current study.

A meta analysis on efficacy of pregabalin in acute postoperative pain by Zhang et al concluded that postoperative opioid consumption and opioid related side effects were reduced but pain scores were not reduced. These conflicting results could possibly be due to differences in dosage, dosing regimen, type of surgery, the use of other analgesic regimes such as opioid or non opioids, different anesthetic technique and surgical procedure.

Most studies showed pregabalin to be well tolerated and associated with dose dependent adverse effects that are mild to moderate and usually transient. Different doses of pregabalin have been used in the literature and doses ranging from 75 mg to 300 mg. It has been shown that higher doses are associated with increased frequencies of side effects. The common adverse effects of pregabalin are nausea and vomiting, visual disturbances, headache, dizziness and somnolence. Most of the studies showed no significant adverse effects when a lower dose of pregabalin was used. Nausea and vomiting were the common side effects in the current study followed by headache and dizziness. There were no documented side effects of somnolence or visual disturbances.

There are a few limitations in study. The pain score was assessed immediately in the postoperative period in the recovery area which makes it difficult to assess the effects of pregabalin at that point of time. Another confounding factor is the use of IV tramadol as a rescue drug which may affect the assessment of pain score postoperatively and incidence of side effects.

**Conclusion**

In conclusion, single dose of 150 mg pregabalin given preoperatively compared to placebo significantly reduced the postoperative pain scores after mastectomy.
References


CONSUMPTION TRENDS OF RESCUE ANTI-PSYCHOTICS FOR DELIRIUM IN INTENSIVE CARE UNITS (ICU DELIRIUM) SHOW INFLUENCE OF CORRESPONDING LUNAR PHASE CYCLES: A RETROSPECTIVE AUDIT STUDY FROM ACADEMIC UNIVERSITY HOSPITAL IN THE UNITED STATES


Abstract

Background: The etiology of delirium in intensive care units (ICU) is usually multi-factorial. There is common “myth” that lunar phases affect human body especially human brains (and minds).

Objective: In the absence of any pre-existing studies in ICU patients, the current retrospective study was planned to investigate whether lunar phases play any role in ICU delirium by assessing if lunar phases correlate with prevalence of ICU delirium as judged by the corresponding consumptions of rescue anti-psychotics used for delirium in ICU.

Materials and Methods: After institutional review board approval with waived consent, the daily census of ICU patients from the administrative records was accessed at an academic university’s Non-Cancer Hospital in a Metropolitan City of United States. Thereafter, the ICU pharmacy’s electronic database was accessed to obtain data on the use of haloperidol and quetiapine over the two time periods for patients aged 18 years or above. Subsequently the data was analyzed for whether the consumption of haloperidol or quetiapine followed any trends corresponding to the lunar phase cycles.

Results: A total of 5382 pharmacy records of haloperidol equivalent administrations were analyzed for this study. The cumulative prevalence of incidents of haloperidol equivalent administrations peaked around the full moon period and troughed around the new moon period. As compared to male patients, female patients followed much more uniform trends of haloperidol equivalent administrations’ incidents which peaked around the full moon period and troughed around the new moon period. Further sub-analysis of 70-lunar cycles across the various solar months of the total 68-month study period revealed that haloperidol equivalent administrations’ incidents peaked around the full moon periods during the months of November-December and around the new moon periods during the month of July which all are interestingly the major holiday months (a potential confounding factor) in the United States.

Conclusion: Consumption trends of rescue anti-psychotics for ICU delirium revealed an influence by lunar phase cycles particularly that of full moon periods on female patients in the ICU.

Introduction

* MD.
** PhD.

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Critically ill patients in the Intensive Care Units (ICUs) frequently experience delirium which is an acute reversible dysfunction of the brain. The etiology of ICU delirium is usually multi-factorial. There is common “myth” that lunar phases affect human body especially human brains (and minds). This “myth” has often been studied in various scenarios including automobile accidents and injury accidents, peri-operative blood loss, clustering of seizures, mental status changes in schizophrenics, and human and animal behavior and physiology. The results of these studies reveal much ambiguity of the issue due to poorly understood underlying mechanisms; and hence results of various studies have either supported or refuted this norm/”myth” altogether. The common thread of this “myth” is that as lunar phases affect the oceans (tidal forces), these phases may affect the human body because it is composed of 70% water (fluids) that may result in “human tidal waves” generated by lunar influences.

Based on this background and in the absence of any pre-existing studies in the ICU patients, the current retrospective study was planned to investigate whether lunar phases have any role in ICU delirium by assessing if lunar phases correlate with prevalence of ICU delirium as judged by the corresponding consumptions of rescue anti-psychotic medications used for delirium in ICU.

**Materials and Methods**

After institutional review board approval with waived consent, the daily census of ICU patients from the administrative records was accessed at an academic university’s Non-Cancer Hospital in a Metropolitan City of United States. Thereafter, the ICU pharmacy’s electronic database was accessed to obtain data on the use of haloperidol and quetiapine over the two time periods for patients aged 18 years or above. Haloperidol and quetiapine are the two rescue anti-psychotic medications primarily used to manage ICU delirium in our hospital. The two time periods analyzed in this study were: 2008-2012 (five year period before the standardized protocol for ICU delirium was instituted in our hospital) and March 2013-October 2013 (eight month period after the standardized protocol for ICU delirium was instituted in our hospital). Since March 2013, our hospital’s standardized protocol for ICU delirium include (a) daily screening for delirium with Intensive Care Delirium Screening Checklist (ICDSC) to recognize patients with positive ICDSC scores ≥4 followed by (b) their initial non-pharmacological management with sleep promotion, ambient noise reductions during night-time, early and aggressive ambulation, and circadian rhythm cycle promotion, and thereafter reserving (c) pharmacological treatment for intractable cases in form of haloperidol 2.5mg every 6hrs as needed intravenous boluses (maximum single dose 5mg and maximum daily dose 40mg) or quetiapine 25-50mg by mouth every 12hrs (maximum dose 200mg every 12hrs) besides ensuring maximization of pain management strategies and minimization of benzodiazepine use among the ICU delirium patients.

Subsequently, the day-to-day lunar phases (from new moon to first quarter to full moon to third quarter) for these time periods were accessed from the freely available public domain web-address http://www.timeanddate.com/calendar/moonphases.html. Thereafter, the daily prevalence of ICU delirium was adjudged by recording the daily percentage of ICU patients who had received haloperidol or quetiapine. Subsequently, the data was analyzed for whether the incidents of haloperidol or quetiapine administrations followed any medication consumption trends corresponding to the lunar phase cycles (any time-sensitive-trends across the 29-plus days of a standard lunar cycle as described in Table 1). Additionally, the data was compared for patients’ age and sex, and their actual haloperidol/quetiapine usage. For uniformity during comparisons, all anti-psychotic usage was equated to per mg oral haloperidol equivalents as per the below-mentioned explanations for bio-equivalence.

Using a multiplication factor of 1.6, intravenous haloperidol dose was converted to oral haloperidol equivalent as per the recommendations of the freely available public domain web-address http://www.globalph.com/haloperidol_dilution.htm. Similarly, although Woods (2003) advised using a conversion of 75mg quetiapine as equivalent to 2mg oral haloperidol, Andreasen et al (2010) described the changing arena of patients’ requirements for very
high doses of quetiapine for efficacy and hence calculated and recommended the changed equivalent doses as 151.97mg quetiapine equivalent to 2 mg oral haloperidol. Therefore, for our retrospective study, we followed the latest 2010 recommendations and used 76 mg quetiapine per mg oral haloperidol equivalent for study results analysis.

For statistical analysis, ANOVA (Analysis of Variance) tests (Repeated measures 2 way ANOVA treatment) were used to compare the continuous data. Fisher exact test and Chi square analysis were used to compare categorical data. For post-hoc analyses, the Student Newman-Keuls test was used. P-values <0.05 were considered statistically significant.

Results

As described in the CONSORT Diagram (Figure 1), a total of 5382 pharmacy records of haloperidol equivalent administrations were analyzed for this study (4734 administrations during 2008-2012 period and 648 administrations during 8-month period in 2013). The time-trends analysis for these administrations were tabulated based on a minimally modified popular nomenclature of lunar phases (Table 1) where the focus was comparisons between new moon period vs. full moon period; and inter-phase comparisons among the four lunar phases. As shown in Table 2, although there were variations for ICU delirium incidence among lunar cycles with the widest values ranging from one-in-four ICU patients to one-in-nine ICU patients receiving haloperidol equivalents (P <0.001), most commonly every 5th or 6th ICU patient based on daily ICU census was receiving haloperidol equivalent during 2008-2013 combined period irrespective of lunar cycle phase. However, the cumulative prevalence of incidents of haloperidol equivalent administrations (Table 2; Figure 2) were significantly different in both study periods (2008-2012 and 8-month 2013) wherein the incidents of haloperidol equivalent administrations peaked around the full moon period and troughed around the new moon period. There was a significant difference between the incidents of haloperidol equivalent administrations based on the patients’ sex (Table 3; Figure 3) wherein as compared to male patients, female patients followed much more uniform...
trends of haloperidol equivalent administrations’ incidents which peaked around the full moon period and troughed around the new moon period during both study periods (2008-2012 and 8-month 2013). On further analysis of the actual administered haloperidol mg equivalent doses, the statistical significance for differences in the administered doses across lunar cycle phases were only observed when the patient-doses were compared across the combined 2008-2013 period (Table 4: section B); and even though there was a statistical significance, the average clinical doses were 0.6-0.7 haloperidol mg equivalent per daily

ICU census across all the lunar cycle phases (Table 4: section B). Further sub-analysis of 70-lunar cycles across the various solar months of the total 68-month study period (Figure 4) revealed that haloperidol equivalent administrations’ incidents peaked around the full moon periods during the months of November-December and around the new moon periods during the month of July; however, interestingly, the actual administered haloperidol mg equivalent average doses were highest around the new moon periods during the months of November-December.

<table>
<thead>
<tr>
<th>LUNAR PERIOD</th>
<th>Percentage Incidence of Haloperidol Equivalent Administration per Daily Census</th>
<th>Incidence of Haloperidol Equivalent Administration per Daily Census On Average</th>
<th>P Value (F-Test)</th>
<th>Cumulative Prevalence of Incidents of Haloperidol Equivalent Administrations</th>
<th>P Value (F-Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMBINED 2008-2013</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Moon Period</td>
<td>16.7% ±16.6%</td>
<td>1-in-6 Patients</td>
<td>0.88</td>
<td>n=337</td>
<td>0.006</td>
</tr>
<tr>
<td>Full Moon Period</td>
<td>16.9% ±14.7%</td>
<td>1-in-6 Patients</td>
<td></td>
<td>n=412</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 1</td>
<td>18.3% ±18.3%</td>
<td>1-in-5 Patients</td>
<td>0.18</td>
<td>n=1194</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Lunar Phase 2</td>
<td>17.6% ±16.2%</td>
<td>1-in-6 Patients</td>
<td></td>
<td>n=1453</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 3</td>
<td>17.5% ±14.5%</td>
<td>1-in-6 Patients</td>
<td></td>
<td>n=1427</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 4</td>
<td>18.7% ±19.2%</td>
<td>1-in-5 Patients</td>
<td></td>
<td>n=1308</td>
<td></td>
</tr>
<tr>
<td>2008-2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Moon Period</td>
<td>16.1% ±15.0%</td>
<td>1-in-6 Patients</td>
<td>&lt;0.001</td>
<td>n=309</td>
<td>0.03</td>
</tr>
<tr>
<td>Full Moon Period</td>
<td>17.8% ±15.4%</td>
<td>1-in-6 Patients</td>
<td></td>
<td>n=361</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Moon Period</td>
<td>23.8% ±28.3%</td>
<td>1-in-4 Patients</td>
<td></td>
<td>n=28</td>
<td>0.008</td>
</tr>
<tr>
<td>Full Moon Period</td>
<td>10.7% ±5.2%</td>
<td>1-in-9 Patients</td>
<td></td>
<td>n=51</td>
<td></td>
</tr>
<tr>
<td>2008-2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 1</td>
<td>18.8% ±18.6%</td>
<td>1-in-5 Patients</td>
<td>0.16</td>
<td>n=1051</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Lunar Phase 2</td>
<td>18.3% ±17.1%</td>
<td>1-in-5 Patients</td>
<td></td>
<td>n=1269</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 3</td>
<td>17.9% ±15.0%</td>
<td>1-in-6 Patients</td>
<td></td>
<td>n=1248</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 4</td>
<td>19.6% ±20.0%</td>
<td>1-in-5 Patients</td>
<td></td>
<td>n=1166</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 1</td>
<td>14.1% ±15.1%</td>
<td>1-in-7 Patients</td>
<td></td>
<td>n=143</td>
<td>0.02*</td>
</tr>
<tr>
<td>Lunar Phase 2</td>
<td>12.9% ±6.1%</td>
<td>1-in-8 Patients</td>
<td></td>
<td>n=184</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 3</td>
<td>14.6% ±9.1%</td>
<td>1-in-7 Patients</td>
<td></td>
<td>n=179</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 4</td>
<td>11.8% ±6.5%</td>
<td>1-in-8 Patients</td>
<td></td>
<td>n=142</td>
<td></td>
</tr>
</tbody>
</table>

*All pair-wise post-hoc comparisons are significantly different (P<0.05) when compared to their expected frequencies
Discussion

To summarize the key points of the study results: (a) ICU delirium events, as adjudged by haloperidol equivalent administrations’ incidents, occurred on an average in approximately 20% of ICU patients daily at our hospital during 2008-2013; (b) ICU delirium events peaked around full moon; (c) ICU delirium events trended similarly across the lunar cycles during pre-standardized protocol time period (2008-2012) as well as during post-standardized protocol time period (2013); (d) as compared to male patients, ICU delirium events in female patients more uniformly followed lunar cycle trends; (e) after removing patients’ age as confounding factor, haloperidol mg equivalent doses’ trends were statistically different (though differences were clinically inconspicuous) in relation to lunar cycle phases; and (f) ICU delirium events happening in relation to lunar cycle phases were more common in the solar months of July, November and December which are interestingly the major holiday months (a potential confounding factor) in the United States besides July being first month-in-training for new resident/fellow ICU physicians and November-December being severe winter weather months in our Metropolitan city.

