"For some must watch, while some must sleep"

HAMLET - Act. III, Sc.ii
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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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¹ Train-of-four
² Post tetanic count
³ Second twitch

**REFERENCES**

1. BRIDION Summary of Product Characteristics (SPC).

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VENTILATION-PERFUSION MATCHING DURING ONE LUNG-VENTILATION IN THE LATERAL DECUBITUS POSITION

In the awake patient, breathing spontaneously in the lateral decubitus position (LDP), gravity results in a higher pleural pressure around the dependent lung which places the dependent lung on the steep part of the compliance (pressure-volume) curve. Also, gravity results in a higher pulmonary blood flow to the dependent lung than the blood flow to the nondependent lung. In the awake patient breathing spontaneously, and probably during natural sleep, the dependent lung receives more perfusion matched with more ventilation during the lateral decubitus position than the nondependent lung. Thus, adequate ventilation-perfusion matching is insured in both the dependent and the nondependent lungs of the awake patient during the LDP.

Induction of general anesthesia decreases the functional residual capacity (FRC) in both the dependent and non-dependent lungs with a consequent change of compliance; the dependent lung moves from the steep compliant position to the lower flat non compliant position of the compliance curve, while the nondependent lung moves from the upper flat non compliant position of the flow-volume curve down to the steep compliant portion. This will shift more ventilation away from the dependent to the nondependent lung. However, because of the gravity, blood flow to the dependent lung remains higher than the blood flow to the nondependent lung. Thus, following general anesthesia in the LDP, the dependent lung is more perfused than ventilated resulting in a shunt effect. In contrast, the non-dependent lung is more ventilated than perfused, resulting in a dead space effect. In order to maintain adequate oxygenation and carbon dioxide elimination, moderate hyperventilation with a high FiO2 is required. An alternative approach is to apply PEEP to the two lung, which can restore their FRC, and their original position on the pressure-volume curve, and optimize ventilation-perfusion matching during general anesthesia in the LDP.

During one-lung ventilation in the lateral decubitus position, the dependent lung is only ventilated. Also, the blood flows predominantly to the dependent lung. In contrast, the non-dependent lung is not ventilated, but is still perfused by about 40-50% of the cardiac output, creating a shunt effect. The degree of shunt is decreased by decreasing the blood flow to the nondependent nonventilated lung by gravity and by lung collapse. However, the most important factor which decreases the degree of shunt from about 40-50% down to 20% is hypoxic pulmonary vasoconstriction (HPV) of the vessels of the nonventilated lung. HPV is obtunded in COPD patients, as well as in patients with respiratory bronchiolitis-associated interstitial lung disease (RB-ILD). Thus, transpulmonary shunting may persist in the non-ventilated lung, resulting in severe hypoxemia during OLV. In contrast, HPV remains very active in patients having left-to-right cardiovascular shunt such as patent ductus arteriosus and ventricular septal defect, which explains the high PaO2 during OLV of these patients.
Distribution of perfusion according to the lung disease is another factor which determines the degree of shunt during OLV. Patients with large central tumors undergoing pneumonectomy or lobectomy will most probably have less perfusion to the operated non-ventilated lung, as compared with patients with peripheral masses. Lung perfusion studies showed that perfusion is already impaired in patients with large central tumors, may be secondary to activation of HPV. That is why, patients undergoing pneumonectomy or lobectomy have a much better oxygenation during OLV than those presenting for peripheral masses.

Hypoxemia during OLV is not only related to the lung disease, but is also determined by several interrelated factors that determine the balance between oxygen consumption, and oxygen delivery:

Cardiac output x \( \left( \text{Hb} \times \text{SaO}_2 \times 1.34 \right) + \left( \text{PaO}_2 \times 0.0031 \right) \)

Thus, hypoxemia during OLV is determined by both ventilation and perfusion, and hence may be attenuated by manipulation of ventilation and perfusion independently.

Protective ventilation strategy using a tidal volume of 5-6 mlKg-1 associated with PEEP versus ventilation by 10 mlkg-1 has been followed by a significantly lower inflammatory response. The inflammatory mediators may be also significantly lower in patients receiving inhalation sevoflurane than those who had intravenous propofol. It may be concluded that hypoxemia release of inflammatory mediators during one-lung ventilation may be attenuated by manipulation of ventilation and perfusion independently. From a ventilator perspective, protective ventilation strategy using a low tidal volume and positive end-expiratory pressure and avoidance of high tidal volume may attenuate the development of acute lung injury during one-lung ventilation. Hypoxemia during OLV may be also attenuated by adequate oxygen delivery, which can be achieved by maintenance of cardiac output, and avoidance of excessive hemodilution.

A sevoflurane-based volatile anesthetic regimen has been also shown to provide protection against inflammatory mediators release during OLV, and better cognitive function following open heart surgery than intravenous proprofol-based anesthesia, suggesting preconditioning of cerebral hypoxemia by the inhalational anesthetic.

Despite optimizing ventilation by the protective ventilation strategy and optimizing perfusion by maintaining cardiac output and avoiding excessive hemodilution, serious hypoxemia during OLV can result from malpositioning of the lung isolation devices such as the double-lumen tubes and the bronchial blockers. The safety margin following left bronchial intubation is greater than following right bronchial intubation because the distance from the carina to the inlet of left upper lobe bronchus is longer than the distance to the inlet of the right upper lobe bronchus. Unfortunately, despite the safety margin, blocking of the inlet of the left upper lobe bronchus by down migration of the tube which may occur during positioning of the patient will result in severe hypoxemia because ventilation will be limited to the left lower lobe only, and hence hypoxemia will not be effectively counteracted by the HPV. Also, overinflation by limiting ventilation to one lobe can result in catastrophic barotrauma. Achieving one-lung ventilation by a tracheal tube and bronchial blocker may be also complicated by severe hypoxemia and unilateral pulmonary oedema whenever suction via the bronchial blocker lumen in practiced while the cuff of the blocker is inflated before thoracotomy. In this situation, suction can result in excessive negative pressure within the lung resulting in excessive congestion of the lung complicated by unilateral pulmonary edema and severe hypoxemia. Also, prolonged suctioning even via the tracheal lumen during OLV can result in hypoxemia whenever ventilation is interrupted for a prolonged period, because the oxygen store will be limited to FRC of one lung only.

The factors that influence distribution of ventilation and perfusion are also important postoperatively. In adults with unilateral lung disease; gas exchange is optimal when the good lung is dependent (down with the healthy lung). In contrast, gas exchange in infants is optimal when the healthy lung is nondependent, a finding opposite to that achieved in adults. Ventilation may be distributed differently in infants and adults. The more unstable rib cage in infants result in a lower FRC close to residual volume, making airway closure likely to occur in the dependent lung, even during tidal volume breathing, and thereby redistribute ventilation
to the non dependent lung. It is not known at which age the adult pattern appear. It is suggested that during the postoperative period, the child with unilateral lung disease should be nursed in both the lateral decubitus position, as well as the supine position to determine the position of optimal gas exchange.

In conclusion, hypoxemia during one-lung ventilation can be predicted preoperatively by severity of the lung pathology, by lung scan, and by the oxygen saturation during two-lung ventilation. Whenever hypoxemia develops following one-lung ventilation, the proper position of the intubation device should be ensured by fiberoptic bronchoscopy. Also, protective ventilation strategy using inhalation anesthetic in 100% oxygen can improve oxygenation and decrease inflammatory mediators. In addition, cardiac output should be optimized, and severe hemodilution avoided. Whenever hypoxemia persists, two-lung ventilation must be resumed, and PEEP to the dependent lung optimized after recruitment. Applying CPAP using 100% oxygen to the nondependent non-ventilated lung may also improve oxygenation significantly. However, the technique is not welcomed during thoracoscopy since it will distend the lung on the operative side, and may interfere with the surgical procedure. NO inhalation can be also used to improve perfusion of the ventilated lung during one-lung ventilation. As a last resort, pulmonary artery clamping on the operated side by the surgeon can improve oxygenation by discontinuing perfusion of the non-ventilated lung, and shifting the cardiac output to the ventilated lung with a consequent decrease of shunt.

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References


THE FIRST INTERNATIONAL ANESTHESIOLOGY CONFERENCE: BEIRUT 1965

BERNARD BRANDSTATER
PROFESSOR OF ANESTHESIOLOGY
LOMA LINDA UNIVERSITY

After many years there are still among us a few senior colleagues who have recollections of the First International Anaesthesiology Conference held in Beirut October 30 to November 2, 1965. This assembly of physicians was a turning point for our specialty in the Middle East region, a foundational event that we should know about and remember. For the sake of nostalgia, and for the many new recruits who have joined our ranks since then, I want to place on record the story of that conference and the personalities who made it happen.

In 1964 I was a young department chairman at the American University of Beirut. I had recently returned from spending an exhilarating year as research fellow at the University of California, San Francisco. Under the watchful eye of Dr. Stuart Cullen who had earlier enjoyed a week-long visit to Beirut, I had immersed myself in the tedious experiments of the original MAC studies with Doctor Ted Eger, and also in studies of adaptation to high altitude with Doctor John Severinghaus. Both of these men were congenial but demanding teachers. In neighboring labs Dr. John Clements and his associates were making the first exciting discoveries of lung surfactant, and always in the background, encouraging and provoking us, was our famous Institute Director Dr. Julius Comroe. Here was a bracing intellectual climate that confronted me with the inevitable question: How could I convey even a small fraction of this energy and excitement back to Beirut, and also to other anesthesiology leaders in nearby countries?

This question still burned in my mind unanswered as I resumed my work at A.U.B. in 1964. And a partial answer came from an unexpected source: a visit by two representatives from ASTRA, the widely respected pharmaceutical company based in Sweden. These two persons were not your usual sales people. They were senior professionals in the company who had a more expansive vision than the immediate sales of their products. Looking at the big picture, they were devising strategies for long-term company growth; and for this to happen, they saw that a strong and flourishing anesthesiology specialty was needed. Perhaps their company could help. One of these visitors was Mr. Mogens Green-Petersen, a business executive from Sweden. The other was a surgeon, Doctor Halina Proscher. Her practice in cosmetic surgery was in Hamburg, but she also worked as a consultant to ASTRA. Her role was to speak as an equal medical colleague to doctors and professors.
Our first meeting was formal and routine, discussing the A.U.B. department, our teaching program, and what I could tell of the professors and teachers in other medical schools in the region. I had to admit I had almost no knowledge of colleagues in other universities, even close to Beirut. We were working separately, in isolation. But I did have some clinical interests which caught their attention. I seized the opportunity to describe my enthusiasm for continuous epidural analgesia in childbirth, and my own design and fabrication of a new disposable nylon catheter. I described my personal experience with the first one thousand epidurals in our hospital. Over several months, I had given all of them myself, remaining on-call 24 hours a day, so I could make mistakes and learn how to avoid them, and teach technique to others. Even before obstetric epidurals were introduced into Europe, these early trial cases were the first in our hospital and doubtless the first in the whole Middle East.

That conversation apparently stimulated some ideas in my visitors. ASTRA was a world leader in producing local anesthetic drugs, lidocaine and others; and epidural anesthesia was a prime use for them. They phoned me later and requested another meeting, this time over dinner. And it was at this second encounter that they unveiled a proposal in which they sought my help. They wanted to give anesthesiology a boost throughout the whole region. They described their impressions after visiting anesthesiology leaders in several countries. These included Lebanon, Syria, Egypt, Turkey, Iraq, Jordan and Iran. In these countries they had observed that anesthesiology was experiencing a painfully slow maturing as a proud and respected specialty. It was financially disadvantaged compared with some other specialties, and did not enjoy high public recognition and respect. The leaders in these countries, beyond expressing a vague paranoia, revealed a key handicap: they worked in isolation and were not acquainted with even their close neighbors. There was no feeling of a professional community that crossed national boundaries, no collaboration, no friendship and mutual stimulation, and little support.