The moon and its effects on animal and human
### Table 3

Demographics of Patients who received Haloperidol Equivalent Administrations

<table>
<thead>
<tr>
<th>LUNAR PERIOD</th>
<th>Age (Mean ±SD) (in years)</th>
<th>P Value (F-Test)</th>
<th>Cumulative Prevalence of Incidents of Haloperidol Equivalent Administrations</th>
<th>Gender Distribution of Incidents of Haloperidol Equivalent Administrations</th>
<th>P Value (F-Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMBINED 2008-2013</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Moon Period</td>
<td>57.8 ±13.5</td>
<td>0.2</td>
<td>n=337</td>
<td>Females 39% Males 61%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Full Moon Period</td>
<td>59.1 ±14.2</td>
<td></td>
<td>n=412</td>
<td>Females 54% Males 46%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 1</td>
<td>58.3 ±13.7</td>
<td>0.15</td>
<td>n=1194</td>
<td>Females 43% Males 57%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lunar Phase 2</td>
<td>57.6 ±15.2</td>
<td></td>
<td>n=1453</td>
<td>Females 50% Males 50%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 3</td>
<td>57.5 ±13.7</td>
<td></td>
<td>n=1427</td>
<td>Females 51% Males 49%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 4</td>
<td>58.5 ±13.8</td>
<td></td>
<td>n=1308</td>
<td>Females 45% Males 55%</td>
<td></td>
</tr>
<tr>
<td><strong>2008-2012</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Moon Period</td>
<td>57.2 ±13.5</td>
<td>0.09</td>
<td>n=309</td>
<td>Females 39% Males 61%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Full Moon Period</td>
<td>59.0 ±14.0</td>
<td></td>
<td>n=361</td>
<td>Females 53% Males 47%</td>
<td></td>
</tr>
<tr>
<td><strong>2013</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Moon Period</td>
<td>65.0 ±11.6</td>
<td>0.16</td>
<td>n=28</td>
<td>Females 50% Males 50%</td>
<td>0.34</td>
</tr>
<tr>
<td>Full Moon Period</td>
<td>60.1 ±16.0</td>
<td></td>
<td>n=51</td>
<td>Females 63% Males 37%</td>
<td></td>
</tr>
<tr>
<td><strong>2008-2012</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 1</td>
<td>57.9 ±13.6</td>
<td>0.09</td>
<td>n=1051</td>
<td>Females 41% Males 59%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lunar Phase 2</td>
<td>56.9 ±15.3</td>
<td></td>
<td>n=1269</td>
<td>Females 48% Males 52%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 3</td>
<td>57.4 ±13.9</td>
<td></td>
<td>n=1248</td>
<td>Females 49% Males 51%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 4</td>
<td>58.2 ±14.1</td>
<td></td>
<td>n=1166</td>
<td>Females 45% Males 55%</td>
<td></td>
</tr>
<tr>
<td><strong>2013</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 1</td>
<td>61.3 ±14.5</td>
<td>0.009</td>
<td>n=143</td>
<td>Females 57% Males 43%</td>
<td>0.03</td>
</tr>
<tr>
<td>Lunar Phase 2</td>
<td>62.9 ±13.5</td>
<td></td>
<td>n=184</td>
<td>Females 60% Males 40%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 3</td>
<td>58.4 ±12.6</td>
<td></td>
<td>n=179</td>
<td>Females 63% Males 37%</td>
<td></td>
</tr>
<tr>
<td>Lunar Phase 4</td>
<td>61.2 ±10.5</td>
<td></td>
<td>n=142</td>
<td>Females 47% Males 53%</td>
<td></td>
</tr>
</tbody>
</table>
Table 4

*Haloperidol mg Equivalent-Strength Administration Dose Per Daily Intensive Care Unit Census*

<table>
<thead>
<tr>
<th>Lunar Period</th>
<th>Characteristic that Acted as Confounding Factor/Covariate</th>
<th>P Value (F-Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study Period 2008-2012</strong></td>
<td><strong>Number of Administrations (n)</strong></td>
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Fig. 2
Graphical Presentation of Haloperidol Equivalent Administrations’ Incidents across the Whole Study Period: New Moon vs. Full Moon AND Lunar Phases 1-4 (Comparative P-Values reported in Table 2)

Fig. 3
Graphical Presentation of Haloperidol Equivalent Administrations’ Incidents’ Distribution per Patients’ Sex/Gender: New Moon vs. Full Moon AND Lunar Phases 1-4 (Comparative P-Values reported in Table 3)
behavior have fascinated mankind since ancient times. Similarly, the medical profession has not been naive or immune to these discussions. Thakur and Sharma (1984) observed that crime rates in three different cities in India during 1978-1982 increased threefold from new moon period to full moon period; and the authors explained this effect secondary to “human tidal waves” in human physiology as similar to gravitational effects of moon on the oceans. However, Laverty and Kelly (1998) reviewed a nine-year period with almost 300,000 accidents and observed periodic changes secondary to calendar changes and season changes but no relationship was apparent in relation to lunar cycle phases including full moon period.

Barr (2000) revisited the historical aspect of term “lunacy” wherein during pre-modern times, mentally ill patients were supposedly displaying behavior changes in accordance to the changes in moon (“lunar”) phases. Among 100 patients who were followed for two-and-half years, Barr observed significant changes during full moon period in the schizophrenic patients as compared to the non-schizophrenic patients; and concluded that further investigations were required to validate the findings. Zimecki (2006) further expanded these discussion by reviewing the lunar phase effects on the animal kingdom in regards to phylogenesis, fishes’ fertility cycles, hormonal level changes in birds, sensory system of rats, and human reproduction. Zimecki tried to explain lunar effects on animal physiology as due to possible induction of changes in electromagnetic milieu around animals due to the periodic changes in the moon. Around same time, Polychronopoulos et al (2006) reported neurology emergency department experience over five year-period that as compared to 21.4% epileptic seizures that occurred during new moon period, 34.2% epileptic seizures occurred during full moon period.

Recently, Voracek et al (2008) reviewed over 65,000 suicides in Austria from 1970-2006. They
did not find any significant difference in completed suicides’ incidence between new moon period vs. full moon period, and the completed suicides’ incidence was equally divided among the four lunar phases. Voracek et al (2008) suggested that as compared to their almost four-decade long study period, other researchers’ short duration study periods can be the reason for other studies reporting lunar effects on human behavior events because they themselves also observed new moon as well as full moon sporadically affecting completed suicide rates during a few individual years among their cumulative 37-year long study period. Similarly, Schuld et al (2011) questioned the idea of patients scheduling their elective major surgeries in accordance to avoid lunar phases like full moon period because their analysis of emergency surgeries’ ten-year data revealed absence of statistical significance in regards to any differences in peri-operative blood loss and complications when measured in concurrence to lunar phases.

The limitations of our study are that (a) it is a retrospective analysis, (b) it measured primarily the action (rescue anti-psychotics use) and assumed the corresponding cause (ICU delirium), (c) it puts forth only our observations but does not provide evidence for the interpretation how (if any) lunar phases affect ICU delirium, and (d) it does not differentiate the effects of lunar phases (if any) on the ICU delirium patients vs. their medical care providers who had diagnosed ICU delirium and decided to administer haloperidol equivalents.

**Conclusion**

In summary, consumption trends of rescue anti-psychotics for ICU delirium revealed an influence by lunar phase cycles particularly that of full moon periods on female patients in the ICU.

**Acknowledgement**

The authors are deeply indebted to the appreciative efforts of Ms. Connie Tourangeau, Pharmacist, and Mr. Xavier Bell, Field Engineer, Department of Pharmacy, Harper Hospital, Detroit Medical Center, Detroit, Michigan, United States in regards to their retrospective enlisting of the ICU patients according to the medications that they had received per their databases. The authors are also grateful to Ms Sapna Parmar, Information Systems Division Application Staff, for her help in enlisting daily ICU patients’ census data for our retrospective study period.
References

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THE USE OF PARAVERTEBRAL BLOCKADE FOR ANALGESIA AFTER ANTERIOR-APPROACH TOTAL HIP ARTHROPLASTY.

ALBERTO E. ARDON* MD MPH, ROY A. GREENGRADE MD, UPASNA BHURIA† MBBS, STEVEN B. PORTER* MD, CHRISTOPHER B. ROBARDS* MD AND KURT BLASER** MD

Abstract

Background: Anterior approaches for total hip arthroplasty (ATHA) are becoming increasingly popular. We postulated that the use of PVB of the T12, L1, and L2 roots would provide adequate analgesia for ATHA while allowing motor sparing.

Methods: The medical records of 20 patients undergoing primary ATHA were reviewed. T12, L1 and L2 paravertebral blockade was accomplished with 3-4ml of 1% ropivacaine with epinephrine 1:200,000 and 0.5mg/ml of preservative-free dexamethasone per level. Primary outcomes were mean opioid consumption in intravenous morphine equivalents and worst recorded visual analog scale (VAS) pain scores during postoperative days 0 to 2 (POD 0 to 2).

Results: Mean opioid consumption was 8.4mg on POD0, 16.6mg on POD1, and 9.8mg on POD2. Median worst VAS scores were 2 for all time intervals except POD 0, which had a median value of 0. All patients had full hip motor strength the evening of POD0. 19 patients were able to ambulate the afternoon of POD1.

Conclusion: T12-L2 PVB, when utilized as part of a multimodal analgesic regimen, results in moderate opioid consumption, low VAS scores, preservation of hip motor function, and may be an effective regional anesthesia technique for ATHA.

Keywords: Paravertebral blockade, anterior total hip arthroplasty, multimodal analgesia, opioid consumption.

Introduction

Anterior approaches for total hip arthroplasty are becoming increasingly popular due to advantages of less muscle trauma, resulting in enhanced convalescence.
Unfortunately, similar to posterior approaches, anterior total hip arthroplasty (ATHA) is associated with significant pain requiring moderate to large doses of opioids with attendant side effects. Multimodal analgesia including regional analgesic techniques such as posterior lumbar plexus block (psoas compartment block) have been utilized to treat the pain of total hip arthroplasty with encouraging results. However, the motor weakness associated with psoas compartment block may limit ambulation and decrease effective physiotherapy, possibly increasing the risk of falls. It is felt by many surgeons that motor sparing analgesic techniques would be of benefit to patients.

While opioids are commonly used for postoperative analgesia in hip arthroplasty patients, the use of these medications is associated with a significant negative side effect profile that includes nausea and vomiting, respiratory depression, prolonged recovery room stay, increased healthcare burden, and decreased patient satisfaction. Consequently, the use of a regional anesthetic technique as a part of a multimodal analgesic plan aimed at reducing postoperative opioid consumption would be advantageous.

The paravertebral block (PVB) is a block of the mixed nerve soon after it exits the intervertebral foramen. It provides intense unilateral analgesia of long duration and has become the primary anesthetic for many applications. We postulated that the use of PVB of the T12, L1 and L2 roots would provide adequate analgesia for ATHA while allowing motor sparing. In this study we present our initial expanded case series of 20 patients who received PVB for ATHA.

Methods

The Institutional Review Board (IRB) approved this study. From June 2013 to February 2014, the medical records of 20 patients undergoing primary ATHA were reviewed. No patient had preoperative motor deficit or opioid consumption requiring long-acting opioids.

After a preoperative interview, informed consent for both surgical anesthesia and peripheral nerve blockade was obtained by an anesthesiologist. All blocks were performed in the preoperative area in a sterile fashion after placement of American Society of Anesthesiologists standard monitors and verification of patient identity and laterality of the procedure. Sedation was at the discretion of the attending anesthesiologist, and included sedative doses of midazolam, fentanyl, ketamine, and/or propofol.