The ASTRA duo informed me they were authorized to offer financial help towards developing a trans-national anesthesiology organization in which goodwill and collaboration could flourish. In an improved climate, proud professional excellence and high specialty standards could be more effectively promoted. They had in mind an initial conference to which would be invited the anesthesiology leaders from a long list of countries. They felt that Beirut, which in those days was a lively and popular tourist destination, would be a suitable place to hold the first conference. Did I see wisdom in such a plan, and would I be willing to help host such a conference, perhaps at the American University campus?

Guardedly I agreed that the proposal had merit; it seemed to be headed in the direction I had hoped for, following my invigorating year in San Francisco. By all means let us aim for professional excitement, collegiality, sharing of ideas and problems, even some rivalry, and work to build a regional community of academic friends. Perhaps here was a means for breaking out of the isolation that had restricted our growth for so long.

We took time out for thinking through the issues. Then we met again to develop a plan of action. An early result was to be a series of visits by myself, with the two ASTRA friends, to other centers, including Cairo, Damascus, Baghdad and Teheran. In due course, this tour did take place. At each center we made new friends and spoke hopefully of starting a new organization for anesthesiologists in the Middle East.

Because no one except the ASTRA representatives accompanied me on these visits, it seems worthwhile to mention some of the names of men, leaders in their time, who appear prominently in my memories of those early ice-breaking visits. In Cairo I was welcomed by Professor Mahmoud El Hakem, and toured Kasr El Aini Hospital. At Ain Shams University I was welcomed by Professor Wadid Bakhoum and by Doctor Shaker, who superintended a junior giving a spinal, using a needle of truly impressive size. At an evening meeting I met the energetic Dr. Adly Shirbini, and listened to an energetic lecture from a bright new faculty member recently returned from Liverpool, Dr. Anis Baraka. Also at that time I befriended the engaging Dr. Ezzat Abouleish. And at a later time I was impressed to see the accomplishments and professional standing achieved by the professor in Alexandria, Dr. Hashem Nassar.
This list of significant names is lengthened when we move to other major cities. Accompanied by Mr. Green-Petersen and Dr. Proscher, we three were received graciously everywhere, and my horizons were being constantly expanded. Barriers between neighbors were breaking down; our plan was working! Dr. Bourhan Abed in Damascus organized a meeting, and toured us through his department at the Mouasat Hospital. In Aleppo we met Doctor Kayyali, and I began a friendship with Professor M. Taha Jasser that has continued for many years since then. In Baghdad we had an evening reception where I made the acquaintance of Dr. Enaizi and Dr. Abdul Amir Al-Uzri. Further afield, in Teheran, I met Dr. Ali Farr, Dr. Fotoohi and Dr. Mohamed Tashayod. From Shiraz came Dr. Morteza Badii. On a separate trip I spent time in Istanbul, and established a personal relationship with Professor Sadi Sun and with Dr. Oner. Later in Beirut I met Dr. Ozdemir Demir from Ankara.

These men listed here greeted us in their home cities during those early first visits. They deserve to be placed on record here because they were true foundation-builders. In those years they were known and respected leaders in their own countries. But in the larger international world of anesthesiology most of them were not widely known. Today a new generation of able followers have taken their place. Yet we who are devoted Middle-Easterners must remember and honor them gratefully. They remained my good friends and supporters throughout my remaining years in Beirut.

Recognition must also be given here to my Lebanese associates and colleagues. Prominent among them were Dr. Adib Abu Haidar, Dr. Raymond Asmar, Dr. Robert Haddad, Dr. Wajih Sabbagh, Dr. Khattar Kanaan, Dr. Musa Muallem and Dr. Fouad Haddad. They were stout-hearted friends and supporters. Of course they had no understanding of the plans I was making, helped by ASTRA. And I suspect they were sometimes puzzled by my talk of bringing into existence a new organization that could win the enthusiastic support of diverse anesthesiologists from different lands and cultures.

I must confess that all of the persons named here are drawn wholly from my memory today, after the passing of nearly fifty years. Of course there were others, equally worthy of mention, whose names I do not recall at the time of this writing. I regret any such omissions. My contemporaries from that era may remind me of others who helped fight those early battles. I now gladly acknowledge the contributions of all who, named or not, helped during those early times of dreaming and hopeful planning. Here I am simply relating my main theme: How, with the help of my new ASTRA friends, I was able to quickly enlarge my circle of professional acquaintances in the Middle East. These personal connections were the foundation on which we hoped to build an effective community of colleagues. We were on our way.

I have tried to describe the state of anesthesiology in 1964, and my hope that we might make a bold new beginning. Those early visits to major cities were a necessary introduction. But much remained to be decided. My fellow-conspirators and I agreed that a regional society was the desired end-result, and we confidently expected this goal could be accomplished, given the goodwill we were experiencing on every side. We would call it “The Middle East Society of Anaesthesiologists”.

To get the ball rolling, we hoped to hold an international conference in Beirut in October-November 1965, the first ever held in the Middle East. ASTRA would provide funding, including travel and hotel costs, to bring together all the significant thought leaders from the whole region. In preparation beforehand, we would draft a proposed constitution for the Society, and get advance support for this by calling together a Constitution Planning Committee that would convene prior to the main Conference program in October. Later we decided we should start publishing a journal to serve as a communications link between our newly discovered friends and neighbors.

As these ideas took firm shape we became more excited. It seemed we were indeed giving birth to a new era for anesthesiology in our region. The organizing details were a huge task, almost entirely in the hands of our staff in the University department in Beirut. The program had to be put together, and it must include prominent leaders in our own countries, but also some distinguished leaders from Europe and North America. We needed some big names, to give the event some serious weight in the view of the wider observing community. We selected carefully some of the most
respected leaders in anesthesiology, and to the best of my recollection, every single one of them accepted warmly our invitation to share in a ground-breaking event. My office at A.U.B. was often swamped with mail, in the days before word processors and the internet.

It fell to my task to put together a conference program that gave prominence to our international guests. We had to design an attractive program book, and for this we needed a logo that might become, in time, a symbol of our new professional society. For this I sought help from the graphic artists connected with l’Imprimerie Catholique in Beirut. I told them (using my halting French) that historically the opium poppy had long been honored as the most effective source of pain relief. Could they please propose an image of a poppy, stylized in a way that was suitable for a logo. They came up with a poppy design that I liked. It made its first appearance on the cover of our program book, and ever since then it has been prominently displayed on the cover of the Middle East Journal of Anesthesiology. Inside our program book I boldly entered this dedication of the new logo:

Long before there was an anaesthesiologist, long before medicine became a science, when healing the sick called for both art and magic, the opium poppy was working its magic in the Ancient East, bringing comfort to the bodies of men, and to their minds peace. It was in our own countries that the poppy was first cultivated…in Persia, in Syria, in Asia Minor. This same flower, after thousands of years, still gives us our best analgesic drugs. We hail it as the symbol of the Middle East Society of Anaesthesiologists.

But this bold dedication to the proposed new Society turned out to be only a hopeful dream. When October 1965 came at last, our honored guests from other lands arrived, and our Constitution Planning Committee set to work. I thought we had drafted a fine constitution, and to win support for it we invited from London none other than Geoffrey Organe, the urbane, dignified President of the World Federation of Societies of Anaesthesiologists. He was the consummate diplomat, appointed to serve as the Committee chairman who could add his authority to the proceedings, and bring our new Society’s constitution to the assembled delegates for their approval.

But it did not happen this way. With all his august dignity and aplomb, Dr. Organe was no match in Committee for the complexities of the political sensitivities in our region. In our consideration of the constitution, any issue that involved national pride could not be compromised by a national spokesman. At a personal level our Committee members were gentle and good-humored colleagues. But back home they would be accountable to political authorities, and they could not publicly sign off on the draft constitution we had set before them. Unresolvable differences arose over such issues as naming the famous Gulf either the Persian Gulf or the Arabian Gulf. To some it may seem a trivial detail, but not to them. When national pride and sensitivity were at stake, no one could yield. In short order Doctor Organe was out of his depth, unable to steer the discussion towards a workable conclusion. The prickly politics were too much for him.

Throughout these lively discussions my heart sank. I was present and witnessed it all. Desperately I sought for a compromise, a way to emerge with the functions and benefits of a society, even if there was no agreed constitution. And that was my final plea. The anatomy of a society was not as important as its physiology, what it actually accomplished. Let us move forward and organize international congresses. Let us visit one another’s departments, and invite neighbors to come as visiting lecturers. And by all means let us take steps to publish a journal that could be an effective voice, a link to join us together in a common bond of friendship and collegiality, neighbors with shared interests and similar goals. This was the decision that finally came out of the Planning Committee’s deliberations.

Meanwhile the First International Conference, the main public event, moved forward, convening immediately on the heels of our frustrating impasse in the Constitution Planning Committee. Simply stated, it was a great success, richly enjoyed by all who were lucky to be there. By my count the registrants numbered 127, and came from 21 different countries. Lectures were given in Dodge Hall on the campus of the American University of Beirut. We were welcomed by the Lebanese Minister of Health Dr. Knio, and music was provided by the Lebanese Military Brass Band. Dignitaries from the Government and the University
graciously appeared at our opening ceremony.

In my judgment the lectures were excellent, the subjects treated being appropriate for that era, a time of simpler technology. In addition to delegates from Middle East countries, we welcomed a galaxy of outstanding speakers from far afield, men whose names were household words amongst anesthesiologists everywhere. Sir Robert Macintosh came from Oxford, in addition to his fellow-Brits Geoffrey Organe from London and Bruce Scott from Edinburgh. The great Martinson-Holmdahl was there from Uppsala. Bill Hamilton came from Iowa, and Guy Vourc'h from Paris. From Copenhagen came J. Kirchhoff and H. Engell, both of them connected with the notorious W.H.O. anesthesiology course in their city. By any standards, this was a distinguished assembly.

Naturally at this event the traditional Lebanese hospitality was on prominent display. The social program was a delight. Participants took tours to Biete'ddine and to Baalbek, and there was a reception at the Phoenicia Hotel. As a final celebration there was a dazzling banquet and floor show at the famed Casino du Liban. In all my many years of attending conferences, I cannot remember another medical meeting that matched this one. It was big enough to be serious, yet small enough to get to know everyone. There was great congeniality and a sheer pleasure at being together, of making new friends after many years working in isolation. I have a treasured photograph of Sir Robert standing amongst the gigantic stones of Baalbek. After many years I visited him in his Oxford home. Though he was then in his nineties, his mind was clear, and he reminisced warmly about his memorable time with us in Beirut.

So were our hopes and our goals achieved? Some of them undoubtedly were. Friendships and next-door collegiality sprang into existence where it had not existed before. We showed that international conferences could accomplish many good things for our profession; they should become a planned part of our scholarly agenda. Our ASTRA friends were at first perplexed that the Planning Committee had not completed all of its task. But in time they came to agree that we could proceed to live and plan as if a Middle East Society did exist, but without formal membership and subscriptions. We could carry out its functions, plan conferences, and eventually publish a journal, the Middle East Journal of Anaesthesiology. We could do all this with or without a constitution, and cultivate simple good-neighborliness. They gave strong encouragement to me, since the Committee had entrusted to me the task of designing and publishing a journal. During the three years I served as the Journal's Founding Editor, ASTRA continued their generous support, through paid advertisements and other means.