For PVB placement, patients were positioned in the sitting position. The T12, L1 and L2 spinous processes were identified in the sitting position either by counting from the L4 spinous process at the level of iliac crest and/or from the T7 spinous process at the level of lower border of the scapulae. Needle entry points were marked 2.5 cm lateral to the spinous process as described previously by Greengrass et al. After skin infiltration with 2% lidocaine with epinephrine 1:200,000 at the marked sites, a sterile 22 g, 10 cm Tuohy needle (B Braun, Melsungen, DE) was introduced perpendicular to the skin until the transverse process was contacted. The needle was then redirected in a caudad direction and advanced 1-1.5 cm. After negative aspiration, 3-4 ml of 1% ropivacaine with epinephrine 1:200,000 and 0.5mg/ml of preservative free dexamethasone were injected per level. Injections were repeated at the other two levels. Sensory deficit in the distribution of T12, L1 and L2 dermatomes were confirmed with ice testing prior to surgical anesthesia. Absence of motor blockade upon hip flexion, assessed with the modified Bromage scale, was also confirmed preoperatively. The modified Bromage scale is defined as follows: 1 = unable to move foot or knee; 2 = able to move foot only; 3 = just able to move knee; 4 = full flexion of knee; 5 = no detectable weakness of hip flexion while supine. One patient required an additional injection at all levels to establish appropriate sensory deficit.

Surgical anesthesia was achieved with an intrathecal injection of 12.5 to 13mg of preservative-free isobaric 0.5% bupivacaine. The same surgeon performed all surgeries utilizing a modified Smith-Peterson anterior approach. No patients had intraoperative complications. At the discretion of the surgeon, patients received an intra-articular injection consisting of morphine 10mg, ketorolac 30mg, and epinephrine 200mcg. Daily opioid and non-opioid analgesic consumption, visual analog scale (VAS) pain scores, and length-of-stay data were extracted from the electronic medical record.
Postoperatively, patients received scheduled intravenous acetaminophen every 6 hours for the first 24 hours, and thereafter on an as-needed basis. All patients received oral celecoxib 200mg twice daily.

**Primary Outcomes**

Mean opioid consumption in intravenous morphine equivalents during the time intervals of postoperative day 0 (POD 0, defined as the period of time from surgical incision until 07:00 on postoperative day 1), postoperative day 1 (POD 1, defined as 07:00 until 07:00 on POD2), and postoperative day 2 (POD 2, defined as .07:00 on POD2 until 18:00

Worst recorded visual analog scale (VAS) pain scores, rated from 0 - 10, during time intervals from POD 0 .to 2

**Secondary Outcomes**

Secondary outcomes included maximum opioid consumption, non-opioid analgesic consumption, ability to ambulate, and distance ambulated.

**Results**

Patient characteristics are shown in Table 1. A total of 20 patients were included, all of whom received a spinal anesthetic. Mean operative time was 78 minutes. Three patients had documented preoperative opioid consumption with short-acting agents. However, none of these patients consumed more than 30mg of oral morphine equivalents per day. The remaining patients denied use of preoperative opioids. No patients developed complications from the paravertebral blocks while hospitalized. No falls

---

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Table 3
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<td>3</td>
</tr>
<tr>
<td>18</td>
<td>0</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>19</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>n/a</td>
<td></td>
</tr>
</tbody>
</table>

n/a: not recorded secondary to lack of record or patient discharge
occurred during hospitalization. Six patients were discharged on POD 2.

Opioid consumption in IV morphine equivalents by patient is shown in Table 2. Mean opioid consumption was 8.4mg on POD0, 16.6mg on POD1, and 9.8mg on POD2. Median opioid consumption was 9.5mg, 15mg, and 9.5mg for POD0, POD1, and POD2, respectively. Maximum opioid consumption was 21.7mg on POD0, 42.3mg on POD1, and 30mg on POD2. The three patients with documented preoperative opioid use had postoperative opioid consumption greater than the median on POD 0, 1 and 2.

Worst VAS scores recorded for each patient are shown in Table 3; values ranged from 0 to 8. Median worst VAS scores, shown in Table 4, were 2 for all time intervals except POD0, which had a median value of 0.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Median worst visual analog pain scores (minimum, maximum)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD0 to 19:00</td>
<td>0 (0,6)</td>
</tr>
<tr>
<td>POD 0-1 overnight</td>
<td>2 (0,8)</td>
</tr>
<tr>
<td>POD1 AM</td>
<td>2 (0,6)</td>
</tr>
<tr>
<td>POD1 PM</td>
<td>2 (0,4)</td>
</tr>
<tr>
<td>POD 1-2 overnight</td>
<td>2 (0,7)</td>
</tr>
<tr>
<td>POD2 AM</td>
<td>2 (0,5)</td>
</tr>
<tr>
<td>POD2 PM</td>
<td>2 (0,4)</td>
</tr>
</tbody>
</table>

Regarding non-opioid analgesics, median acetaminophen and celecoxib doses are shown in Table 5. Median acetaminophen dose was highest on POD 0 (4000mg), while median celecoxib dose was higher on POD1 and POD2 (400mg).

<table>
<thead>
<tr>
<th>Table 5</th>
<th>Median acetaminophen and celecoxib consumption among patients (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen Consumption</td>
<td></td>
</tr>
<tr>
<td>POD 0</td>
<td>4000</td>
</tr>
<tr>
<td>POD 1</td>
<td>2650</td>
</tr>
<tr>
<td>POD 2</td>
<td>1000</td>
</tr>
<tr>
<td>Celecoxib Consumption</td>
<td></td>
</tr>
<tr>
<td>POD 0</td>
<td>200</td>
</tr>
<tr>
<td>POD 1</td>
<td>400</td>
</tr>
<tr>
<td>POD 2</td>
<td>400</td>
</tr>
</tbody>
</table>

All patients had modified Bromage scores of 5 the evening of POD 0; 2 patients were able to ambulate at that time. On the morning of POD 1, 15 patients were able to ambulate, while 19 were able to do so by that afternoon (Table 6). Median distances ambulated on the morning and afternoon of POD1 were 30 feet and 80 feet, respectively.

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Ambulation among study patients, with distance ambulated in feet [median (range)]</th>
</tr>
</thead>
<tbody>
<tr>
<td># of patients ambulated POD0</td>
<td>2</td>
</tr>
<tr>
<td># of patients ambulated POD1 AM</td>
<td>15</td>
</tr>
<tr>
<td># of patients ambulated POD1 PM</td>
<td>19</td>
</tr>
<tr>
<td>Distance ambulated POD1 AM</td>
<td>30 (1, 500)</td>
</tr>
<tr>
<td>Distance ambulated POD1 PM</td>
<td>80 (5, 980)</td>
</tr>
</tbody>
</table>

Discussion

Although the concept of the paravertebral block (PVB) originated in the early 20th century, its popularity has waxed and waned. Recently, a renewed interest in the technique has developed, as it has been found to be an effective analgesic technique that minimizes hemodynamic compromise. The injection of local anesthetic in the paravertebral space blocks conduction in the dorsal and ventral rami of the exiting spinal nerve root. Paravertebral blockade also inhibits conduction through the sympathetic chain, resulting in only a unilateral sympathectomy. At the levels of thoracic vertebrae, the paravertebral space is a wedge shaped space defined anterolaterally by the parietal pleura, posteriorly by the superior costotransverse ligament, and medially by the vertebral, vertebral disk, and intervertebral foramina. The superior and inferior borders are provided by the heads of the ribs. In the lumbar vertebrae, the inter-transverse ligament provides the posterior border of the paravertebral space. As explained by Greengrass et al, the paravertebral space provides an area where exiting spinal nerves are not tightly enveloped by fascia, possibly facilitating nerve blockade.

Paravertebral blockade is commonly used for breast surgery, video-assisted thoracic surgery, minimally invasive cardiac surgery, herniorrhaphy, and hand-assisted laparoscopic nephrectomy. To our
knowledge, use of this analgesic technique in anterior-approach hip arthroplasty has not been described in the literature. While the use of PVB was reported by Bogoch and colleagues in 2002 for postoperative analgesia following total hip and knee arthroplasty, the technique described suggests a psoas compartment blockade, not a true paravertebral block, as the initial needle approach was made 4cm lateral to the spinous process rather than 2.5cm. Lee et al reported excellent analgesia in two patients who patients received L1/L2 paravertebral blocks along with local anesthetic infiltration of the joint for hip arthroscopy. Wardhan and colleagues described continuous L2 paravertebral blockade to be slightly inferior to a lumbar plexus catheter when comparing opioid consumption in posterior approach total hip arthroplasty patients, with no motor strength advantage. However, patients in that study received 15ml of local anesthetic during placement of the paravertebral catheter. Injection of a large amount of local anesthetic in the paravertebral space may result in epidural and/or unpredictable spread. In one radiographic study, 25% of patients who received 20ml injectate at a single paravertebral level had epidural spread evident on MRI. Observed weakness in PVB patients after a large volume injection could be secondary to neuraxial or extensive paravertebral spread of local anesthetics. In our current study, we have limited the injectate to a maximum of 4ml per level, which we believe minimizes the risk of these complications. In our case series, no patient had a modified Bromage score less than 5 the evening of POD 0. Additionally, no patient was noted by physical therapy as having significant ipsilateral lower extremity weakness that prevented full participation in physical activity.

Studies addressing opioid consumption among patients who undergo anterior approach total hip arthroplasty are limited. In a prospective study by Barrett et al, ATHA patients consumed a mean of 32.2mg, 50.7mg, and 33.7mg IV morphine equivalents on POD 0, 1 and 2, respectively. Another study by Restrepo describes POD0, POD1, and POD2 mean intravenous morphine consumption as 11.2mg, 13.9mg, and 6.82mg, respectively. However, patients in this study received intrathecal morphine as part of their analgesic plan, thus our results are not directly comparable. Additionally, the risk of postoperative respiratory depression after an intrathecal opioid injection is unnecessary when non-opioid modalities are available. Bogoch et al’s study which used a single-injection lumbar plexus block showed an opioid consumption of 18.7mg of morphine equivalents in the first 8 hours after surgery, which is significantly higher than our results. Some studies contend that there is little difference in opioid consumption or pain scores when comparing an anterior approach hip arthroplasty to a classic posterior approach. Rodriguez et al found no difference in either metric when comparing the two surgical methods. Even with a lumbar plexus catheter in place, opioid consumption may be high in the classic posterior approach. For example, Wilson et al documented a mean opioid consumption of 54.67mg of IV morphine equivalents in the first 24 hours after THA, even with a properly functioning lumbar plexus catheter. If indeed little difference in opioid consumption exists between the two surgical techniques, our results suggest that multimodal analgesia including a PVB at T12-L2 may decrease opioid consumption significantly in ATHA patients.

During the time intervals studied, all median VAS scores were 2 or less. Reports of perioperative VAS scores for the ATHA patient population are limited. One study described mean POD 0, 1, and 2 VAS scores to be (4.2 ± 1.4), (4.0 ± 1.0) and (3.8 ± 1.1), respectively. The low median VAS scores in our study, combined with moderate opioid consumption, are thus encouraging.

The potential efficacy of paravertebral blockade in this study may be explained on anatomic grounds. First, the cutaneous analgesia provided by paravertebral blocks at T12, L1 and L2 is suited for coverage of the surgical incision. Second, as described by Wetheim in 1952, the peripheral nerve innervation of the hip joint is provided by the obturator nerve, femoral nerve, and branches of the sacral plexus. The spinal nerves at the levels of T12, L1 and L2 provide sensory fibers to the iliohypogastric, ilioinguinal, genitofemoral, lateral femoral cutaneous, femoral and obturator nerves. Thus, a significant proportion of the sensory fibers to the hip joint are affected by T12-L2 paravertebral blockade. Lastly, the bony innervation of the hip joint may indeed be affected by this paravertebral approach. Although osteotominal anatomy of the hip...
joint is much less well defined, Brown and colleagues
describe L2 as providing innervation to the medial
midshaft femur, iliac crest, and anterior superior iliac
spine; L3 provides innervation to the femoral neck and
acetabulum. In our study we did not conduct an L3
block so as to decrease the total anesthetic dose and
minimize the risk of motor block. Based on our results,
separate blockade of L3 may indeed not be required for
adequate analgesia after ATHA. Femoral nerve fibers
arise from L2, L3, and L4 nerve roots. Blockade with
moderate volume only at L2, while giving sensory
block in that dermatomal distribution and having
limited caudal spread, may allow full motor function
of the femoral nerve. We recognize, however, that until
further studies delineating osteotomal hip innervation
are conducted, the exact contribution of PVB analgesia
to the hip joint may not be well defined.

The patients in this case series received both
acetaminophen and celecoxib as part of a multimodal
approach to postoperative analgesia. Acetaminophen
use was highest on POD0-1, which may have contributed
to the low opioid consumption and very
low median worst VAS of zero. Likewise, twice-daily
celecoxib administration may also have contributed
to decreasing the total opioid consumption among
these patients. While the exact contribution of
acetaminophen and celecoxib in reducing opioid
requirements in these anterior hip arthroplasty patients
is not known, previous studies in total knee and
posterior-lateral approach hip arthroplasty suggest that
multimodal analgesia reduces opioid burden. The
low overall pain scores and opioid consumption in this
case series certainly suggest that the use of multimodal
analgesia may contribute to the analgesic efficacy of
paravertebral blockade.