I still have in my possession a copy of the program book prepared for that First International Conference. It is a monument to much hard work, and to the vision and dreams of many good friends who helped make the event the delightful success that it became. But for me, the book is also a monument to a remarkably rich teamwork that developed between myself and the representatives of ASTRA. I could not have asked for more helpful and understanding collaborators. For me they represented an admirable relationship of mutual respect, the kind that is possible and should be expected between physicians and the companies that supply their drugs.

In recent years there has developed a climate of suspicion in which profit motives of industry are viewed as sinister, possibly hostile to the noble ideals of medical science.

These suspicions, so prevalent in Euro-American culture, lack balance. Economic interests are legitimate and should be respected, transparent and not resented. When openly recognized they need not threaten our professional autonomy or judgment. My experience working closely with a major drug company in 1964-65 was one of mutual respect and pleasurable teamwork. It was clear to all that ASTRA would win new friends and achieve greater visibility by helping anesthesiology to flourish in the burgeoning Middle East. The Company's goals overlapped with those of our young specialty. To launch new initiatives, and to break out of our old constrictedness...these were equally our goals in universities, in operating theaters and also in Company boardrooms. We were moving in the same direction, and we needed each other.

After these many years I salute those friends in industry who perceived our needs in 1964 and were willing to contribute financial resources and also add their unique suggestions on how best to promote...
forward progress in anesthesiology. They made possible some memorable firsts for anesthesiology in the Middle East. Their vision and our dreams coincided ideally, in the quest for excellence that we shared. The spirit of hope and expectation and trust that we shared then, allied with focused hard work, remains for me as a splendid example of altruism at its finest.

Time has marched on. Political and cultural strife has sadly clouded the atmosphere in some of the lands that were represented so happily at the 1965 conference. There is still no Middle East Society of Anesthesiologists, but we press forward without it. There are some national societies, and there have been energetic Pan-Arab congresses. Our early isolation is a thing of the past. One noteworthy success has been the continuing vigor of The Middle East Journal of Anesthesiology. Published first in 1966 following that first International Conference, I was pleased in 1969 to entrust its editing and management to Dr. Anis Baraka and his associate Dr. Fouad Haddad. After many years of superb work they in turn have passed the torch to Dr. Ghassan Kanazi and his team at the American University of Beirut. It serves a diverse community of clinicians and thought-leaders in many countries. May it long continue and flourish.

The science and technical sophistication of anesthesiology have come a long way since 1965. My hope and my prayer is that those advances on the technical side will be matched by a parallel and equal devotion to the ethics of medicine, to the dignity and value of human life, and to the ideals of selfless service to those who need our help. At our conference in 1965 we heard references to our ancient forefather, Hippocrates. In his clinic and school for physicians on the Greek island of Kos, he was located close to us in Beirut. Now, decades after our conference, let us resolve to preserve the spirit and ideals of that ancient master in our hospitals, and especially in our hearts. We must insist, as did the ancient Greek, on the high value of all human life. Compassion and devoted service should be our constant guiding torch, especially when the political climate seems to be threatening. Before God and before all mankind, the relieving of pain and the safeguarding of life are goals that belong to no single race or color, language or culture. They belong to all of our human family.

Bernard Brandstater
November 2013
EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE ON POSTOPERATIVE PAIN FOLLOWING SPINAL ANESTHESIA. A RANDOMIZED DOUBLE BLIND CONTROLLED STUDY

Mahendra Kumar*, Neha Dayal**, R.S. Rautela***, A.K. Sethi*

Abstract

Background: Magnesium sulphate (MgSO₄), NMDA receptor antagonist, is known to reduce perioperative requirement of anesthetics and analgesics. However, no studies assessed the effect of MgSO₄ on onset and recovery from spinal anesthesia. A prospective, randomised, double blind study was designed to assess the effect of intravenous (IV) MgSO₄ on onset and recovery from spinal anesthesia and post operative analgesic requirement following below umbilical surgery.

Methods: Sixty patients (ASA class I & II) were selected randomly and divided into two groups. Patients were given either MgSO₄ 50mg kg⁻¹ in 10mL within 10min, followed by an infusion of MgSO₄ 10mg kg⁻¹ hr⁻¹ IV in 4mL (MG group) for 12 hrs or normal saline in same volume and rate for 12 hrs as used in MG group (NS group). After initiating the infusion, spinal anesthesia was given with 0.5% bupivacaine (Hyperbaric) 2.5mL at L3/4 or L4/5 space. Time taken for sensory block at the level of T-10 and motor block (modified Bromage Score-1) was noted. Postoperatively, time taken for recovery from spinal anesthesia, pain score and requirement of postoperative analgesic in 24 hours were observed and compared between the two groups.

Results: The first rescue analgesia was required after 334 ± 202 min in MG group and after 233 ± 141 min in NS group with significant difference (p <0.05). The morphine required over 24 hours for analgesia was significantly less in MG group (3.99 ± 1.25 mg) as compared to NS group (7.13 ± 2.68 mg) (p <0.000).

Conclusion: Intravenous MgSO₄ improves postoperative analgesia without affecting the onset and recovery from spinal anesthesia.

Key words: Magnesium sulphate, spinal anesthesia, postoperative analgesia.

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Introduction

Post operative pain may result into various physiological changes with physical and psychological trauma. Various techniques and drugs are used to make a patient pain free in the post operative period. Magnesium sulphate (MgSO₄), a NMDA receptors antagonist, has been tried to control perioperative pain by modifying the pain mechanism. Search of literature shows many studies assessing the analgesic effect of magnesium sulphate following general anesthesia. Only few studies assessed the effect of magnesium sulphate on postoperative pain following regional anesthesia. However to our knowledge, no studies have evaluated the effect of MgSO₄ on the onset and recovery from spinal anesthesia as well as postoperative pain control. The aim of the present study is to assess the effect of intravenous magnesium sulphate on onset and recovery of spinal anesthesia and postoperative analgesic requirement following below umbilical surgery.

Methods

After getting approval from institutional research board, sixty adult patients of either sex, aged 18-60 yrs, to ASA class I and II with the ability to understand the Visual Analogue Scale, scheduled for elective below umbilical surgery under spinal anesthesia were selected randomly. All patients were asked to give informed consent to participate in the study. Patients having compromised renal, hepatic, cardiac functions, bleeding disorder, skeletal muscles disorder or any other neurological deficit or not willing to participate in the study were excluded. Patients on alcohol, analgesics, narcotics or any other drug containing magnesium were also excluded from the study. The selected patients were randomized by blocks into two equal groups.

The demographic parameters of each patient were recorded. Continuous monitoring of electrocardiograph (ECG), heart rate, non-invasive blood pressure (NIBP - systolic, diastolic and mean arterial blood pressure) and pulse oximetry (SpO₂) was started and continued throughout the study period by using Colin-BP 508 monitor.

Patients of MG group were pre-treated with magnesium sulphate 50 mg kg⁻¹ body weight intravenously (IV) in 10 ml volume over 10 minutes, followed by IV infusion of 10 mg kg⁻¹ hr⁻¹ in 4 ml for 12 hrs. Similarly, patients of NS group received normal saline 10 ml IV within 10 min, followed by IV infusion of normal saline 4 ml hr⁻¹ for 12 hrs. Infusion was given by using Soveta-S1 syringe infusion pump. After initiating the infusion, as per the group allocated, fluid co-loading was started with 500 mL ringer lactate solution. Spinal anesthesia was administered to each patient with 0.5% heavy bupivacaine 2.5 ml at L3-L4 or L4-L5 intervertebral space in the sitting position using a midline approach with a 25 G Whitacre needle. Level of sensory block by pin prick method and motor block by modified Bromage score was assessed at every 2 minutes following subarachnoid injection, and the time taken to achieve complete loss of sensations up to T-10 level and complete motor block (modified Bromage score-1) was noted. Surgery was allowed when there was no sensation. Oxygen 4L/min through face mask and adequate fluid therapy was given to all patients.

Postoperatively, block was assessed every 15 min

<table>
<thead>
<tr>
<th>Demographic profile of the two groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group MG</strong></td>
</tr>
<tr>
<td><strong>(n = 30)</strong></td>
</tr>
<tr>
<td>Age (Yrs)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>M:F</td>
</tr>
</tbody>
</table>

(p-value <0.05 significant)
EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE ON POSTOPERATIVE PAIN FOLLOWING SPINAL ANESTHESIA: A RANDOMIZED DOUBLE BLIND CONTROLLED STUDY

and time taken for regression of sensory block to the level of L-1 and recovery of motor block to modified Bromage score 6 was noted. Pain at rest was assessed by using the visual analogue scale (VAS) every 30 minutes for three hours and then every three hours for next 21 hours (total 24 hours). Rescue analgesia was given in the form of morphine 0.05 mg kg⁻¹ body weight IV when VAS score was more than 3. Period of analgesia (from the time of subarachnoid injection to the time of first rescue analgesia required) and total requirement of analgesic in 24 hours was recorded. Both the observer of the parameters and the patient were blind to the drug injected IV and in the subarachnoid space. The collected data were statistically analyzed by using ‘repeated measures ANOVA test’ and Group ‘t’ test.

### Results

Demographic data was statistically comparable for both groups (p > 0.05) (Table 1). There was no statistical difference between two groups for their mean time required to achieve complete sensory block up to the level of T-10, motor block to modified Bromage score -1, complete recovery from sensory block to the level of L-1 and complete motor recovery to modified Bromage score-6 (p > 0.05) (Table 2). The period of analgesia (the time interval between subarachnoid injection and requirement of first rescue analgesic) was longer in MG group (333.91 ± 202.41 min) as compared to NS group (232.68 ± 140.62 min) with statistical significant difference (p value < 0.05) (Table 2). The mean postoperative rescue analgesia requirement

### Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group MG (n = 30)</th>
<th>Group NS (n = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min) taken to achieve-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory block up to T-10</td>
<td>7.47 ± 2.67</td>
<td>7.93 ± 3.25</td>
<td>0.54</td>
</tr>
<tr>
<td>Motor block to MBS-1</td>
<td>8.13 ± 1.96</td>
<td>8.33 ± 2.17</td>
<td>0.70</td>
</tr>
<tr>
<td>Time (min) taken for recovery from</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory block to L-1</td>
<td>237.10 ± 37.19</td>
<td>242.80 ± 23.88</td>
<td>0.48</td>
</tr>
<tr>
<td>Motor block to MBS - 6</td>
<td>227.87 ± 31.61</td>
<td>270.40 ± 24.87</td>
<td>0.39</td>
</tr>
<tr>
<td>Duration of post operative analgesia (min)</td>
<td>333.91±202.41</td>
<td>232.68±140.62</td>
<td>0.04</td>
</tr>
<tr>
<td>Total morphine (mg) required in 24 hrs</td>
<td>3.99 ± 1.25</td>
<td>7.13 ± 2.68</td>
<td>0.000</td>
</tr>
</tbody>
</table>

(p value: <0.05 significant difference, < 0.000 highly significant difference)

(MBS-Modified Bromage Score).

### Table 3

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Group MG</th>
<th>Group NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inguinal hernioplasty</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Appendicectomy</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Patellar fracture-(Wiring)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Varicose vein-ligation</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Below knee amputation</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Interlock nailing-tibia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Fistulectomy</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

**Modified Bromage Score**

1- Complete block (unable to move feet and knees).
2- Almost complete block (able to move feet only).
3- Partial block (able to move knees).
4- Detectable weakness of hip flexion while supine (full flexion of knees).
5- No detectable weakness of hip flexion while supine.
6- Able to perform partial knee bend.
Post operative pain is associated with physical and psychological trauma\(^1\), it is treated with various drugs and techniques to make a patient pain free\(^2\). Magnesium sulphate has been tried to control perioperative pain by modifying pain mechanism. Magnesium sulphate is a noncompetitive NMDA receptor antagonist \(^3\) having antinociceptive effects by two mechanisms: i) it prevents central sensitization which occurs due to peripheral nociceptive stimulation\(^4\), ii) it also acts as physiological calcium antagonist by inhibiting calcium entry inside the cells at different voltage gated calcium channels by blocking NMDA receptors\(^5\).

During the study, no side effects of magnesium sulphate were observed except for burning sensation in four patients at the injection site.

Discussion

Post operative pain is associated with physical and psychological trauma\(^1\), it is treated with various drugs and techniques to make a patient pain free\(^2\). Magnesium sulphate has been tried to control perioperative pain by modifying pain mechanism. Magnesium sulphate is a noncompetitive NMDA receptor antagonist\(^3\) having antinociceptive effects by two mechanisms: i) it prevents central sensitization which occurs due to peripheral nociceptive stimulation\(^4\), ii) it also acts as physiological calcium antagonist by inhibiting calcium entry inside the cells at different voltage gated calcium channels by blocking NMDA receptors\(^5\).

It has been used as an adjuvant to the analgesics
and anesthetic agents for intra and postoperative analgesia\(^6,7\). Intravenous administration of magnesium sulphate as bolus and intraoperative infusion during general anesthesia reduces the requirement of narcotics and anesthetic agents with low postoperative pain score\(^6,7,8,9\). Comparing magnesium sulphate to fentanyl showed better intraoperative antinociceptive efficacy of intravenous magnesium sulphate\(^10\). Postoperative morphine requirement has been reported progressively higher following fentanyl as compared to magnesium administration\(^15\).

Only few studies are available with the use of magnesium sulphate following regional anesthesia as compared to general anesthesia. In these studies it was observed that administration of magnesium sulphate as bolus followed by IV infusion under spinal anesthesia was associated with postoperative increased time to analgesic requirement, significantly lower pain score and lower cumulative patient controlled analgesia (PCA) drug consumption\(^12,13\).

But observations of Ko et al were different in this regard, they did not find any reduction in postoperative cumulative analgesic dose requirement with a bolus of intravenous magnesium sulphate followed by infusion in the patients undergoing abdominal hysterectomy under epidural block\(^14\). The difference might be due to the short duration of infusion (6 hours) of magnesium sulphate while pain assessment was done for a prolonged postoperative period (72 hrs).

In our study, the mean time required for the achievement of a sensory, a motor blockade and their recovery in both groups was comparable. Hemodynamic parameters of both groups were also comparable and no patient developed hypotension in any group. As compared to those who received normal saline, patients who received MgSO\(_4\) had a longer duration of post-operative analgesia and required lower doses of morphine. Serum magnesium levels could not be done, but no patient showed any clinical sign of hypermagnesemia. In the literature, many studies have shown that the use of magnesium sulphate in the dose of 40-60 mg kg\(^{-1}\) did not show any clinical sign of hypermagnesemia, even after infusion of magnesium sulphate for many hours\(^6,7,15,16\). In the presence of a normal renal function, magnesium is rapidly eliminated. Magnesium is safe to use, its toxicity begins at the concentration of 2.5-5 mmol L\(^{-1}\), which is much higher than the levels observed (maximum level 1.5 ± 0.2 mmol L\(^{-1}\)) in other studies following magnesium sulphate administration\(^15,17\).

In our study, we used a bolus of magnesium 50 mg kg\(^{-1}\) followed by 10 mg kg\(^{-1}\) hr\(^{-1}\) infusion which was supposed to be a safe dose referring to the results of the above mentioned studies\(^15,17\).

Thus observations of our study suggest that IV bolus (50 mg kg\(^{-1}\)) and infusion (10 mg kg\(^{-1}\) hr\(^{-1}\)) of magnesium sulphate is safe to use; it improves postoperative analgesia and reduces analgesic requirement without having any effect on onset and recovery from spinal anesthesia.
References


LOW CONCENTRATION LIDOCAINE (0.5%) BOLUS EPIDURALLY CAN INITIATE FAST-ONSET, EFFECTIVE AND SAFE ANALGESIA FOR EARLY STAGE LABOR

HENRY LIU* 1,2, SHANGLONG YAO**1, FRANK ROSNIA*2

Abstract

There is no consensus on the optimal local anesthetic agent to initiate labor analgesia for patients in active labor. Currently used local anesthetic agents for initiating labor analgesia include 0.25% bupivacaine, 0.5% bupivacaine, 0.2% ropivacaine without or with various types and doses of opioids. All these agents are administered in incremental doses and are relatively “slow onset” in initiation of labor analgesia. We used 0.5% lidocaine 10ml as the loading dose given as an epidural bolus to initiate epidural analgesia for patients in early stages of labor. We included 32 cases (16 in Lidocaine group and 16 in Bupivacaine group). We found that 0.5% lidocaine is fast-onset, very effective and safe in initiating epidural analgesia for early stage labor.

Introduction

There is no consensus on the optimal local anesthetic agent to initiate labor analgesia1,2,3,4,5. The commonly used agents include 0.25% bupivacaine, 0.5% bupivacaine, and 0.2% ropivacaine with or without various types and doses of opioids and other adjuncts3,4,5,6,7. However all these analgesia-inducing local anesthetic agents/techniques are believed to be slow in initiating labor analgesia, which has led to the gaining popularity of combined spinal and epidural (CSE) analgesia in recent decades5,8,9. Nevertheless CSE has its intrinsic drawbacks: the potentially increased risk of postdural puncture headache10, fetal heart rate changes8,11, pruritus related to intrathecal opioids12, untested epidural catheter if local anesthetic agent is used intrathecally, undetermined amount of local anesthetic agent migrating into intrathecal space after epidural bolus or infusion and other potential problems13,14,15. There is an additional concern for those who use intrathecal opioid for their CSE: opioids are controlled substances with controlled access, certain amount of time is needed to sign out opioids, so the faster onset after intrathecal injection could be offset by the additional time needed to obtain opioids. And the time for the onset of analgesia in laboring parturients should be the total time from anesthesia team is consulted/requested for labor analgesia to the time the patient experiences analgesia and reasonable pain relieve. Since anesthesiologist needs to go to drug-dispensing machine to get opioid, the time spent in the process will be counted to the total time. It won’t be unusual if the total time for dispensing opioids, the insertion of

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CSE, and injection of opioid is longer than regular epidural catheter placement and bolus dose of local anesthetic agent and achieving reasonable analgesia. In 2006 Nafisi found that 1% lidocaine is effective for labor analgesia\textsuperscript{16}. It is well documented that lidocaine is faster in onset of analgesia than bupivacaine\textsuperscript{17}, and bolus of the loading dose at once will achieve even faster analgesia than giving incrementally, as we noticed from our practice. However 10ml loading dose of 1% lidocaine cannot be given with single injection, because 100mg total lidocaine dose is not safe if given intrathecally by accident. It may cause high or total spinal anesthesia. We hypothesized that labor analgesia can be safely induced with bolus loading dose of 10ml 0.5% lidocaine (total 50mg lidocaine), which should be relatively safe even if it is accidentally injected intrathecally. So we conducted this small sample-sized pilot study to investigate the efficacy and safety of 10ml 0.5% lidocaine as a bolus dose to induce labor analgesia, and we found that this strategy was effective and safe in initiating labor analgesia. In this pilot study of prospective nature we compared 10ml bolus of 0.5% lidocaine to 10ml of 0.25% bupivacaine in initiating labor analgesia.

**Methods**

We randomized 32 parturients who are in active labor into two groups: Lidocaine group and Bupivacaine group. This study was approved by our Institutional Review Board. Written consents were obtained from all patients prior to inclusion in the study. Patients in Lidocaine group received 10 ml of 0.5% lidocaine as the bolus loading dose (n = 16), and the Bupivacaine group received 0.25% bupivacaine 10 ml as the bolus loading dose for their labor epidural (n = 16). A pre-epidural intravenous fluid loading was given to both groups. All patients were in sitting position when epidural catheters were placed by the same anesthesiologist. After sterile preparation of the skin and local anesthetic infiltration of skin wheals at L3, L4 level, \#17G Tuohy needle was inserted into epidural space with the technique of "loss of resistance" with 2ml air. The epidural catheter was threaded 4 cm into the epidural space. Then 10ml of 0.5% lidocaine or 10ml of 0.25% bupivacaine was epidurally injected respectively in Lidocaine group or Bupivacaine group. A continuous infusion of 0.2% ropivacaine at 14 ml per hour was used for both groups and started as soon as patient lays down from sitting position. After the injection of the loading dose of local anesthetic agents, a senior anesthesiologist examined the patients to get the following parameters: sensory blockade is assessed with pinprick technique; motor blockade is graded according to Bromage Scores (I = free movement of legs and feet, II = free movement of feet, only flex knees, III = free movement of feet, unable to flex knees, IV = unable to move legs and feet)\textsuperscript{18}; pain relieve is assessed by asking patient “do you feel better now or not yet?”, the time was documented when patient reported “feeling better”.

We documented patients' age, height, and body weight; the total volume of pre-epidural intravenous fluid loading; the cervical dilatation status indicating the stage of laboring process; the time from skin preparation to epidural loading dose injection to reflect the technical difficulties of the epidural placement; the time patient started feeling better or achieving pain relieve; and the time the sensory blockade level to reach stable levels.

For the comparison of age, height, body weight, pre-epidural fluid loading volume, the time from skin preparation to epidural loading dose injection, and cervical dilatation (in centimeters), we used Student T test for statistical analysis. For the comparison of the time to start feeling analgesia, and the time to achieve stable levels, we used Wilcoxon method for statistical analysis. For the analysis of delivery methods, total top-off doses and the incidence of motor blockade, we used Chi-Square Test. For all the statistical analyses, \( P <0.05 \) is considered significant.

**Results**

Pre-epidural intravenous fluid loading was given to both groups, Lidocaine group received 1537 ± 144.6 ml on average and the Bupivacaine group received 1418 ± 187.8 ml on average (\( P = 0.62 \)). The cervical dilatation when epidural catheter was placed was 3.44 ± 1.9 cm for Lidocaine group and 3.38 ± 1.15 cm for Bupivacaine group (\( P = 0.99 \)). There were no statistically significant differences in age, height or
LOW CONCENTRATION LIDOCAINE (0.5%) BOLUS EPIDURALLY CAN INITIATE FAST-ONSET, EFFECTIVE AND SAFE ANALGESIA FOR EARLY STAGE LABOR

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weight between the two groups (Table 1). The time from skin preparation to epidural loading dose injection were 4 ± 1.21 minutes in Lidocaine group and 4.81 ± 2.56 minutes in Bupivacaine group (P = 0.26). We did not experience significant technical difficulties in placing the epidural catheters in both groups.