All but two of the study patients were able to
participate in physical therapy to some degree by the
evening of their surgical day. The two patients who
did not were limited by a late discharge from the
recovery room, as they were both mid-afternoon cases.
By the morning of POD1, 15 of the 20 patients were
able to ambulate. Median distance ambulated during
the morning physical therapy session was 30 feet. By
the afternoon of postoperative day 1, 19 patients were
ambulating, with a median distance of 80 feet. These
results, when considered in the context of low median

VAS scores on POD1, suggest that paravertebral
blockade may provide significant analgesia to facilitate
ambulation during the first 24 hours after surgery.

As mentioned previously, 13 patients received
intraarticular morphine, ketorolac and epinephrine.
The evidence supporting the use of these medications
within the articular space without local anesthetic,
however, is not robust. While some studies do suggest
that the use of intraarticular local anesthetic may
enhance postoperative analgesia, the analgesic
properties of intra-articular morphine or epinephrine
without local anesthetic are yet to be supported
by data. To our knowledge, there are no studies
regarding the analgesic properties of sole epinephrine
when injected into an articulation. Regarding opioids,
one murine-model study suggests that subcutaneous
administration of morphine may have some analgesic
properties at the site of injection, but these effects
have not been validated in the intra-articular space
in humans. Another study in patients undergoing
knee surgery showed no difference in postoperative
opioid consumption when morphine is added to intra-
articular bupivacaine in the presence of a femoral
nerve block. The efficacy of ketorolac when injected
into a joint without local anesthetic has also not been
studied extensively. One small study by Vintar et
al studied the impact of 10mg ketorolac on an on-
demand intraarticular bolus of 25mg ropivacaine
and 2mg morphine available every 60 minutes.
Patients who received intraarticular ketorolac had
decreased opioid use 24 hours postoperatively.
However, another study showed that patients who
only received intraarticular ketorolac had higher
pain scores and shorter time to first analgesic request
compared to patients who only received intraarticular
bupivacaine. In our study, when patients who did
not receive this intra-articular injection are analyzed
separately, mean and median opioid consumption are
similar to those of the overall cohort (Table 7). Thus,
given these results and the paucity of evidence for
the efficacy of this intra-articular mixture, we do not
believe this modality affected our primary outcome.
However, as shown in Table 8, median worst VAS
scores did seem to be slightly higher in those patients.
Thus, we realize that the theoretical possibility of a combined analgesic effect cannot entirely be
discounted.
Table 7
Mean and median opioid consumption in mg IV morphine equivalents, patients who did not receive intra-articular injection

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD 0</td>
<td>8.96</td>
<td>10</td>
</tr>
<tr>
<td>POD 1</td>
<td>12.43</td>
<td>10</td>
</tr>
<tr>
<td>POD 2</td>
<td>7.04</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 8
Median visual analog pain scores (minimum, maximum), patients who did not receive intra-articular injection

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>POD0 to 19:00</td>
<td>0 (0,5)</td>
</tr>
<tr>
<td>POD 0-1 overnight</td>
<td>5 (0,9)</td>
</tr>
<tr>
<td>POD1 AM</td>
<td>0 (0,3)</td>
</tr>
<tr>
<td>POD1 PM</td>
<td>2 (0,6)</td>
</tr>
<tr>
<td>POD 1-2 overnight</td>
<td>4 (0,6)</td>
</tr>
<tr>
<td>POD2 AM</td>
<td>5 (0,8)</td>
</tr>
<tr>
<td>POD2 PM</td>
<td>6 (0,7)</td>
</tr>
</tbody>
</table>

The limitations in our case series include the retrospective nature of the study, the small number of patients, and the lack of randomization. Additionally, the VAS scores were recorded by ward nursing staff per regular protocol, without mention of activity status during the patient’s self-assessment of pain. However, since we have collected the worst recorded VAS rather than the entire range of pain scores, we hope to capture as many VAS scores associated with activity as possible. We also recognize that while appropriate sensory deficit was confirmed preoperatively, the duration of this sensory deficit was not documented. Thus, we can only speculate on the exact duration of the paravertebral block. Given the steady level of opioid requirements throughout postoperative day 2, though, we suspect that the analgesia associated with nerve blockade continued to some degree during this time period.

Conclusion

T12 through L2 paravertebral blockade, when utilized as part of a multimodal pain management plan, results in low VAS scores, preservation of hip motor function, moderate opioid consumption, and may be an effective analgesic modality for patients undergoing anterior approach total hip arthroplasty. The outcomes of our retrospective case series are encouraging. Prospective studies are warranted.
References


17. Wilson SH, Auboux AM, Elov JD, Merhan RB, Chelly JE: Ropivacaine 0.1% versus 0.2% for continuous lumbar plexus nerve block infusions following total hip arthroplasty: a randomized, double blind study. Pain Medicine; 2014, 15:465-472.


SUBTENON BUPIVACAINE INJECTION FOR POSTOPERATIVE
PAIN RELIEF FOLLOWING PEDIATRIC STRABISMUS SURGERY:
A RANDOMIZED CONTROLLED DOUBLE BLIND TRIAL

RADWA H BAKR** AND HESHAM M ABDELAZIZ*

Abstract

**Background:** Strabismus surgery in children is often associated with undesirable intraoperative and postoperative side effects including pain, postoperative nausea and vomiting (PONV), and oculocardiac reflex (OCR). Systemic analgesics have side effects and are contraindicated in some cases. We hypothesized that the preoperative subtenon injection of bupivacaine would reduce postoperative pain and the incidence of side effects adverse effects.

**Methods:** Sixty children (2 to 6 years of age, ASA status I to II) were randomized to receive either subtenon bupivacaine 0.5% or a saline injection before the beginning of surgery in a double-blind manner. Pain scores using the Face, Legs, Cry, Activity, and Consolability (FLACC) scale, incidence of OCR and PONV, requirement of additional systemic analgesia, and time to discharge from the recovery room were compared.

**Results:** The pain scores were significantly lower in the subtenon bupivacaine group at 0 min \( (p = 0.0056) \) and at 30 min \( (p = 0.013) \). There was no significant difference between the two groups at the other time intervals. There was a significant reduction in the incidence of oculocardiac reflex and the incidence of vomiting in the subtenon bupivacaine group. Eight of the 27 patients in the subtenon bupivacaine group required additional systemic analgesia compared to 19 of 29 controls. The time to discharge from recovery room was lower in the subtenon bupivacaine group.

**Conclusion:** These data provide some evidence that a preoperative subtenon block with bupivacaine combined with general anesthesia allows efficient control of postoperative pain as well as a reduction in the incidence of OCR and PONV in young children undergoing strabismus surgery.

**Keywords:** Bupivacaine, Pain, Pediatrics, Strabismus surgery, Subtenon anesthesia.

Introduction

Following strabismus surgery children often experience severe discomfort and are unable to open the operated eye. The surgical manipulation of the medial rectus muscle causes severe bradycardia because of the oculocardiac reflex. The postoperative period is marked by frequent obvious discomfort, caused by a high frequency of postoperative nausea and vomiting and pain. Pain after strabismus correction is thought to be in the conjunctival area, but Tenon’s capsule, sclera, and stretched muscles may also contribute to its intensity. This pain represents a source of distress to the child and the parents. Different modalities of treatment have been proposed and found to be variably effective. Opioids are helpful but carry the risk of nausea, vomiting, and drowsiness.

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Non-steroidal anti-inflammatory drugs (NSAIDs) remain controversial in small children. The side effects of these agents are particularly undesirable in the ambulatory surgery setting or are contraindicated in many children. Regional anesthesia has been proposed for management of postoperative pain following strabismus surgery. Topical amethocaine 1% drops and subconjunctival infiltration with bupivacaine 0.5% administered at the conclusion of strabismus surgery have been shown to be effective in reducing postoperative pain\textsuperscript{2,3,4}. Retrobulbar and peribulbar block have been explored in children with varying degrees of success\textsuperscript{5}. Among the different techniques, the subtenon eye block is widely used for anterior and posterior segment surgery in adults. A small quantity of local anesthetic is injected in the subtenon space by use of a smooth cannula after surgical incision of the conjunctiva. This technique ensures adequate postoperative analgesia in adults\textsuperscript{6,7} although it has not been sufficiently explored when used before the start of surgery in children.

We performed a prospective, randomized, double-blind, controlled study to determine the efficacy of subtenon’s bupivacaine injection at reducing postoperative pain, the incidence of postoperative complications, and the requirements of postoperative analgesics in pediatric patients undergoing strabismus surgery.

Patients and Methods

Approval to perform the study was granted by the Institutional Review Board. Informed written consent was obtained from the parents prior to their children’s enrollment in the study. Sixty children aged 2-6 years of age with ASA status I to II scheduled for primary surgical correction of unilateral or bilateral strabismus were included in the study. Patients were randomly allocated to one of 2 equal groups. The inclusion criteria were: age 6 years or under, unilateral or bilateral surgery, primary surgery or reoperation, horizontal, vertical, or oblique muscle surgery. Exclusion criteria were: known drug sensitivity or body weight less than 8 kg.

A standard anesthetic protocol was used for all children included in the study. Midazolam (0.3 mg/kg) and atropine (10 μg/kg) were given rectally 30 minutes before anesthesia. EMLA (eutectic mixture of local anesthetics) cream was applied rectally 30 min before anesthesia over two potential venipuncture sites. Induction was by sevoflurane inhalation and maintenance was by spontaneous ventilation of sevoflurane in oxygen and nitrous oxide via laryngeal mask airway. Intraoperative analgesia was in the form of rectal paracetamol 20 mg/kg. Patients were monitored intraoperatively by electrocardiography, pulse oximetry, noninvasive blood pressure, and end-tidal CO\textsubscript{2} measurements. Heart rate and blood pressure were recorded before induction and every 5 minutes during anesthesia and surgery until the end of the procedure. After induction, bupivacaine 0.5% or a placebo saline solution were slowly injected in the subtenon space with a curved, blunt 25-mm 20 gauge cannula introduced through a small conjunctival and subtenon limbal aperture. The dose of bupivacaine was titrated according to the child’s body weight to ensure a subtoxic dose of less than 2.5 mg/kg. The efficacy of the block was judged satisfactory if the pupil was widely dilated and fixed, thus confirming ciliary ganglion blockade.

The anesthesiologist, surgeon, and nurses were blinded to the nature of the injected solution. All operations were performed by the same surgeon. Surgery was started 5 minutes after the subtenon injection. The surgical protocol was standardized; for surgery on the vertical rectus muscles the conjunctiva was opened over the insertion. The inferior oblique was approached via limbal peritomy if surgery on the lateral rectus was also being performed, or via a circumferential conjunctival incision 10 mm from the limbus if not. The conjunctiva was closed with 6-0 or smaller Vicryl\textsuperscript{®}. All patients received 1 drop of amethocaine 1% onto the operated eye at the conclusion of surgery. After emergence from anesthesia patients were transferred to the recovery ward. On arrival in the recovery room, the patient’s behavior was assessed by a nurse who was not aware of the nature of the solution injected in the subtenon space. The pain scale used for assessment was the Face, Legs, Activity, Cry, Consolability scale (FLACC)\textsuperscript{8} (Table 1). This behavioral pain assessment scale is widely accepted as a method of assessment for pain in children by direct observation. The scale consists of 5 categories. Each category is scored on a 0-2 scale, which results in a total score of 0-10. A score
Subtenon bupivacaine for pediatric strabismus surgery

Pain assessment was performed after the removal of the laryngeal mask, and then at 30 min intervals until discharge from the recovery ward. Children with a FLACC score equal to or higher than 4 were given 20 mg/kg rectal paracetamol. The following parameters were collected in the recovery room: pain scores, at 0 min, 30 min, 1 hr, 2 hrs, 3 hrs, incidence of occurrence of occulo-cardiac reflex (indicated by a sudden decrease of the heart rate higher than 20% and concomitant with muscular traction), incidence of postoperative nausea and vomiting, number of patients requiring additional systemic analgesia, and the mean time to first analgesia.

Statistical analysis was done using SPSS (version 14.0, SPSS Inc., Chicago, IL, USA). Continuous data, such as age, weight, anesthetic duration, time to discharge from the recovery ward and time to eye opening, were expressed as mean and SD and were analyzed using Student’s t-test. A chi-squared test was performed for the comparison between qualitative variables. A Mann-Whitney U test allowed intergroup comparison between quantitative variables. A P value < 0.05 was considered as significant. Results were expressed as mean ± SD. Confidence intervals of 95% are provided for statistically significant results.

Results

Fifty six children completed the study. One child in the control group and three in the treatment group were excluded after recruitment due to incomplete data. 46 (82.0%) underwent unilateral and 10 (18.0%) underwent bilateral surgery. 45 operations (81.1%) were primary procedures and 11 (18.9%) were reoperations. 27 children (48.6%) were randomized to the treatment group and 29 (51.4%) were randomized to the control group. The groups were similar with regards to age, weight, sex, proportions having bilateral surgery or reoperations, and number of muscles operated upon (Table 2).