The number of top-up doses, the onset time of pain relieve, the time of sensory blockade to reach stable level, and the rate of cesarean section between the two groups were listed in Table 2. There were statistically significant differences in the onset time of pain relief, 2.88 ± 0.89 minutes in Lidocaine group and 4.81 ± 1.56 minutes (P <0.0001) and incidence of motor blockade between the two groups, Lidocaine group zero while Bupivacaine group had 6/16 (P <0.01). All motor blockades observed in the Bupivacaine group were Grade II on the Bromage Score. Other documented parameters included hematocrit (33.58 ± 3.9 in Lidocaine group, 34.69 ± 3.16 in Bupivacaine group, P = 0.4) and platelet count (211.69 ± 43.78 in Lidocaine group and 232.06 ± 43.06 in Bupivacaine group, P = 0.19), no significant differences between the two groups.

Discussion

The ultimate goal in obstetric anesthesia is to achieve safe and fast relieve of labor pain. The onset time to achieve analgesia should not only be the time from injection of anesthetic agents (opioids and/or local anesthetic agent) to pain relieve. Obstetric anesthesia service should target the shortest time between anesthesia team is consulted/requested for epidural placement to the time patient achieves reasonable analgesia. The agents used via traditional epidural catheter are believed not fast enough to initiate labor analgesia, thus CSE is designed to achieve faster onset by injecting local anesthetic agent or opioids into intrathecal space. However, CSE does have its intrinsic drawbacks: if local anesthetic agent is used intrathecally, it is very difficult to test the epidural catheter placement, because the intrathecally injected local anesthetic agent will produce sensory and/or motor blockade; the potentially increased risk of postdural puncture headache, though this has not been confirmed by meta-analyses if opioids is used intrathecally, patient may complain pruritus, fetal heart

Table 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Hematocrit</th>
<th>Platelet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>24.9 ± 5.3</td>
<td>161.6 ± 7.8</td>
<td>85.9 ± 21</td>
<td>33.58 ± 3.92</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>23 ± 4.9</td>
<td>161.3 ± 6.1</td>
<td>82.5 ± 20</td>
<td>34.6 ± 3.16</td>
</tr>
<tr>
<td>P value</td>
<td>0.33</td>
<td>0.9</td>
<td>0.64</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Cervix dilation (cm)</th>
<th>Time to pain relieve (min)</th>
<th>Motor blockade</th>
<th>Top-up injection</th>
<th>C-section rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>3.44 ± 1.93</td>
<td>2.9 ± 0.9</td>
<td>0/16</td>
<td>4/16</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>3.38 ± 1.81</td>
<td>4.8 ± 1.6</td>
<td>6/16</td>
<td>3/16</td>
</tr>
<tr>
<td>P value</td>
<td>0.99</td>
<td>0.00017</td>
<td>0.01</td>
<td>0.67</td>
</tr>
</tbody>
</table>

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rate changes and other symptoms; if opioids is used, anesthesia provider(s) needs to spend some time to obtain opioids from a dispensing machine/storage. This process will take some time and delay the combined spinal and epidural placement in some hospitals; there will be some local anesthetic migration into intrathecal space after initiation of continuous epidural infusion, the rate and total amount of this migration will be very difficult to assess\textsuperscript{13,14,15}, this may necessitate the dose adjustment of continuous epidural infusion. The dose adjustment can be very difficult because it is extremely difficult to quantify how much local anesthetic agent will diffuse into the intrathecal space via the dural puncture. Currently epidural analgesia in many medical centers is usually initiated with a loading dose of 10-12 ml 0.25% bupivacaine, 0.2% ropivacaine, less popularly with 0.5% bupivacaine, or 1% lidocaine with or without opioids, in 3-5ml incremental boluses. The problems with this traditional epidural technique are its slow onset of analgesia and potential motor blockade. As we notice from our practice, bolus of the whole loading dose will induce analgesia faster than incremental boluses, especially when we inject with slightly higher pressure. Unfortunately the above-mentioned commonly-used loading dose agents are not safe to be injected epidurally as a bolus because if the catheter is accidentally placed intrathecally, the loading dose will induce high or total spinal anesthesia, which can be detrimental to the parturients. This led us to test 0.5% lidocaine 10ml bolus injection to initiate labor analgesia. Injection of 0.5%lidocaine 10ml as an epidural loading dose can be relatively safely because even if the total 50mg lidocaine loading dose is accidentally given intrathecally, patient will likely develop spinal anesthesia, but the risk of high spinal or total spinal anesthesia will be significantly minimized. However, bolus injection of 0.25% bupivacaine 10ml as the loading dose is not within the scope of standard practice, though some anesthesiologists do give bolus of 0.25% bupivacaine 10ml epidurally. We used 0.25% bupivacaine as control group so we could compare the onset time of analgesia and incidence of complications. The epidural catheter placement in this study was executed by one senior experienced obstetric anesthesiologist, and if the anesthesiologist encountered any technically difficult or felt possible misplacement, 0.25% bupivacaine wouldn’t be given as bolus, and the case would be excluded from the study, but this did not happen during this pilot study.

This study showed that 0.5% lidocaine caused significantly less motor blockade than 0.25% bupivacaine. Lidocaine group did not have any motor blockade (0/16) while 0.25% bupivacaine group had 37.5% (6/16) Grade II motor blockade. We are not sure whether bolus dose of 10ml 0.25% bupivacaine increased the incidence of motor blockade or not comparing with incremental doses of 0.25% bupivacaine with a total volume 10ml. Our result indicated that lidocaine group achieved significantly faster onset than 0.25% bupivacaine group (2.9min versus 4.8min, $P < 0.001$). With an onset time of analgesia reported by patients as quick as 2.9 min on average, 10ml 0.5% lidocaine loading dose given as a bolus will be indicated for those patients in early stage of labor, if this technique can be validated by larger scale clinical trials for its efficacy and safety. However, 0.5% lidocaine 10ml loading dose given as a bolus epidurally may or may not be adequate for more severe pain experienced by patients in later stage of labor. This needs to be elucidated by further investigations. The rate of cesarean section can be related to different techniques of epidural analgesia, but it can also be dependent upon the tradition of the obstetric team.

**Conclusion**

The result of this small pilot study indicated that loading dose of 0.5% lidocaine 10ml given epidurally as a bolus injection can induce fast onset of labor analgesia. This technique can be used effectively and safely in initiating epidural analgesia in early stage labor.
LOW CONCENTRATION LIDOCAINE (0.5%) BOLUS EPIDURALLY CAN INITIATE FAST-ONSET, EFFECTIVE AND SAFE ANALGESIA FOR EARLY STAGE LABOR

References


JAHAN PORHOMAYON*, PAMELA K. WENDEL**, LESLIE DEFRANKS-ANAIN***, KAY B. LEISSNER****, NADER D. NADER*****

Abstract

Objectives: The primary goal of this study was to assess the impact of airway devices on the incidence of nausea after knee arthroplasty and their interaction with the use of nitrous oxide.

Methods: Charts were reviewed for 499 patients after knee arthroplasty under general anesthesia. Demographic data, type of airway device, nitrous oxide, sevoflurane, desflurane, isoflurane, fentanyl, metoclopramide, ondansetron, dexamethasone, rocuronium and neostigmine were analyzed. Fisher’s exact test was used to compare the categorical factors and t-test was used for continuous variables. Sinclair scores were used for post-operative nausea and vomiting (PONV) risk stratification. Multivariate logistic regression model was constructed to identify the factors contributing to the frequency of PONV.

Results: PONV was documented in 10.3% of patients. Nitrous oxide was associated with a higher frequency of PONV than those received air mixture (12.5% vs. 8.7%, P < 0.01). Prior to risk stratification, the frequency of PONV was 17% in the endotracheal tube (ETT) vs. 6.7% in the laryngeal mask airway (LMA) group (P < 0.01). Sinclair score was 0.51 ± 0.17 for the ETT group and 0.74 ± 0.12 for the LMA group (P <0.001). After risk stratification and matching, the incidence of PONV was 15.8% with the use of ETT compared with 7.9% for LMA (P <0.05).

Conclusion: The frequency of PONV was almost twice with ETT as with LMA. Longer duration of anesthesia, neuromuscular blockade and non-standardized antiemetic regimen may have contributed to the increase PONV in ETT group. Prospective randomized studies are necessary to further explore whether and to which extend airway devices influence the incidence of PONV.

Key words: postoperative nausea, vomiting, anesthesia, nitrous oxide, adult males

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Introduction

Post-operative nausea and vomiting (PONV) is a common occurrence that can lead to additional escalated care and increased costs, as well as discomfort to the patient. There are known risk factors for PONV\(^1\),\(^2\), but the role of airway devices on PONV is less clear\(^1\). Previously published conflicting results in regards to the influence of airway device on PONV are outlined in Table 1. PONV can increase length of stay in the post-anesthesia care unit (PACU)\(^1\),\(^2\).

Nader et al. reported that barometric changes in the middle ear pressure upon discontinuation of nitrous oxide anesthesia could predict PONV\(^3\). The authors specifically demonstrated that the gradient in the middle ear pressure was greater with the use of nitrous oxide, and therefore a larger gradient was associated with PONV. Increased PONV with the use of nitrous oxide is possibly dose-dependent. This occurrence was also found in another study that looked at gynecological surgeries\(^4\), and in a study that measured specifically severe PONV\(^5\).

In a single-blinded, randomized, controlled study, Swann et al. found a higher incidence of PONV in patients with laryngeal mask airways (LMA) than those with endotracheal tubes (ETT) following inhalational anesthesia with nitrous oxide\(^6\). Nader et al. noticed a trend in use of a LMA increasing the pressure gradient in the middle ear compared with the use of an ETT\(^3\). The possible mechanisms may have been related to the obstruction of Eustachian canal or stimulation of different parts of the airway. However, this difference did not reach statistical significance in regards to the incidence of PONV. Another study contradicted this finding, concluding that middle ear pressure did not change with the choice of airway device\(^7\). Yet, this study did not specifically address the issue of PONV in relationship to the various airway devices or gaseous agents used. The same author reported that LMA reduced the absolute risk of PONV by 40% in comparison to ETT in females undergoing general anesthesia without nitrous oxide\(^8\).

Other investigators have demonstrated that in otologic surgeries the use of ETT versus LMA created no statistically significant difference in terms of PACU recovery time and PONV. Therefore, the multiplicity of factors involved in PONV and the contradicting results in the literature left the possibility that selection of airway device may change the incidence of PONV [Table 1]\(^9\),\(^10\).

We undertook this retrospective review to assess the differences in the incidence of PONV between the LMA and ETT groups in patients undergoing knee arthroplasty. Secondary aim was to assess influence of the airway choices on PONV in a subgroup of patients receiving nitrous oxide as well as to explore predictors for PONV in the study population. We hypothesized that the use of LMA was associated with a higher frequency of PONV after general anesthesia.

<table>
<thead>
<tr>
<th>Author</th>
<th>Surgery</th>
<th>N</th>
<th>Anesthesia &amp; Duration</th>
<th>ASA Class</th>
<th>Airway Device</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holhrieder(^a)</td>
<td>Breast &amp; GYN</td>
<td>200</td>
<td>(\text{N}_2\text{O} 88-95\text{ min})</td>
<td>I &amp; II</td>
<td>LMA vs. ETT</td>
<td>Less PONV in LMA group</td>
</tr>
<tr>
<td>Holhrieder(^7)</td>
<td>Orthopedic</td>
<td>80</td>
<td>(\text{N}_2\text{O}/\text{Air 70 min})</td>
<td>I &amp; II</td>
<td>LMA vs. ETT</td>
<td>No significant change in MEP</td>
</tr>
<tr>
<td>Nader(^3)</td>
<td>Orthopedic</td>
<td>27</td>
<td>(\text{N}_2\text{O}/\text{Air &lt;120 min})</td>
<td>I &amp; II</td>
<td>LMA vs. ETT</td>
<td>(\text{N}_2\text{O} \rightarrow \text{PONV, Similar PONV in LMA and ETT})</td>
</tr>
<tr>
<td>Swan(^6)</td>
<td>GYN</td>
<td>60</td>
<td>(\text{N}_2\text{O})</td>
<td>I &amp; II</td>
<td>LMA vs. ETT</td>
<td>LMA 13.0% VS ETT 9.4% PONV</td>
</tr>
<tr>
<td>Klockgethe(^9)</td>
<td>PED-Eye</td>
<td>100</td>
<td>(\text{N}_2\text{O})</td>
<td>I &amp; II</td>
<td>LMA vs. ETT</td>
<td>ETT group more PONV followed up for 24 hours</td>
</tr>
</tbody>
</table>

LMA = Laryngeal Mask Airway, ETT = Endotracheal Tube, PED = Pediatric, \(\text{N}_2\text{O}\) = Nitrous Oxide, GYN = Gynecology, MEP = Middle Ear Pressure
PONV = Post-operative nausea and vomiting, PACU = Post anesthesia care unit, LOS = length of stay
Methods

Patients and Data Collection:

The study was reviewed and approved by the Institutional Review Board at the Veteran’s Administration Western New York Health Care System. Due to its retrospective nature, the study was exempted from obtaining informed consents. Electronic charts were reviewed retrospectively from 499 ASA physical status I through III patients with age ranging 18-80 years old who had undergone knee arthroplasty surgery under general anesthesia, from September 30, 2004 to October 1, 2009. Patients were excluded from the review if they received regional anesthesia or had preexisting nausea, vertigo, and otitis media. Patients, who required neostigmine in excess of 2.5 mg for reversal of muscle relaxants, were also excluded. Patients, who received general anesthesia by the use of an airway device other than ETT or LMA, were also excluded from the study as well as patients in lateral and prone positions. Furthermore, patients whose duration of surgery was longer than 240 minutes were excluded.

Demographic data analyzed patient’s age, history of motion sickness, smoking history, PONV, race, gender, ASA physical status, and body mass index (BMI). The intra-operative use of nitrous oxide was limited to 50% in all patients. The use of volatile anesthetics (sevoflurane, isoflurane or desflurane), total intraoperative dose of fentanyl, neuromuscular blocking drugs (rocuronium), neuromuscular reversal agents (neostigmine), prophylactic antiemetic drugs (metoclopramide, ondansetron or dexamethasone), and the duration of surgery were recorded. Perioperative fluid strategy in our hospital is restrictive and all patients received Plasmalyte 4-6 mL/Kg/hour.

Upon transfer to the PACU, the patients were monitored and supplemental oxygen was provided in supine position with mild (20°) head of the bed elevation. Nausea was defined as the feeling of sickness with an inclination to vomit. Vomiting, or emesis, was defined as the expelling of gastric content through the mouth. The incidence of PONV was assessed and recorded electronically by a certified post-anesthesia nurse (CPAN) in the PACU and a registered nurse on the surgical floor for a period of 24 hours. The use of prophylactic antiemetic drugs included dexamethasone 4 mg, metoclopramide 10 mg and ondansetron 4 mg with fixed dose and not calculated based on body weight. Ondansetron 4 mg was administered for the first episode of PONV and repeated if symptoms persisted. If the patient did not respond to second dose of ondansetron, metoclopramide was administered in the PACU. PACU length of stay (PACU LOS) was calculated from the time of arrival until the patients were deemed to meet the criteria to leave the PACU as document in the Nurses’ note.

Furthermore, we recorded the incidence of a composite adverse events including: hypoxia defined as arterial oxygen saturation less than 90%, hypoventilation defined as respiratory rate of less than 8 per minute, reintubation, acute congestive heart failure requiring inotropic drug and positive pressure ventilation, hypotension with the systolic pressures <20% of the baseline and intractable pain documented by an 11 point numeric pain score (0-10). Patients were medicated with pain scores of more than 4 and if unresponsive to low dose opioid treatment (hydromorphone <2 mg) with an intravenous administration of 30 mg ketorolac, provided adequate renal function.

Statistical Analysis

NCSS 2007 (Salt Lake, UT) was used for statistical analysis. All identifiable information was removed before exporting the data into the statistical software. The primary endpoint was the occurrence of PONV until discharge criteria’s were met. The secondary outcome variable included PACU LOS. Fisher’s exact test with chi-squared cross tabulation was used to identify the difference in the incidence of PONV. Continuous variables such as age, duration of surgery, and length of stay in the PACU were examined by Student’s t-test and the data were expressed mean values with standard deviation were reported if the given variable passed the normality test, otherwise median values were reported with interquartile range. Since neuromuscular blockade was only used in patients whose airway was established by endotracheal intubation, the use of these drugs and related reversal
agents were only analyzed for ETT subgroup of patients. Sinclair score was calculated for every patient using the following formula and was used for risk stratification:

$$\text{logit}(P) = -5.97 + -0.14 \times \text{Age} + -1.03 \times \text{Sex} + -0.42 \times \text{Smoking} + 1.14 \times \text{PONV History} + 0.46 \times \text{Duration} + 2.36 \times \text{GA} + 1.48 \times \text{ENT} + 1.9 \times \text{Plastic} + 1.2 \times \text{Gyn}.$$  

Sinclair scoring uses age, sex, smoking status, previous PONV, type of anesthesia, duration of anesthesia, and type of surgery to identify independent predictors of PONV. This model predicted PONV accurately and yielded an area under the receiver operating characteristic curve of 0.79 ± 0.01 using an independent validation set. Calculated predictive risk score was used as the propensity scoring in order to match the data based on the airway choice. Therefore, equal numbers of ETT and LMA patients were compared. Multivariate logistical regression was used with PONV as the primary outcome variable. The following variables were listed in constructing the multivariate model: the use prophylactic antiemetic, rocuronium, neostigmine, nitrous oxide, volatile anesthetics (sevoflurane, isoflurane vs. desflurane), gender, race, ASA status and the airway device (ETT vs. LMA). $P$ values of less than 0.05 were considered significant.

### Table 2

<table>
<thead>
<tr>
<th>Basic Preoperative characteristics of the patients with and without postoperative nausea and vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PONV (N =446)</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Race</strong></td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td><strong>BMI</strong> (Kg/m$^2$)</td>
</tr>
<tr>
<td>28.5 ± 5.8</td>
</tr>
<tr>
<td><strong>ASA Class</strong></td>
</tr>
<tr>
<td>PS-1</td>
</tr>
<tr>
<td>PS-2</td>
</tr>
<tr>
<td>PS-3</td>
</tr>
<tr>
<td><strong>Smoking Status</strong></td>
</tr>
<tr>
<td>Smokers</td>
</tr>
<tr>
<td>Ex-smokers</td>
</tr>
<tr>
<td>Non-smokers</td>
</tr>
<tr>
<td><strong>Airway Device</strong></td>
</tr>
<tr>
<td>ETT/LMA</td>
</tr>
</tbody>
</table>

$P<0.05$ is statistically significant

BMI: body mass index; ASA: American Society of Anesthesiologists; PS: physical status; ETT: endotracheal tube; LMA: laryngeal mask airway; *signifies significant difference

Ex-smokers were defined, as people who were formerly daily smokers but currently do not smoke at all.

Table 3
Intra-operative and anesthetic characteristics of the patients with and without PONV

<table>
<thead>
<tr>
<th></th>
<th>No PONV (N = 446)</th>
<th>PONV (N = 51)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anesthetics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2O</td>
<td>280 (62%)</td>
<td>40 (78%)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Sevofluorane</td>
<td>396 (88%)</td>
<td>43 (84%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Desflurane</td>
<td>39 (9%)</td>
<td>6 (11%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>10 (2.2%)</td>
<td>2 (3.9%)</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>VAS pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl citrate (mcg/kg)</td>
<td>2.25 ± 2.13</td>
<td>2.77 ± 3.8</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Duration of Surgery (min)</strong></td>
<td>61.8 ± 41.0</td>
<td>72.3 ± 46.5</td>
<td>0.03*</td>
</tr>
<tr>
<td><strong>Length of PACU Stay (min)</strong></td>
<td>96.4 ± 63.0</td>
<td>130.7 ± 78.8</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Table 4
Demographic characteristics and Perioperative Data

<table>
<thead>
<tr>
<th></th>
<th>LMA (N = 327)</th>
<th>ETT (N = 170)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Match</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinclair Score</td>
<td>0.74 ± 0.12</td>
<td>0.51 ± 0.17</td>
<td>0.001</td>
</tr>
<tr>
<td>N2O</td>
<td>216 (66%)</td>
<td>102 (60%)</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>37 (11%)</td>
<td>17 (33%)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>279 (87%)</td>
<td>147 (86%)</td>
<td>NS</td>
</tr>
<tr>
<td>Black</td>
<td>45 (13%)</td>
<td>19 (11%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Others</td>
<td>8 (3%)</td>
<td>4 (3%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>46 ± 15</td>
<td>62 ± 13</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BMI (Kg/m2)</td>
<td>28.4 ± 5.2</td>
<td>28.7 ± 5.9</td>
<td>NS</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS-1</td>
<td>47 (47%)</td>
<td>0 (0%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PS-2</td>
<td>203 (77%)</td>
<td>83 (50%)</td>
<td>0.38</td>
</tr>
<tr>
<td>PS-3</td>
<td>77 (23%)</td>
<td>87 (51%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Fentanyl (mcg/kg)</td>
<td>2.4 ± 2.9</td>
<td>2.2 ± 2.0</td>
<td>0.38</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>94 ± 47</td>
<td>47 ± 28</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Prophylactic Antiemetic</td>
<td>194 (59%)</td>
<td>89 (52%)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

BMI: body mass index; ASA: American Society of Anesthesiologists; PS: physical status; ETT: endotracheal tube; LMA: laryngeal mask airway;  
• Asterisks signify significant difference between ETT and LMA groups  
Data matching was done using Sinclair PONV risk score as the propensity score:  
Logit (P) = -5.97 + -0.14 *Age + -1.03 *Sex + -0.42 *Smoking + 1.14 *PONV History + 0.46 *Duration + 2.36 *GA + 1.48 *ENT + 1.9 *Plastic + 1.2 *Gyn.
Results

The charts from 499 patients were reviewed. Two patients were excluded because their airways were controlled by means other than ETT or LMA. There were a total of 43 female patients in the review. The average age was 51.4 ± 16.1 years for all patients. PONV occurred in 51/497 (10.3%) patients. The incidence of PONV was 29/170(17%) with the use of ETT and 22/327 (6.7%) with LMA (P <0.001) [Table 2]. Average PACU length of stay for all patients was 107 ± 61 minutes. The average PACU length of stay for patients without and with PONV was 96 ± 63 minutes and 130 ± 79 minutes, respectively (P <0.001). When nitrous oxide was used as a part of anesthetic mixture, the incidence of PONV was 18 out of 102 (17.5%) in the ETT group vs. 22/216 (10.1%) in the LMA group. Additionally, an ETT was used in 55 out of 177 patients and a LMA for the remaining 122 patients without nitrous oxide. The incidence of PONV among patients not receiving nitrous oxide was 11 out of 177 (8.7%). However, there was no statistical difference among the patients with ETT and LMA in the subgroup analysis without nitrous oxide. All intraoperative parameters for patients with or without PONV are shown in Table 3. Neostigmine was used in 11/51 patients who had PONV while it was used in 37/446 (8.2%) patients without PONV [Table 3].