The pain scores at each time interval are summarized in Table (3). The treatment group experienced significantly less pain than the control at the 0-h observation ($P = 0.005$) and at 30 min ($P = 0.013$). There was no significant difference between the two groups at the other time intervals. There was a significant reduction in the incidence of occurrence of occulocardiac reflex that required a temporary interruption of traction on the muscles and the injection of atropine in the study group (5 patients) compared to (11 patients) in the control group. The incidence of nausea was not significantly decreased in the study group (3 patients compared to 4 patients in each group)
the control group); however, the incidence of vomiting was significantly lower in the study group (6 patients) than the control group (10 patients) (Table 4). Eight of the 27 patients in the subtenons group required additional systemic analgesia (30%) compared to 19 of 29 controls (65%). This difference was borderline with regards to statistical significance ($P = 0.052$). The median time to first analgesia was 2hrs 45min in the control group compared to 1 hour in the study group (Table 5). The length of stay in the recovery room was reduced to a significant degree in the bupivacaine group; two hours after the removal of the LMA, 22 of 29 children recruited in the control group were still present in the recovery room in contrast to 4 of the 27 children in the study group.

Discussion

Strabismus surgery in children is frequently performed as an outpatient procedure. A large proportion of children experience clinically significant pain after strabismus surgery. Additionally, Pediatric strabismus surgery often leads to postoperative behavioral problems during the recovery period as a result of pain, visual disturbances, nausea and vomiting, and separation from parents. A study demonstrated that altered behavior was encountered on emergence in 44% of operated children, and that 20% of them exhibited complex symptoms simulating delirium.

Symptoms such as PONV and pain are the main cause of delayed discharge, contact with the hospital after discharge, and hospital readmission after outpatient surgery for these children.

Pain after strabismus surgery may be caused by sectioning and traction exerted on the extraocular muscles. Many strategies have been proposed for treatment of the pain experienced by these children. Topical analgesia using drops containing a NSAID was efficient in some studies, but not effective in others.

Table 3

<table>
<thead>
<tr>
<th></th>
<th>Subtenon Group (N = 27)</th>
<th>Control Group (N = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min</td>
<td>1.77 ± 1.12</td>
<td>3.41 ± 1.12</td>
<td>0.005</td>
</tr>
<tr>
<td>30 min</td>
<td>1.66 ± 1</td>
<td>3.17 ± 1.04</td>
<td>0.013</td>
</tr>
<tr>
<td>1 hr.</td>
<td>2.11 ± 0.89</td>
<td>2.14 ± 0.1</td>
<td>0.91</td>
</tr>
<tr>
<td>2 hrs.</td>
<td>2.55 ± 0.89</td>
<td>2.86 ± 1.41</td>
<td>0.57</td>
</tr>
<tr>
<td>3 hrs.</td>
<td>3.04 ± 1.4</td>
<td>2.72 ± 1.47</td>
<td>0.38</td>
</tr>
</tbody>
</table>
Opioid analgesia is frequently used to reduce postoperative pain after strabismus surgery; however, these drugs often cause nausea, vomiting, and drowsiness. A study showed that opioid analgesia is associated with more prolonged recovery times after anesthesia, a longer stay in hospital, and delayed return to normal activity when compared to other analgesics\textsuperscript{15}.

Intravenous NSAID such as ketorolac have been shown to be as effective as morphine and pethidine for the relief of pain after strabismus surgery in children, and with a lower incidence of postoperative nausea and vomiting\textsuperscript{16,17}.

Other studies showed that systemic NSAIDs such as ketoprofen were efficient in reducing pain after strabismus surgery in children when compared to placebo\textsuperscript{18,19}.

On the other hand certain NSAIDs such as ibuprofen and simple analgesics such as paracetamol were shown to be less effective\textsuperscript{20}.

Asthma occurs in 30% to 40% of children, 20% of those are sensitive to aspirin and other NSAIDs\textsuperscript{21,22}. In addition, reactions to NSAIDs include urticaria, angioedema, rhinitis\textsuperscript{23}, and exacerbation of asthma or bronchospasm\textsuperscript{24-27}, which may be fatal\textsuperscript{28}. These side effects occur after administration in common ophthalmic procedures and have been shown to occur with NSAIDs such as ibuprofen, diclofenac, and ketorolac\textsuperscript{28}. Therefore the use of NSAIDs may not be appropriate for many children undergoing strabismus surgery.

Different techniques of regional anesthesia combined with general anesthesia have been proposed for the young child undergoing strabismus surgery. In addition to controlling postoperative pain, it has been suggested that suppression of the trigeminal reflex by regional anesthesia may correlate with a decrease in the incidence of vomiting\textsuperscript{29}.

These techniques have yielded conflicting reports. Postoperative topical tetracaine compared with topical saline in pediatric strabismus surgery was shown to provide a short-lived but significantly better pain relief as judged by both pain score and analgesic requirement\textsuperscript{30}.

Topical amethocaine 1% drops and subconjunctival infiltration with bupivacaine 0.5% administered at the conclusion of strabismus surgery have been shown to be equally effective in reducing postoperative pain\textsuperscript{31}, although another study did not show any additional analgesic effect of either of these interventions when compared to placebo\textsuperscript{32}. Similarly, a study showed that the subconjunctival injection of bupivacaine 0.5% as compared with a placebo decreased postoperative pain scores in 36 young children. Another study compared subconjunctival bupivacaine to topical tetracaine in children undergoing squint surgery, with both giving effective analgesia.

<table>
<thead>
<tr>
<th>Subtenon Group (N = 27)</th>
<th>Control Group (N = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 (18%)</td>
<td>11 (38%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Incidence of nausea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (11%)</td>
<td>4 (14%)</td>
<td>0.575</td>
</tr>
<tr>
<td>Incidence of vomiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (22%)</td>
<td>10 (34%)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subtenon Group (N = 27)</th>
<th>Control Group (N = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients requiring additional systemic analgesia n (%)</td>
<td>8 (30%)</td>
<td>19 (65%)</td>
</tr>
<tr>
<td>Median time to first analgesia</td>
<td>2 hours 45 minutes</td>
<td>1 hour</td>
</tr>
</tbody>
</table>

M.E.J. ANESTH 23 (1), 2015
However, some investigators found no difference in pain score after pediatric squint surgery using postoperative topical saline, topical tetracaine or subconjunctival bupivacaine. Although subconjunctival local anesthetics have had some success in the relief of postoperative pain, the source of pain after strabismus surgery is believed to be receptors in tenon’s fascia and muscle tendons as well as conjunctival receptors.

Regional blocks have also been explored in children. Retrobulbar anesthesia by the administration of 2 mL of bupivacaine 0.5% before surgery was as effective as a subconjunctival injection given after the operation in 10 children. However the block reduced the incidence of OCR from 60% (control group) to 4% in children. Similarly, a study proved that peribulbar block (0.3 mL/kg of a bupivacaine 0.5% and lidocaine 2% mixture) reduced postoperative pain in 25 children 5 to 14 years of age to a significant degree; two thirds of these children were operated on for strabismus. The authors also reported a major reduction in the incidence of oculocardiac reflex and postoperative nausea and vomiting compared with the control group treated with pethidine.

However, when comparing different eye blocks in children, subtenon anesthesia seems to offer some advantages over retrobulbar or peribulbar blocks in pediatric strabismus surgery; All these techniques require the cooperation of patients by asking them to move their eyes laterally to exclude perforation of the globe or nerve injury during the procedure. Small children are unable to cooperate in this way, which leads to performance of the block under general anesthesia, with poor clinical control.

Thus, in the current study, we elected to perform subtenon anesthesia in pediatric patients undergoing squint surgery. Subtenon’s anesthesia results in excellent anesthesia and akinesia and is widely used for adult anterior and posterior segment surgery. The anesthetic agent is delivered into the subtenon’s space posterior to the globe’s equator using a blunt cannula inserted through a conjunctival incision, usually located in the inferonasal quadrant. The drug spreads rapidly through the subtenon’s space and anesthetizes the long and short ciliary nerves as they pierce Tenon’s capsule around the optic nerve.

These nerves carry sensory fibers from the sclera, cornea, and uveal tract. Spread of the drug into the muscle sheaths and eyelids results in anesthesia of these structures.

The surgery is then started through the same conjunctival incision which allows access to extraocular muscles. Therefore, application of anesthetics is no more invasive than the operation itself. Moreover, the required volume of local anesthetics to provide adequate analgesia is less important and limits the risks of damage caused by rapid injection or myotoxicity from the anesthetic solution.

Complications after subtenons anesthesia are uncommon but orbital hemorrhage, extraocular muscle injury, and globe perforation with scissors during dissection of the subtenons space have all been reported. There is also a risk of damage to structures crossing the subtenons space during rapid or high volume injection, and of myotoxicity from the anesthetic agent, but neither of these has yet been reported after subtenons administration. This was fully explained to parents at the time of consent. There were no complications resulting from subtenon injection in this study.

We chose to administer the block preoperatively rather than postoperatively since regional blocks are associated with fewer episodes of bradycardia and hypertension intraoperatively caused by the oculocardiac reflex which results from the traction on the extraocular muscles, this was evident in our study where a significant difference in the occurrence of oculocardiac reflex was observed.

Preoperative administration also offered the advantage of facilitation of surgical dissection and delivery of a controlled volume. The administration of local anesthetic, postoperatively is usually associated with protrusion of Tenon fascia and leakage of anesthetic through the incision. The administration of a preoperative subtenon block did not result in any surgical difficulty from tissue distortion.

In this study we looked at the administration of a long acting anesthetic; bupivacaine has an onset of action of approximately 20 min, preoperative administration ensures analgesic effectiveness as the general anesthetic wears off. We, found significant reduction in postoperative pain score as measured by...
the FLACC score.

Similar results have been obtained in a randomized controlled trial that investigated the postoperative use of sub-Tenon lignocaine in 111 children undergoing squint surgery. Pain was reduced significantly in the first hour after surgery, but thereafter there was no effect\(^{46}\). Lignocaine is a shorter-acting anesthetic with a duration of 1-2h when given as a sub-Tenon block, while the effect of bupivacaine lasts for 3-3.5h\(^ {45}\).

Our findings are also similar to those obtained by Steib et al. who explored the preoperative administration of bupivacaine in 40 children. The authors found a significant reduction in pain scores in the study group. The incidence of oculocardiac reflex and postoperative nausea and vomiting were also reduced in the study group\(^ {47}\).

On the other hand, in a study by Morris et al. the authors used preoperative levobupivacaine to perform subtenon block in 27 children undergoing strabismus surgery and found no significant reduction in pain scores in the study group\(^ {49}\). However, their study had several limitations; a placebo was not used in the control group, and not all patients received exactly the same general anesthetic agents or additional analgesia. These two factors may have influenced the results obtained by these investigators. These factors were avoided in our study which may explain our favorable results. However, the results obtained by these authors matched previous results obtained by Carden et al.\(^ {33}\).

No data in the literature suggests the optimal volume to inject in the pediatric population. Use of a large volume to produce akinesia is not essential, as general anesthesia is always used with young children, which allows satisfactory operating conditions by itself\(^ {49,52}\).

A significant reduction in PONV was observed in our study during the recovery period. This undesirable effect after strabismus surgery is caused by pain, traction of the muscles, and perioperative use of opioids. A similar reduction in PONV was also encountered in the study conducted by Steib et al.\(^ {47}\).

In conclusion, a preoperative subtenon block with bupivacaine combined with general anesthesia allowed efficient control of postoperative pain as well as a reduction in the incidence of OCR and PONV in young children undergoing strabismus surgery. We recommend that further studies be conducted to determine the optimal volume to inject in the subtenon space and to compare different local anesthetics.

Acknowledgements

The authors sincerely acknowledge the support of the Ain Shams University Ophthalmology Department in supporting this anesthesiology research. The authors also acknowledge the efforts of Mr. Deepak Gupta in the statistical calculations and analysis.
References


Straight to Video: Tonsillar Injury during Elective Glidescope®-Assisted Pediatric Intubation

JASON D. RODNEY*, ZULFIQAR AHMED*, DEEPAK GUPTA*, and MARIA MARKAKIS ZESTOS*

Abstract

Airway management in pediatric patients presenting for tonsillectomy and adenoidectomy may prove challenging given the enlarged upper airway structures. Video laryngoscopy (VL) can be very helpful but it does not come without risks. In this case report, we report an unfavorable outcome of VL in a pediatric patient with adenotonsillar hypertrophy.

Introduction

Airway management in pediatric patients presenting for tonsillectomy and adenoidectomy may prove challenging given the enlarged upper airway structures. Video laryngoscopy (VL) as a modality of airway instrumentation has the potential to facilitate an unobstructed view of the vocal cords in situations where the oral, pharyngeal and laryngeal axes are difficult to align. Such may be the case due to body habitus, trauma or neoplasm, among other indications. For this reason, VL is an important tool in the anesthesiologist’s armamentarium. It has been suggested that VL has earned a place high up in an algorithm for dealing with a difficult airway, particularly in a “can’t intubate/can’t ventilate” patient scenario1-4. VL may also be considered in patients where minimizing the force required during laryngoscopy is desirable such as a patient with loose teeth. Even though VL can be very helpful, it does not come without risks. There have been numerous case reports describing injury to various oropharyngeal structures. Hereby, we report an unfavorable outcome of VL in a pediatric patient with adenotonsillar hypertrophy undergoing tonsillectomy and adenoidectomy.