Preoperative risk of PONV was calculated for every patient using the Sinclair formula. Sinclair score for the ETT group was 0.51 ± 0.17 while the risk for the LMA group was 0.74 ± 0.12 (P <0.001). The LMA group was identified as higher risk group for PONV based Sinclair scoring system. In order to evenly distribute the patients into airway groups, Sinclair risk was used as propensity score to match the patients for equal risk of PONV. All the values were reanalyzed before and after match demonstrated in Table 4. The incidence of PONV was 25/157 (15.8%) with the use of ETT compared with 12/157 (7.9%) for the LMA group (P <0.05) after matching [Table 4].

We also analyzed the data examining the use of prophylactic antiemetic drugs. Notably, prophylactic antiemetic medications were administered to 52.4 % of patients with ETT and 59.3%, of the patients with LMA (P = 0.13). When specifically looking at the use of ondansetron, 32.7% of patients in ETT group received this medication prophylactically versus 37% of patients in the LMA group (P = 0.4). The average length of surgery for patients with ETT was 94 ± 45 minutes and for patient with LMA was 47 ± 28 minutes (P <0.001).

Multivariate logistic regression model was constructed for all preoperative risk factors as listed in the Methods section. This analysis showed that gender, age, duration of surgery and nitrous oxide use to be independent risk factors for PONV [Fig. 1]. The odds ratio for the length of surgery was 1.008 [1.000-1.920]. Therefore for each added minute of surgery, the risk of PONV increased by 0.8%. Age had the opposite effect on PONV with an odds ratio of 0.993 [0.962-0.998]. Therefore each added year of age protected an individual from PONV by 0.7%.

Discussion

We have shown that the incidence of PONV is significantly higher in patients who had an ETT

compared to those with a LMA in univariate analysis. This association seemed to be related to some other confounding variables since multivariate analyses indicated that an airway device was not an independent predictor of PONV. There has been very little data on the influence of airway device and post-operative incidence of nausea and vomiting. Several publications report contradictory results6,8,9. More information and research is needed to establish the role of airway devices on PONV. Previous study by our group had suggested that changes in middle ear pressure might have contributed to the PONV3. But since the etiology of PONV is multifactorial in origin, it would be difficult to draw any solid conclusion on the cause and effect relationship.

The use of nitrous oxide is a known risk factor for PONV12 and our study confirms that nitrous oxide is an independent factor for PONV and the relative risk of nitrous oxide is greater among those with ETT than those with LMA. A meta-analysis from 1996 states that nitrous oxide was associated with increased emesis in 24 of 27 studies analyzed, but did not record the type of airway device used for anesthesia13. More recent studies have also identified nitrous oxide as a risk factor for PONV, but the influence of choice of airway device on PONV was not reported. Apfel et al. limited the study to surgeries of less than one hour14. Many of the surgeries (65.7%) recorded in our study were of a shorter time frame usually less than 60 minutes. Selection of an airway device was influenced by the duration of surgery and experience of the anesthesiologist15. In view of these findings, we suggest that several risk assessment tools that are used in clinical setting to predict the incidence of PONV should modify to include nitrous oxide as part of their formula.

The LMA has been in use since 1984, so presumably some of the above studies may have included patients using this airway device16. Other investigators have reported the type of airway device used, but only matched this variable across study populations instead of examining its effect on PONV17. One meta-analysis found that eliminating the use of nitrous oxide did not reduce the incidence of nausea, but it did reduce the incidence of early and late vomiting2. Perhaps, the findings in our study also represent a subset of patients in which nitrous oxide is not the predictor for PONV, namely in patients in which LMA was used as the airway device. Future studies will help us to delineate this finding.

Increased duration of surgery is a well-accepted risk factor for PONV and has been repeatedly supported by the literature in the pediatric population11,17,19. Of note, our study did not include any pediatric patient. One study found that the incidence of PONV increased by 59% for every 30 minute increase in duration of surgery11. Our findings followed the same trend (24% increases for every additional 30 minutes). Additionally, we found that when variables were matched, the incidence of PONV was significantly different between the ETT and LMA groups. If the groups were separated, patients with ETT had a significantly longer length of surgery compared with LMA. This finding could have accounted for the fact that ETT was associated with significantly more PONV than LMA.

It has been noted in previous publication that children and young adults are at risk for increased PONV20. Publications have found many variations on this trend over time. One author found that age over 50 showed a linear decrease in incidence of PONV11. Another researcher found that age under 50 increased the risk of PONV as compared to age over 70 years old21. Our study did not have any pediatric subjects and the average age of our subjects was 51 years with a range from 20 to 80 years. Similarly, our findings demonstrated that increasing age was protective against PONV. For every one year increase in age, the risk decreased by 0.7%.

We were unable to establish any correlation between the ASA physical status and the incidence of PONV. Lower ASA class has been suggested by two studies as a risk factor for PONV21,22, and they were adopted by the Consensus Practice Guidelines published in 200323. However, these studies were survey-based and therefore might have missed patients with higher ASA class. Since in our study we have excluded ASA 4 and ASA 5 patients, we cannot comment on the true effect of ASA class on PONV. Furthermore, it is likely that ETT would have been the main airway device in this high-risk population (ASA-4 and ASA-5 patients).
We also established that PONV increased PACU length of stay. Intuitively this makes sense and has been supported by studies in the past. One study found that each episode of vomiting increased time in the recovery room by about 20 minutes. Our study does not address data encompassing the number of episodes of vomiting.

One factor that could not be controlled for between patients using ETT and those with LMA was neuromuscular blockade. ETT patients were all paralyzed while LMA patients were not. Neostigmine was the only reversal agent used to reverse neuromuscular blockade at the end of surgery. Neostigmine has been associated with PONV at doses greater than or equal to 2.5 mg. We excluded patients receiving doses of greater than 2.5 mg.

One limitation of this study is its retrospective nature. PONV could only be determined by chart review of electronic medical records entered by PACU nurses during post-anesthesia recovery. Patients who experienced the subjective sensation of nausea but did not report these symptoms or did not want medications may have been missed.
References


MARKED VARIABILITY IN PERI-PARTUM
ANESTHETIC MANAGEMENT OF PATIENTS ON
BUPRENORPHINE MAINTENANCE THERAPY (BMT):
CAN THERE BE AN UNDERLYING ACUTE OPIOID INDUCED
HYPERALGESIA PRECIPITATED BY NEURAXIAL
OPIOIDS IN BMT PATIENTS?

DeePaK GuPTA*, CArL CHRISTENSEN**, VITALy SOSKiN***

Abstract

Objectives: To compare adequacy of peri-partum pain management with or without neuraxial opioids in patients on buprenorphine maintenance therapy (BMT).

Methods: After institutional review board approval for the study protocol, retrospective peri-partum anesthesia/analgesia data of BMT patients for five-year period were accessed and analyzed.

Results: Out of reviewed 51 patient charts, nineteen patients were found eligible for final comparative analysis. The daily amounts of peri-partum rescue analgesics with vs without neuraxial opioids were equianalgesic doses of parenteral hydromorphone (10.7 ± 13.8 mg vs 2.6 ± 0.7 mg, P = 0.45 for vaginal delivery; 16.4 ± 21.1 mg vs 5.3 ± 3.6 mg, P = 0.42 for elective cesarean section (CS)), oral ibuprofen (1.1 ± 0.5g vs 0.8 ± 0.4g, P = 0.37 for vaginal delivery; 1.1 ± 0.2g vs 1.6 ± 0.6g, P = 0.29 for elective CS), and acetaminophen (0.2 ± 0.4g vs 0 ± 0g, P = 0.56 for vaginal delivery; 0.3 ± 0.3g vs 0.2 ± 0.2g, P = 0.81 for elective CS). In the patients who underwent emergent CS after failed labor (all had received epidural opioids), there was clinical trend for higher daily amounts of peri-partum rescue analgesics (parenteral hydromorphone 35.6 ± 37.5 mg; oral ibuprofen 1.2 ± 0.4g; oral acetaminophen 1.2 ± 0.5g), when compared with vaginal delivery patients or elective CS patients who all had received neuraxial opioids.

Conclusions: As the study was underpowered (n = 19), future adequately powered studies are required to conclude for-or-against the use of neuraxial opioids in BMT patients; and pro-nociceptive activation by neuraxial opioids may be worth investigating to improve our understanding of peri-partum pain management of BMT patients.

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Introduction

The treatment of choice for maintenance therapy in opioid-dependent pregnant patients is methadone1. Buprenorphine maintenance therapy (BMT) is FDA-approved for community-based treatment of opioid dependence2, but not during pregnancy. However, women may choose to continue BMT during pregnancy if they are stable in treatment3 or if methadone is not available or refused. In addition, the preliminary results indicate that buprenorphine-exposed fetuses and neonates have superior well-being and outcomes as compared to methadone-exposed fetuses and neonates4-6. Buprenorphine has high affinity for mu receptors, but only activates them partially. Moreover, based on clinical experiences and incompletely understood mechanisms/phenomena, there is an ongoing debate whether peripartum neuraxial opioids improve or worsen peri-partum analgesia in BMT patients7,8. Therefore peri-partum pain management becomes challenging and unpredictable in patients on BMT9.

The goal of this retrospective analysis was to compare adequacy of peri-partum pain management with and without neuraxial opioids in patients on BMT.

Methods

After the institutional review board approval for the study protocol, the retrospective data for a five-year period (2007-2011) were accessed at an academic university’s women’s hospital. The pharmacy and information technology team were asked to screen the patients admitted to the obstetric floors in the abovementioned five-year period for the administration of buprenorphine in any form (sublingual, oral, intravenous or intramuscular). This pharmacy data review and analysis provided the research team with the detailed number of patients who were on buprenorphine during their hospital stay in our obstetric floors. Additionally, for accessing the patients that might have been missed by abovementioned analysis, Medical Center Business Objects as well as Medical Records were screened for inpatient admissions with the admitting diagnosis codes as 648.3 [drug dependence in pregnancy]. Subsequently, the electronic medical records (and as needed the paper medical records) of all the eligible patients were accessed for the following observation parameters:

Pre-procedure (labor epidural or cesarean section):
- Patient’s age, height and weight, and ASA class
- Daily dose and route of administration of buprenorphine
- Whether patient had taken the scheduled dose before the procedure
- Any other documented pain medication

Intra-procedure:
- Type of procedure
- Whether neuraxial access was obtained
- What type of neuraxial access was obtained
- Whether neuraxial opioids were given
- Types and total doses of neuraxial opioids/local anesthetics given were calculated based on our standard practices for neuraxial medications administration and total duration of neuraxial analgesia-anesthesia
- Any other pain medication given during the procedure

Post-procedure (till the time of discharge):
- Daily dose and route of administration of buprenorphine
- Whether neuraxial opioids were given in post-operative epidural analgesic solutions
- Type and total dose of neuraxial opioids/local anesthetics given
- Type and daily dose of non-steroidal anti-inflammatory drugs (NSAIDs) given
- Type and daily dose of parenteral opioids given
- Type and daily dose of pain medications at discharge

Subsequently, the following primary peri-partum anesthesia/analgesia data were compared between the patients who had or had not received neuraxial opioids [the patients were stratified whether they received epidural or intrathecal opioids, and whether they delivered vaginally or with cesarean section (CS)]: daily home dose of buprenorphine, daily
MARKED VARIABILITY IN PERI-PARTUM ANESTHETIC MANAGEMENT OF PATIENTS ON BUPRENORPHINE MAINTENANCE THERAPY (BMT): CAN THERE BE AN UNDERLYING ACUTE OPIOID INDUCED HYPERALGESIA PRECIPITATED BY NEURAXIAL OPIOIDS IN BMT PATIENTS?