Case Presentation

A 6-year old female with comorbidities of sickle cell disease and a history of numerous blood transfusions presented for elective tonsillectomy-adenoidectomy due to obstructive sleep apnea. Preoperative airway examination revealed Mallampati Class I with full range of neck

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and jaw mobility, adequate thyro-mental distance, and as expected, enlarged tonsils. In addition to tonsillar hypertrophy, it was noted that the patient had loose upper incisors about which the parent was very concerned. The anesthesia team decided to use GlideScope® Cobalt AVL for endotracheal intubation in an effort to avoid inadvertent pressure or traction on the loose teeth.

After the induction of anesthesia, endotracheal intubation was attempted by the anesthesiology resident with the GlideScope®. A Cormack Lehane grade I laryngoscopic view was easily achieved with a size 2 GlideScope® blade. A 6.0 internal diameter (ID) oral RAE endotracheal tube, without stylet, was unsuccessfully introduced to the oropharynx. The rigid GlideRite® stylet was not used during the initial attempts to pass the endotracheal tube because when inserted into the endotracheal tube, the tip of the stylet protruded beyond the end of the oral RAE endotracheal tube. The RAE endotracheal tube of ID 6.0 mm was removed, and it was noted that blood was present on the tip of the endotracheal tube.

Mask ventilation was resumed with oxygen and sevoflurane and at this time, it was much more difficult to manually ventilate than during induction despite head-tilt-chin-lift and jaw thrust maneuvers. A subsequent attempt at VL by the supervising anesthesiologist revealed that the tonsils were almost completely obstructing the laryngoscopic view. Further attempts at intubation were withheld, and assistance was sought from the otorhinolaryngology surgical team due to the apparent injury to the enlarged tonsils during the initial intubation attempt.

The examination by the otorhinolaryngologist revealed Brodsky Grade 4+ tonsils with one partially detached tonsil having minimal mucosal bleeding. Endotracheal intubation was achieved by an attending physician with a Miller 2 blade with no observable effect to the loose teeth. At this time, the decision was made to proceed with the tonsillectomy-adenoidectomy as planned. After discussion with the concerned parent, the loose tooth was removed by the attending dentist. The remainder of the peri-operative course was unremarkable.

Discussion

Even though VL has been shown to improve the ability of novices to obtain laryngeal exposure when compared to Direct Laryngoscopy (DL) in adults, there is evidence for and against ease of use with respect to pediatric patients. Fonte et al demonstrated that pediatric residents, who were unfamiliar with VL, failed at tracheal intubations at a higher rate while using VL than when performing DL with a Miller blade in pediatric patients with a normal airway or tongue edema. Ilies et al found no difference between an attending physician’s and an experienced resident’s ability to obtain an improved view of vocal cords using VL after DL. Despite a perceived disadvantage to using VL for tracheal intubation by novices, it has been shown that in the hands of experienced anesthesiologists, VL does improve the ability to successfully intubate pediatric patients. VL may prove to be a useful tool in obtaining laryngeal exposure, but there have been numerous reports of injury to various oropharyngeal structures in adults including abrasion, perforation and laceration of tonsils, palatopharyngeal wall, lingual nerve as well as dental injury. It has been suggested that both the blind insertion and pathway of the endotracheal tube and the rigid stylet may be contributing factors to oropharyngeal injury during VL.

Although the decision for airway instrument choice was ultimately influenced by the patient’s dentition rather than a perceived difficult airway (even though the loose tooth was eventually removed by a dentist), this case shows one instance wherein use of GlideScope® for pediatric endotracheal intubation may have contributed to more harm than good. Even if the rigid stylet is not used to facilitate intubation, there is an inherent risk of oropharyngeal injury when using the video laryngoscope due to the inability to visualize the endotracheal tube passing from the opening of the mouth to the point where it enters the field of focus of the camera lens.

The GlideScope® has become a popular tool among peri-operative, critical care and emergency room care providers. Few would dispute that it has earned a place in the American Society of Anesthesiologists’ Difficult Airway Algorithm which
states that providers managing difficult airway should give appropriate considerations to the comparative benefits vs. workability potential of options including VL as the initial intubation attempt. In the presence of a known pharyngeal mass it may be worth considering DL, flexible fiberoptic (FFO) bronchoscope or a combination of VL and FFO used in conjunction as described by Weissbrod and Merati. We would also recommend caution when using the video laryngoscope for educational purposes. Although VL may facilitate both trainer and trainee to visualize the vocal cords in pediatric patients, its use may increase the risk of oropharyngeal injury or failed intubation in inexperienced hands.

Conclusion

In summary, operators’ tendency to direct and focus their attention ‘Straight To Video’ in VL should be cautioned against in order to avoid potential oropharyngeal injuries along the route of blind insertion of the endotracheal tube from the angle of the mouth until it becomes visible on the screen of the VL.
References


Abstract

Trigeminal neuralgia (TN) is characterized by unilateral, lancinating, paroxysmal pain in the dermatomal distribution area of trigeminal nerve. Percutaneous balloon compression (PBC) of Gasserian ganglion is an effective, comparatively cheaper and simple therapeutic modality for treatment of TN. Compression secondary to PBC selectively injures the large myelinated A-alfa (afferent) fibers that mediate light touch and does not affect A-delta and C-fibres, which carry pain sensation. Balloon compression reduces the sensory neuronal input, thus turning off the trigger to the neuropathic trigeminal pain. In this current case series, we are sharing our experience with PBC of Gasserian Ganglion for the treatment of idiopathic TN in our patients at an academic university-based medical institution in India. During the period of August 2012 to October 2013, a total of twelve PBCs of Gasserian Ganglion were performed in eleven patients suffering from idiopathic TN. There were nine female patients and two male patients with the age range of 35-70 years (median age: 54 years). In all patients cannulation of foramen ovale was done successfully in the first attempt. In eight out of eleven (72.7%) patients ideal ‘Pear-shaped’ balloon visualization could be achieved. In the remaining three patients (27.3%), inflated balloon was ‘Bullet-shaped’. In one patient final placement of Fogarty balloon was not satisfactory and it ruptured during inflation. This case was deferred for one week when it was completed successfully with ‘Pear-shaped’ balloon inflation. During the follow up period of 1-13 months, there have been no recurrences of TN. Eight out of eleven patients (72.7%) are completely off medicines (carbamazepine and baclofen) and other two patients are stable on very low doses of carbamazepine. All patients have reported marked improvement in quality of life. This case series shows that percutaneous balloon compression is a useful minimally invasive intervention for the treatment of trigeminal neuralgia.

Introduction

Trigeminal neuralgia (TN) is characterized by unilateral, lancinating, paroxysmal pain in the dermatomal distribution area of trigeminal nerve. According to International Headache Society (IHS) and International Association for Study of Pain (IASP) trigeminal neuralgia is...
painful, unilateral affliction of face, characterized by brief, electric shock like pain limited to one or more divisions of trigeminal nerve, commonly evoked by trivial stimuli like shaving, talking, washing of face but may also occur spontaneously with abrupt onset and termination\(^2\). Exact cause of TN is not known, and multiple treatment options are available but there is no ideal treatment available for all patients\(^3\). Severity of pain can result in poor health and deterioration of day-to-day functional status\(^4,5\). According to IHS, TN can be classified as classical or idiopathic and symptomatic or secondary\(^6,7\). In 2003, Burchiel classified TN on the basis of clinical features: Type 1 TN which is predominantly episodic and sharp; and Type 2 TN which is constant, dull, and burning in nature\(^8\).

The American Academy of Neurology (AAN) and the European Federation of Neurological Societies (EFNS) Guidelines on TN treatment (2008) recommend medical treatment with carbamazepine and oxcarbazepine or lamotrigine and baclofen as first option for TN\(^7\). In patients refractory to medical treatment or in whom side effects of medications are intolerable, othersurgical treatments are recommended. Various modalities of surgical treatment are possible, from major intracranial operation to minimally invasive percutaneous techniques. Because of the achievable longest duration of pain relief, microvascular decompression (MVD) is recommended as the first option, but it is a major intracranial operation, which may not be suitable for older, debilitated patients. MVD is also complicated with the risk of major neurological morbidity and mortality. Due to their minimally invasive nature and possibility to repeat, percutaneous procedures are widely used for the surgical treatment of TN, mostly in the patients who are not eligible for MVD, are not willing to have MVD or are refractory to previous surgical treatments. One of these procedures is percutaneous balloon compression (PBC) of Gasserian ganglion which was first introduced by Mullan and Lichtor in 1983\(^9\).

PBC is an effective, comparatively cheaper and simple therapeutic modality for treatment of TN. Compression secondary to PBC selectively injures the large myelinated A-alfa (afferent) fibers that mediate light touch and does not affect A-delta and C-fibres, which carry pain sensation. Balloon compression reduces the sensory neuronal input, thus turning off the trigger to the neuropathic trigeminal pain. PBC is not as selective for pain originating from a particular trigeminal division as radiofrequency thermo-coagulation (RFTC) is\(^10,11\).

In this current case series, we are sharing our experience with PBC of Gasserian ganglion for the treatment of idiopathic TN in our patients at an academic university-based medical institution in India.

**Case Series**

During the period of August 2012 to October 2013, a total of twelve PBCs of Gasserian Ganglion were performed in the Department of Anesthesiology and Pain Medicine at Lala Lajpat Rai Memorial Medical College, Meerut, India in eleven patients suffering from idiopathic TN. There were nine female patients and two male patients with the age range of 35-70 years (median age: 54 years). All the patients were suffering from Burchiel Type 1 TN with the classical features of idiopathic TN i.e., electric shock-like lancinating pain in the territory of trigeminal nerve (CN V). Two patients had involvement of both maxillary (V\(_2\)) and mandibular (V\(_3\)) divisions of Cranial Nerve V; three patients had involvement of V\(_2\) division only and remaining six patients had TN along V\(_3\) division only. The duration of the disease ranged from 2.5-12 years. Only three patients could undergo a magnetic resonance imaging because of financial constraints; all other patients were screened for any intra-cranial pathology by computerized tomography scanning. None of our patients had bilateral TN; five patients had involvement of right side CN V and six patients had left-sided involvement. All patients had been treated with carbamazepine and baclofen as part of failed medical management prior to PBC. One patient had already undergone retro-gasserian glycerol rhizotomy, which provided pain relief for only five months. One patient underwent PBC on two occasions secondary to non-satisfactory placement of balloon inside the Meckel’s cave followed by rupture of balloon and venous bleeding. The case was deferred and performed again after one week with satisfactory results.
Procedural Details of PBC: All the procedures were performed under conscious sedation using two-dimensional C-arm fluoroscopic guidance. Patients were placed in supine position with slight extension of neck. C-arm fluoroscope was aligned to take a ‘Modified sub-mental view’, in which foramen ovale was visualized between mandible on the lateral side and maxilla on the medial side (Figure 1). In this view, a 14-gauge cannula with blunt trocar was used to enter the foramen ovale to reach the Meckel’s cave where the Gasserian ganglion is situated (Figure 2). Once entry was confirmed in the Meckel’s cave, lateral view was obtained wherein 4-Fr Fogarty catheter was gently threaded in to the Meckel’s cave up to the clivus. After confirmation of correct position of the balloon in anterio-posterior and lateral views, Fogarty balloon was inflated with 0.8-1 ml of water soluble contrast dye (Omnipaque-240, GE Healthcare) for 1.5-3 minutes. After completion of the intervention, Fogarty balloon was deflated and removed along with the cannula; and manual digital pressure was applied for five minutes against the maxilla to stop any bleeding and cerebrospinal fluid drainage. A small dressing was applied on the skin puncture site and patients were transferred to post-anesthesia care unit for observation. After regaining full consciousness, patients were examined for relief in pain, facial sensation and corneal reflex; and, after two to four hours, patients were discharged home on oral antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs).

Procedural Results of PBC: In all patients cannulation of foramen ovale was done successfully in the first attempt. In eight out of eleven (72.7%) patients ideal ‘Pear-shaped’ balloon visualization could be achieved (Figures 3-4). In the remaining three patients (27.3%), inflated balloon was ‘Bullet-shaped’. In one patient final placement of Fogarty balloon was not satisfactory and it ruptured during inflation. This case was deferred for one week when it was completed successfully with ‘Pear-shaped’ balloon inflation. In one patient, venous bleeding was detected on removal of trocar from cannula that ceased after placement of Fogarty catheter and successful PBC. In another patient, who had not been pre-medicated with atropine, there was sudden asystole on entering in to the foramen ovale, which responded to Inj. atropine 1.2 mg intravenous bolus with no post-operative sequelae. In all other patients, no episode of major bradycardia occurred due to pre-medication with atropine 0.4 mg intravenously. All patients had complete relief of neuralgic pain in the immediate post-operative period. In nine out of eleven patients (81.81 %), there was mild to moderate facial hypoesthesia, which was more prominent with longer compression-duration (3 minutes vs. 1.5 minutes). This hypoesthesia improved within 6-8 weeks and did not cause appreciable discomfort to these patients. Five out of eleven patients (45.4%) complained about mild facial dysesthesias (continuous burning sensation in CN V distribution), which improved in 6-8 weeks with the use of neuro-modulatory drugs such as pregabalin. One patient complained of malocclusion of mandible and difficulty in chewing on the operated side, which
also improved in four weeks without any treatment. Four out of eleven (36.36%) patients revealed mild to moderate asymptomatic masseteric weakness on post-operative physical examination that also improved in 4-6 weeks. None of the patients had loss of corneal reflex and/or anesthesia dolorosa. In two out of eleven (18.2%) patients, there was eruption of herpes labialis on the ipsilateral side, which was treated with anti-viral drugs with resolution of the lesions within two weeks. All patients complained of temporal headache in the immediate post-operative period, which improved in 24-48 hrs with the use of NSAIDs and ice fomentation. None of the patients had any major complication such as corneal ulcer, 4th or 6th cranial nerve palsy, meningitis or death. During the follow up period of 1-13 months, there have been no recurrences of TN. Eight out of eleven patients (72.7%) are completely off medicines (carbamazepine and baclofen) and other two patients are stable on very low doses of carbamazepine. All patients have reported marked improvement in quality of life.

Minimally invasive pain interventions have found a niche among the available treatments for many intractable, chronic painful conditions such as TN. PBC has been found to be an effective intervention in many studies. PBC has an advantage of sparing the corneal reflex over other percutaneous methods. It has a unique mechanism of action of selective injury to large myelinated A-alfa and A-beta fibers and relative sparing of small, unmyelinated C-fibers and poorly myelinated A-delta fibers. So it may be the best technique for addressing ophthalmic division (V1) pain of TN and this observation has been confirmed by Brown et al.

Initially PBC was advocated for older age group and for those who were unfit for major surgical procedure. Now it has been found useful even in many young patients, especially those who do not have any evidence of vascular malformation and/or are unwilling to undergo major surgery. Strojnik and Smigoc and Natraj have used this technique in patients with aberrant basilar artery as well as in young patients. In our study, there was a female patients preponderance, most patients were of advanced age and there was almost equal distribution of right side vs. left side involvement, although some authors have found preponderance of right sided involvement.

In all our patients, modified Mullan’s technique was used for PBC. Though ‘Pear-shaped’ balloon is considered to be the best in some studies, this shape was achieved in only eight out of eleven patients in our series but we did not find any differences in the outcome, possibly due to shorter follow-up in our study (1-13 months). Same can be true in regards to the compression-duration wherein practitioners have used compression time ranging from 1-20 minutes; some authors have reported correlation between the duration of compression and duration of pain relief but with longer duration of compression, more complications like facial dysesthesias have been reported.
Because there is no consensus on the optimal duration of compression during PBC, in our practice we have used the compression times of 1.5 minutes and 3 minutes; and we have found that although the pain relief was complete with both compression-duration, incidence and magnitude of facial hypoesthesia and dysesthesia was more in patients who had received compression for longer duration.

Prolonged masticatory weakness due to masseter-pterygoid weakness has been reported after PBC. We also encountered malocclusion on ipsilateral jaw in one patient and mild masseteric weakness in four patients, which was not bothersome to the patients because pre-procedure, they were not chewing from that side any way due to the precipitation of their neuralgic pain. In all patients, this weakness completely recovered in 4-6 weeks without any intervention. In all patients in our series, complete relief from neuralgic pain was observed, which is similar to other studies. Autonomic changes such as bradycardia and hypotension have been reported on entering the foramen ovale in more than 50% of cases which was not observed in our series because of pre-medication with atropine. Though no mortality has been reported during PBC in the literature, Natrajian had reported an incidence of intra-operative myocardial infarction which was managed successfully. We also encountered a case of sudden asystole on foramen ovale penetration in a patient who was not given atropine pre-operatively in spite of our policy. It was recognized immediately due to continuous electrocardiography and was managed successfully with rescue dose of atropine with no post-operative sequelae. Therefore, it is our suggestion to ensure premedication with atropine prior to penetration of foramen ovale before all percutaneous procedures including PBC. Though review of medical literature elicits rare incidences of anesthesia dolorosa, intracranial fistula formation and cranial nerve injury, corneal ulceration and death during PBC, we did not encounter any such adverse effect.

Recurrence of pain after successful PBC and initial pain relief has been reported very widely in the literature, Baabor and Perez-Limonte had reported 15% recurrence after 3 years, and Skirving and Dan had reported 31.9% recurrence in 20-years duration. In our moderate follow-up period of 1-13 months, we have not found any recurrence so far.

The major limitations in the present study were retrospective nature of the case series, small number of patients (n=11) and short duration of follow-up (1-13 months).

Conclusion

This case series shows that percutaneous balloon compression of Gasserian ganglion is a useful minimally invasive intervention for the treatment of trigeminal neuralgia. If performed appropriately with the help of anatomical landmarks and radiological guidance, it is a low risk procedure with high success rate. Due to very low incidence of corneal anesthesia and anesthesia dolorosa, we recommend PBC as first choice among percutaneous interventions for TN especially involving V1 division as well as in multidivisional pain.
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Abstract

Radial artery insertion is a common procedure in intensive care units. We describe a case of a critically-ill 73-year-old man in the neurocritical care unit with a subarachnoid hemorrhage whose radial arterial catheter tip was transected from the main line and was successfully managed with bedside retrieval of the catheter.

Introduction

Radial artery insertion is usually done in the neurocritical care unit (NCCU) for the purposes of blood pressure monitoring and arterial blood sampling. Several complications are known such as temporary occlusion, thrombosis, pseudoaneurysm formation, hematoma formation, abscess, cellulitis, median nerve involvement and air embolism. Retained radial artery catheter is rare but has been reported in literature. Several causes have been mentioned such as accidental transection, repeated catheterization and repeated wrist movements. Several modalities have been mentioned to confirm the location of the arterial catheter as well as different methods to remove the catheter.

We describe a case of a 73-year-old man who presented with aneurysmal subarachnoid hemorrhage due to an anterior communicating aneurysm and underwent aneurysmal clipping. His course was complicated by cardiopulmonary instability. On his first post-operative day, the radial arterial catheter tip on his left wrist was fractured from the main line as it was being removed. He then underwent a bedside vascular exploration and removal of the foreign body. We also present a review and summary of the available literature regarding retained radial catheters and the available modes of image confirmation and options for treatment.

Case

A 73-year-old man was admitted in our Neurosciences critical care unit (NCCU) for an aneurysmal subarachnoid hemorrhage (ASAHI), Hunt and Hess 3, Modified Fischer Scale 3. He underwent aneurysmal clipping after a four vessel angiogram revealed a 3-millimeter irregular and superiorly projecting anterior communicating artery aneurysm. Post-operatively day 1, he was very agitated and his left radial arterial catheter was discontinued due to very poor waveform. As it was being pulled out, the nurse noticed that the long portion of the distal cannula was not there. It was highly suspected that it was still in the vessel. Pulses and perfusion distally were adequate. A
stat portable 3-view X-ray of the wrist and hand done visualized a 4cm catheter fragment in the anterolateral soft tissue aspect of the distal forearm proximal to the left wrist (Figure 1). A vascular surgery consult was placed and surgical removal and exploration was planned the following day. His family was informed of the incident and consented for the procedure. On the day of the planned exploration, the patient had acute respiratory failure further complicated by an asystolic event. He was immediately resuscitated and was started on norepinephrine, dopamine, epinephrine to maintain his mean arterial pressure. The surgical procedure was postponed due to hemodynamic instability. Three days after, it was deemed that due to the patient’s continued hemodynamic instability, he was not a good surgical candidate to transport to the operating room. The bedside exploration of the left radial artery and the removal of the distal catheter tip were then done with local anesthesia under ultrasound guidance. The incision was made at the top of the radial artery on the left forearm. The catheter was identified right at the entry site of the radial artery. DeBakey pickups were used to extract the catheter out of the radial artery (Figure 2). The radial artery was found to be thrombosed at that location. Dopplers were performed after the procedure to assure adequate pulses and perfusion distally. The procedure was tolerated well and perfusion was maintained throughout the hospital stay.

**Fig. 1**
Plain left hand and wrist x-ray. Panel A is the PA (postero-anterior) view. Panel B is the lateral view. Encircled in red is the retained radial artery catheter fragment

**Fig. 2**
Proximal part of the radial arterial catheter without the retained distal catheter tip

**Discussion**

The radial arterial line for this patient was for strict blood pressure monitoring which is one of the most common reasons for its placement. The reason for the radial artery catheter breakdown in this patient is unclear. Several reasons for this type of breakdown have been reported in the past including accidental transection while separating the arterial line from the intravenous line, possible damage to the catheter sheath due to repeated catheterization attempts, transection while suturing, shearing off of the cannula due to repeated wrist movement postoperatively during recovery, reinsertion of the stylet needle, accidental cutting during suture removal, and dressing removal. In our case, our suspicion is that the patient was probably moving his wrist repeatedly during his post-operative agitation. Prompt vascular surgery consult for possible exploration is very important to prevent the possibility of distal embolization and distal migration with thrombosis. There is also a possibility of proximal migration and the use of ultrasound to confirm the location of the catheter preoperatively is recommended. Described by Aslam et al., this proximal migration, although unlikely, may occur because of arterial spasm distally. Several imaging modalities may be used to confirm the location of the retained fragment (Table 1). In this patient, the most rapid way to confirm the imaging late at night was a plain radiograph. With the vascular surgery team
<table>
<thead>
<tr>
<th>Source</th>
<th>Patient characteristic</th>
<th>Cause of cannula transection</th>
<th>Diagnostic procedure for confirmation</th>
<th>Consulting service/Procedure for removal</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moon et al.</td>
<td>69 y.o., Male</td>
<td>Accidental transection by scissors while separating intravenous and arterial catheter</td>
<td>7.5 MHz high-frequency ultrasonography, 3-D CT</td>
<td>Plastic surgery/OR Surgical exploration and removal of fragment by microforceps</td>
<td>Recovered, no residual sequelae</td>
</tr>
<tr>
<td>Lee SY et al.</td>
<td>69 y.o., Male</td>
<td>Reinsertion may have damaged the catheter sheath, manufacturing defect of angiocatheter is suggested</td>
<td>Wrist CT</td>
<td>Service not mentioned/OR surgical exploration and removal of fragment</td>
<td>Recovered, no residual sequelae</td>
</tr>
<tr>
<td>Ho KS et al.</td>
<td>20 y.o., Female</td>
<td>Repeated wrist movement</td>
<td>Not mentioned</td>
<td>Vascular surgery/OR surgical exploration under local anesthesia</td>
<td>Recovered, no residual sequelae</td>
</tr>
<tr>
<td>Aslam M et al.</td>
<td>63 y.o., Female</td>
<td>Not mentioned</td>
<td>ultrasound</td>
<td>Vascular surgery/OR surgical exploration under local anesthesia</td>
<td>Recovered, no residual sequelae</td>
</tr>
<tr>
<td>Shah U.S. et al.</td>
<td>72 y.o., Female</td>
<td>Transected while securing the arterial catheter with suture.</td>
<td>none</td>
<td>Vascular surgery/OR surgical exploration simultaneous with planned indicated surgery</td>
<td>Recovered, no residual sequelae</td>
</tr>
<tr>
<td>Bengezi OA et al.</td>
<td>58 y.o., Male</td>
<td>Hypothesized to be repeated flushing and manipulation created a vulnerable point along the catheter length</td>
<td>Plain X-ray of wrist and hand with ultrasound confirmation pre- and intraoperatively</td>
<td>Vascular surgery/OR surgical exploration with arteriotomy</td>
<td>Excellent flow with good capillary refill in all fingers.</td>
</tr>
<tr>
<td>Kim IS et al.</td>
<td>74 y.o., Male</td>
<td>Reinsertion of stylet needle through the embedded catheter sheath intraoperatively for pleural decortications</td>
<td>Portable X-ray</td>
<td>Unclear if vascular surgery involved/OR Exploration and removal during scheduled primary surgery</td>
<td>Recovered uneventful</td>
</tr>
<tr>
<td>Moody C et al.</td>
<td>Unknown elderly</td>
<td>Accidental cutting of the plastic cannula</td>
<td>Ultrasound imaging pre-and intraoperatively</td>
<td>Surgical team involved/OR exploration with arteriotomy and removal of catheter</td>
<td>Recovered uneventful</td>
</tr>
<tr>
<td>Ferguson E et al.</td>
<td>62 y.o., Male</td>
<td>Accidental cutting of catheter fragment</td>
<td>Portable X-ray</td>
<td>Vascular surgery/OR arteriotomy and removal of catheter</td>
<td>Uneventful</td>
</tr>
<tr>
<td>Mayne D and Kharwar F</td>
<td>64 y.o., Male</td>
<td>Repeated flexion and extension</td>
<td>Portable X-ray</td>
<td>Unclear if vascular surgery involved/Unclear if OR Exploration and removal or bedside</td>
<td>Uneventful</td>
</tr>
<tr>
<td>Hamid et al.</td>
<td>unknown</td>
<td>Accidental transection with dressing removal</td>
<td>Sonosite, X-ray</td>
<td>Percutaneous approach using a snare</td>
<td>Some spasm on angiography however no complications after removal</td>
</tr>
</tbody>
</table>
on board, they were able to perform their bedside ultrasound localization both preoperatively and during the surgery itself. Ideally, patients are taken to the operating room for surgical exploration and removal of the fragment with generally good outcome (Table 1). However that is not always possible as in our case. The patient was hemodynamically unstable and was unable to tolerate repeated position changes even just for transportation. However, as soon as the patient was deemed able to tolerate the surgical exploration at bedside, it was immediately arranged and another ultrasound was performed preoperatively. The procedure was performed in our NCCU.

Retained radial artery catheter is rare but has been reported. Clinicians should be aware of the various mechanisms by which the catheter may be transected so precautions can be observed. Appropriate wrist stabilization, careful suture placement and removal and avoidance of multiple stylet needle reinsertion are the suggested ways to prevent this complication. Prompt confirmation of the location of the retained fragment is indicated with simultaneous vascular surgery consultation for timely exploration and removal. Intraoperative confirmation of the catheter may be needed. If the patient is unable to tolerate transport to the operating room, it is feasible to perform the procedure at bedside. To the authors’ knowledge this is the first report of a bedside surgical exploration for a retained radial arterial catheter in a hemodynamically unstable patient.
References

Abstract

Esophageal rupture has been described following iatrogenic manipulation. In this report, we present an elderly lady admitted to the operative theater for laparoscopic cholecystectomy. Multiple intra-operative attempts to place a flexible orogastric tube were unsuccessful because of failure to advance.

Post-operatively, the patient developed sepsis and a right pleural effusion. She was transferred to the Intensive Care Unit and she was treated with antibiotics. Radiologic evaluation confirmed an esophago-pleural fistula. Surgical repair was urgently performed for closure of fistula and lung decortication. The patient recovered and was discharged home.

Introduction

Esophageal perforation is a serious complication of procedures performed on or around the esophagus and is mainly iatrogenic. Esophageal perforation is most frequently encountered during endoscopic procedures but also during nasogastric tube placement, endotracheal intubation, stricture dilation and during the use of oesophageal bougies. This complication has a poor prognosis with inadequate management.

While providing anesthesia to surgical patients, anesthesists frequently insert esophageal dilators, nasogastric tubes or orogastric tubes/suction catheters. Such interventions may cause trauma to soft tissue structures. We describe a case of esophageal perforation secondary to the orogastric insertion of a simple 14 French suction catheter used routinely to deflate the stomach during laparoscopic cholecystectomy. To our knowledge, this is the first case report describing esophageal perforation following the insertion of a flexible orogastric 14Fr suction catheter in an adult patient undergoing laparoscopic cholecystectomy.
Case Report

A 79 year old, 70 kg lady known hypertensive and dyslipidemic presented for laparoscopic cholecystectomy and intraoperative cholangiogram secondary to an acute cholecystitis. The patient denied any symptoms or history of dysphagia, odynophagia, gastroesophageal reflux or chest pain. Difficult intubation was anticipated due to short neck and a glidescope assisted intubation was planned.

In the operating room, after lung denitrogenation with 100% oxygen, rapid sequence induction was performed using lidocaine 100 mg (1.5 mg/kg), propofol 140 mg (2 mg/kg) and succinylcholine 100 mg (1.5 mg/kg) intravenously. No bag ventilation was performed. The trachea was intubated by an endotracheal tube (ETT) size 8.0 using the Glidesscope and a 10Fr intubating stylet (Unomedical). Several attempts to insert a well lubricated 14 Fr suction catheter failed (Bicakcilar, suction catheter w/vakon connector ideal tip 4.7 mm x 600mm). The catheter would not advance even with an index finger inserted in the patient mouth guiding the catheter into the pharynx. After multiple attempts using the laryngoscope to have better visualization, the insertion of the orogastric tube was not successful. During the procedure, the surgeon noted that the stomach was inflated and insisted on the placement of an orogastric tube to suction the stomach. We elected then to place an ETT size 7.0 that we advanced in the esophagus and inserted the orogastric tube through it. The advancement of the catheter would always stop at the same level as previously tried with or without the laryngoscope attempts. The resistance upon the insertion of the catheter was encountered at a distance of about 25 cm from the lips. No forcible maneuvers were performed and no blood was recovered over the suction catheter. We decided to abort the placement of the orogastric tube and the surgeon was advised so. His concern was a fully inflated stomach that he is showing us on the video camera. We explained that placement of orogastric tube was difficult, and will treat his concern by extubating the trachea when the patient is fully awake.

After the surgical procedure ended, extubation was uneventful. The patient was transferred to the recovery room. She was fully awake and asymptomatic.

On post-op day one, the patient complained of dry cough and dyspnea after her first meal. On physical exam, she had scattered wheezes and right field crakles. She was afebrile. Chest X ray (CXR) revealed opacification on the right lower and right middle fields. A diagnosis of pulmonary aspiration was suspected and Solumedrol, Combivent, pulmicort and Tazocin were started. The CXR improved in the afternoon. However, clinically the patient was getting worse the following day with progressive desaturation down to 90% and became hypotensive with systolic pressure of 80 mmHg. The patient was transferred to the intensive care unit and Tazocin was shifted to broad spectrum antibiotic coverage consisting of Meropenem, Levofloxacin and Metronidazole. The patient symptoms improved, however the cough and wheezes persisted. A CT chest was done on post op day 7 revealing an air pocket posterior to the carina in continuity with the right lower lobe. A diagnosis of esophageo-pleural fistula in the lower esophagus was suspected and was confirmed with Gastrograffin swallow. On post-op day 9, a thoracotomy for right lung decortication and closure of fistula was performed. The patient was kept intubated and extubation was done on the following day. Antibiotics were continued for 14 days post-op. The radiological findings on CXR resolved on post-op day 17.

A repeated gastrograffin swallow was performed on post-op day 20 showing an outpouching at the level of the fistula but no leak. Another gastrograffin swallow was performed on post-op day 27 showed no leak.

The patient was discharged from the hospital on post-op day 33.

Discussion

Perforation of the esophagus due to instrumentation in the adult is a rare yet potentially devastating event associated with high morbidity and mortality1. The mortality has decreased from 38.7% in the 1970s to 8.3% today18. The leading cause of
Esophageal perforation is mainly iatrogenic with perforations at the thoracic level being the highest. Most of perforations occur during instrumentation of the esophagus i.e. endoscopy procedures, transesophageal echocardiography, esophageal varices sclerotherapy, stricture dilatation, using relatively large stiff probes (endoscope, TEE probe, Sengstaken-Blakemore (SB) tube, bougie). Several risk factors have been described for esophageal perforation such as pre-existing esophageal abnormalities (carcinoma, stricture, diverticuli) and cervical osteophytes. Esophagogastroduodenoscopy was the most commonly litigated procedure, followed by intubation and Nissen fundoplication. But there have been few reported cases of iatrogenic esophageal perforations by a flexible nasogastric tube occurring mainly in neonates or infants.

In our patient the perforation occurred after multiple attempts at inserting the orogastric suction catheter where the obstruction was faced at 25 cm distal to the lips. The most common areas of instrumental esophageal perforation are the relatively narrow portions at the distal esophagus. The perforation is complicated by an inflammatory process and communication with the pleura in 80% of the cases. The thin mediastinal pleura is ruptured by the inflammatory process, producing contamination of the pleural space and a pleural effusion. Then, gastric contents and fluids are drawn into the pleural space by the negative intrathoracic pressure resulting in further inflammation and fluid sequestration, hypovolemia, and the early appearance of tachycardia and systemic sepsis. In our patient the CXR revealed opacifications which reflect consolidation of the lungs that is due to an accumulation of fluids that is most probably edema and inflammation. This explains the scattered wheezes and crackles that were heard on post op day one. In addition, esophageal perforation allows bacteria, usually polymicrobia flora to spread into the mediastinum and subphrenic space leading to mediastinitis. This explains the septic picture of our patient that was revealed by hypotension and progressive oxygen desaturation.

However if delayed diagnosis beyond 48h was made, no patient with esophageal perforation should be deprived from surgical repair. Mortality is decreased in surgical repair versus conservative treatment, for that reason, our patient underwent thoracotomy for fistula closure and repair of esophageal tear.

In any patient with a recent history of esophageal instrumentation, the diagnosis of esophageal injury should be suspected in the presence of any of the symptoms encountered by our patient. Also, the absence of gastric content on naso/orogastric tube or the presence of blood on the catheter elicit a possible diagnosis of perforation. Nevertheless blood was not noted on the suction catheter in our case.

For the first 24 hours following the laparoscopic cholecystectomy, our patient’s only complain was pain over the incision and a mild shoulder pain attributed to the laparoscopic procedure. This pain was controlled by analgesics. She denied any complain or history of dysphagia, odynophagia, dysphonia or dyspnea. However, after her first meal she complained of sudden dry cough and severe dyspnea. Taking into consideration the fact that the patient was extubated with a distended stomach, pulmonary aspiration was the most probable diagnosis.

It was the persistence of the cough and dyspnea and the worsening of these symptoms following meals, along with a problematic naso/orogastric tube insertion that made the suspicion of esophageal perforation high. Because of the failure of insertion of the orogastric catheter and the occurrence of resistance at 25 cm from the lips, an intrathoracic esophageal injury in our case was suspected. The CT chest showed an air pocket adjacent to the carina in continuity with the right lower lobe. This prompted us to perform esophagogram to confirm the diagnosis of esophageal perforation.

The presence of underlying esophageal pathology could explain the difficulty in advancing the orogastric tube. As anesthesiologists we are the experts in inserting orogastric tubes or suction catheters, a maneuver that we perform almost every day in our practice. The advancement of the catheter was impossible past 25 cm of the lips despite so many attempts. This could be
explained by a pre-existing esophageal pouch that the patient is unaware of or by an osteophytic compression of the esophagus due to the patient age, which made the advancement of the catheter impossible. Forcing the catheter insertion through multiple attempts lead to the perforation. On another note, the deviation from our current practice of inserting a suction catheter through an ETT placed in the esophagus is a very rare maneuver that we perform in extreme situations. This also could be the reason of the perforation.

Conclusion

The lesson taken from this case report is not to force the advancement of an orogastric/nasogstric suction catheter especially when different techniques and multiple attempts fail. The other lesson taken is to have a very high threshold inserting an ETT in the esophagus to facilitate the suction catheter insertion by advancing the catheter through the ETT since this could also be a risk factor for esophageal perforation.
References


LETTER TO THE EDITOR

PEDIATRIC ENDOTRACHEAL INTUBATION

Claude Abdallah

Dear Editor,

I have read with interest the manuscript: “Simulation training in endotracheal intubation in a pediatric residency” M. E. J. Anesth 22(5) 2014, by Drs. Sharara-Chami, Taher, Kaddoum, Tamim and Charafeddine. The authors are to be congratulated for taking the time to analyze and publish the study, the discussion highlights interesting points.

Tracheal intubation in pediatric patients is an essential tool in anesthesiology, traditionally acquired in a clinical setting. Factors related to the patient such as the age of the patient and the level of experience of the trainee may be determinant factors in the decision of the anesthesiologist to make a first attempt at tracheal intubation. Learning curves exist for practical skills and despite useful tools to monitor the learning process; competency is difficult to assess by the anesthesiologist in the absence of adequate exposure with the trainee or a previous documentation of the level of execution of involved skills. Literature review shows the advantage of preparing trainees outside the operating room so that clinical training opportunities can be used most effectively when they arise. Scientific reports documenting the effects of simulation training on learning and updating knowledge about airway management showed improvement in decision-making, communication capabilities1-4 and a better learning of crisis management and endotracheal intubation5. Residents achieve proficiency levels in a smaller number of elapsed days of training and in a smaller number of trials in the operating room6. Simulation would represent also an additional tool for assessing the performance of procedures in anesthesia, such as rapid sequence induction, since it represents more clearly behaviors used in clinical practice than is possible to demonstrate using evaluation by questionnaires7. This may be particularly interesting since theoretical lectures and standard mannequin-based driven workshops have shown to improve overall theoretical knowledge but not to translate to practical skill during realistic mannequin-based simulations8.

As discussed by the authors, future studies pertaining to documentation of the trainee’s perspective when faced with a pediatric tracheal intubation with teaching of pediatric endotracheal intubation with and without simulation training would be useful to perform.

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References


ERRATUM

The correct spelling name of the first author of the Letter-to-Editor entitled “Anesthetic management of a patient after functional hemispherectomy using bilateral bispectral index monitoring” and published in the October 2014 issue of the Middle East Journal of Anesthesiology (pp. 627-628) is “Shinichiro Kira” and not “Shinichiri Kira”.

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They should be brief. Individuals named must be given the opportunity to read the paper and approve their inclusion in the acknowledgments.

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