Fig. 1
CONSORT Diagram

For statistical analysis, ANOVA Single factor was applied to compare the means and variance of the continuous data. Chi-Square test was utilized to compare all (expected frequencies equal to or greater than 5) but extremely small sample size based proportions; a two-tailed Fisher exact probability test was used if the sample size was very small. A p-value of <0.05 was considered statistically significant.

Results

A total of 51 patient charts were reviewed; however only nineteen patient encounters remained for comparative analysis after various exclusions as shown in Fig. 1: CONSORT Diagram. Subsequently, the patients were stratified whether they had only received labor epidural analgesia and delivered vaginally (Table 1), and whether they underwent elective CS and received subarachnoid block only (Table 2). Finally, as all emergent CS patients (n = 3) had received epidural opioids, these patients were compared within the strata of patients who all had received neuraxial opioids but had differed in their mode of fetal delivery (Table 3). The daily amounts of peri-partum rescue analgesics (an indicator of adequacy of peri-partum pain relief) with vs without neuraxial opioids were equianalgesic doses of parenteral hydromorphone, oral ibuprofen, and acetaminophen as shown in Tables 1-2 and Fig. 2. Moreover, in the patients who underwent emergent CS after failed labor, there was clinical trend for higher daily amounts of peri-partum rescue analgesics when compared with vaginal delivery patients or elective CS patients who all had received neuraxial opioids (Table 3, Fig. 3). Even though our results were statistically

equianalgesic parenteral dose of hydromorphone, total equianalgesic dose of epidural fentanyl, and daily oral doses of ibuprofen and acetaminophen received. The equianalgesic doses for the parenteral opioids were primarily calculated from the online web-applications10-11. Daily home dose of sublingual buprenorphine 0.4 mg was considered equianalgesic to intramuscular/intravenous buprenorphine 0.3 mg and intrathecal morphine 250 mcg was considered equianalgesic to epidural fentanyl 83 mcg12-14. In view of variable but not yet confirmed equianalgesia reports15-17, intravenous ketorolac 120 mg was considered equianalgesic to oral ibuprofen 2400 mg.

For statistical analysis, ANOVA Single factor was applied to compare the means and variance of the continuous data. Chi-Square test was utilized to compare all (expected frequencies equal to or greater than 5) but extremely small sample size based proportions; a two-tailed Fisher exact probability test was used if the sample size was very small. A p-value of <0.05 was considered statistically significant.

Results

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Fig. 2
Daily Peri-Partum Analgesics Requirements by Patients on Buprenorphine Maintenance Therapy in Peri-Anesthesia Period: A Comparison of Vaginally Delivered Patients and Elective Cesarean Section Patients
Table 1
Comparison Parameters (in terms of rescue analgesics) to adjudge adequacy of Peri-Partum Pain Relief with or without Epidural Opioids in Laboring Patients on Buprenorphine Maintenance Therapy

<table>
<thead>
<tr>
<th></th>
<th>Those who had Epidural Opioids (n = 8)</th>
<th>Those who did not have Epidural Opioids (n = 2)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-Anesthesia Parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>25.13 ± 5.84</td>
<td>24.5 ± 6.36</td>
<td>0.9</td>
</tr>
<tr>
<td>Height (inches)</td>
<td>64.63 ± 3.54</td>
<td>62.5 ± 3.54</td>
<td>0.47</td>
</tr>
<tr>
<td>Weight (pounds)</td>
<td>167.38 ± 21.53</td>
<td>139 ± 0</td>
<td>0.11</td>
</tr>
<tr>
<td>Pre-Anesthesia Daily Home Dose of Buprenorphine (mg)</td>
<td>16 ± 5.66</td>
<td>10 ± 8.49</td>
<td>0.25</td>
</tr>
</tbody>
</table>

**Peri-Anesthesia Parameters after the institution of Labor Epidural Analgesia**

<table>
<thead>
<tr>
<th></th>
<th>Those who had Epidural Opioids (n = 8)</th>
<th>Those who did not have Epidural Opioids (n = 2)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days till Hospital Discharge (n)</td>
<td>3.13 ± 0.64</td>
<td>4 ± 1.41</td>
<td>0.19</td>
</tr>
<tr>
<td>Total Epidural Fentanyl Dose (mg)</td>
<td>0.40 ± 0.14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Epidural Bupivacaine Dose (mg)</td>
<td>164.06 ± 71.48</td>
<td>Unknown</td>
<td>-</td>
</tr>
<tr>
<td>Total Equianalgesic Parenteral Hydromorphone Dose (mg)</td>
<td>31.85 ± 41.58</td>
<td>11.05 ± 6.44</td>
<td>0.52</td>
</tr>
<tr>
<td>Daily Equianalgesic Parenteral Hydromorphone Dose (mg)</td>
<td>10.67 ± 13.82</td>
<td>2.64 ± 0.67</td>
<td>0.45</td>
</tr>
<tr>
<td>Total Equianalgesic Oral Ibuprofen Dose (g)</td>
<td>3.5 ± 1.82</td>
<td>2.8 ± 0.57</td>
<td>0.62</td>
</tr>
<tr>
<td>Daily Equianalgesic Oral Ibuprofen Dose (g)</td>
<td>1.11 ± 0.45</td>
<td>0.77 ± 0.42</td>
<td>0.37</td>
</tr>
<tr>
<td>Total Acetaminophen Dose (g)</td>
<td>0.16 ± 0.35</td>
<td>0 ± 0</td>
<td>0.56</td>
</tr>
<tr>
<td>Daily Acetaminophen Dose (g)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2
Comparison Parameters (in terms of rescue analgesics) to adjudge adequacy of Peri-Partum Pain Relief with or without Intrathecal Opioids in Elective Cesarean Section Patients on Buprenorphine Maintenance Therapy

<table>
<thead>
<tr>
<th></th>
<th>Those who had Intrathecal Opioids (n = 3)</th>
<th>Those who did not have Intrathecal Opioids (n = 3)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td><strong>Pre-Anesthesia Parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>30 ± 4.58</td>
<td>34.67 ± 6.66</td>
<td>0.37</td>
</tr>
<tr>
<td>Height (inches)</td>
<td>62.67 ± 2.31</td>
<td>65.33 ± 1.15</td>
<td>0.15</td>
</tr>
<tr>
<td>Weight (pounds)</td>
<td>177.67 ± 33.26</td>
<td>190.33 ± 31.02</td>
<td>0.65</td>
</tr>
<tr>
<td>Pre-Anesthesia Daily Home Dose of Buprenorphine (mg)</td>
<td>13.33 ± 4.62</td>
<td>13.33 ± 9.24</td>
<td>&gt;0.99</td>
</tr>
</tbody>
</table>

**Peri-Anesthesia Parameters after the institution of Subarachnoid Anesthesia**

<table>
<thead>
<tr>
<th></th>
<th>Those who had Intrathecal Opioids (n = 3)</th>
<th>Those who did not have Intrathecal Opioids (n = 3)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days till Hospital Discharge (n)</td>
<td>3.67 ± 0.58</td>
<td>3.33 ± 0.58</td>
<td>0.52</td>
</tr>
<tr>
<td>Total Intrathecal Morphine Dose (mcg)</td>
<td>250 ± 50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Intrathecal Bupivacaine Dose (mg)</td>
<td>12 ± 0</td>
<td>12 ± 0</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Total Equianalgesic Parenteral Hydromorphone Dose (mg)</td>
<td>52 ± 60.81</td>
<td>19.07 ± 16.25</td>
<td>0.42</td>
</tr>
<tr>
<td>Daily Equianalgesic Parenteral Hydromorphone Dose (mg)</td>
<td>16.39 ± 21.08</td>
<td>5.31 ± 3.62</td>
<td>0.42</td>
</tr>
<tr>
<td>Total Equianalgesic Oral Ibuprofen Dose (g)</td>
<td>4.13 ± 1.36</td>
<td>5.33 ± 2.61</td>
<td>0.52</td>
</tr>
<tr>
<td>Daily Equianalgesic Oral Ibuprofen Dose (g)</td>
<td>1.11 ± 0.22</td>
<td>1.56 ± 0.60</td>
<td>0.29</td>
</tr>
<tr>
<td>Total Acetaminophen Dose (g)</td>
<td>1.2 ± 1.2</td>
<td>0.88 ± 0.82</td>
<td>0.72</td>
</tr>
<tr>
<td>Daily Acetaminophen Dose (g)</td>
<td>0.3 ± 0.3</td>
<td>0.25 ± 0.22</td>
<td>0.81</td>
</tr>
</tbody>
</table>
MARKED VARIABILITY IN PERI-PARTUM ANESTHETIC MANAGEMENT OF PATIENTS ON BUPRENORPHINE MAINTENANCE THERAPY (BMT): CAN THERE BE AN UNDERLYING ACUTE OPIOID INDUCED HYPERALGESIA PRECIPITATED BY NEURAXIAL OPIOIDS IN BMT PATIENTS?

Fig. 3
Daily Peri-Partum Analgesics Requirements by Patients on Buprenorphine Maintenance Therapy in Peri-Anesthesia Period: A Comparison of Emergent Cesarean Section Patients within the Strata of Patients who all received Neuraxial Opioids

Fig. 4
Schematic Diagram of Mechanism of Action underlying the difficult Peri-Anesthesia Management with Neuraxial Opioids in Patients on Buprenorphine Maintenance Therapy (inspired from Jones). Fentanyl attaches to mu-receptor and highly stimulates it; however, buprenorphine can easily displace fentanyl from mu-receptor. Now this receptor is poorly stimulated by buprenorphine; however, fentanyl displacing buprenorphine from mu-receptor is questionable due to very strong affinity of buprenorphine to mu-receptor
significant only for acetaminophen use among neuraxial opioids patients depending on mode of fetal delivery (Table 3), the clinical trends suggest that the study is underpowered and the differences in other analgesic requirements may not have reached level of statistical significance (P < 0.05) because very few pregnant women (nineteen in the five-year study analysis period) chose to continue BMT during pregnancy.

**Discussion**

Peripartum pain management encompasses analgesic coverage for the following: (a) first stage labor pain is visceral in origin and mediated through thoracolumbar spinal segments (T10-L1) secondary to inflammatory mediators released from dilated and effaced cervix, (b) second stage labor pain is somatic in origin and mediated through sacral spinal segments (S2-S4) secondary to a distended perineum, and (c) post-caesarean pain, mediated through thoraco-lumbo-sacral spinal segments (T4-S5), is a combination of somatic origin pain due to surgical incision and visceral origin pain due to uterine exteriorization.

Buprenorphine is 17-(cyclopropylmethyl)-alpha-(1,1-dimethylethyl)-4,5-epoxy- 18,19-dihydro-3-hydroxy-6-methoxy-alpha-methyl-6,14-ethenomorphinan-7-methanol. As buprenorphine is a partial agonist to the mu receptor, it stimulates the mu receptor, but at lower intensity than other opioids (partial agonism). However, as buprenorphine binds more strongly to the receptor, it can displace other opioids from the receptors. Conversely, dissociation of buprenorphine from the receptor is slow, and other
opiates may not be able to stimulate the occupied mu receptor (Fig. 4). Therefore, peripartum analgesia is unpredictable if other opioids are given concomitantly and peripartum pain management becomes challenging in pregnant patients who are on BMT for opioid dependence.

During the peripartum period of BMT patients, the dilemma for obstetric anesthesiologist is whether neuraxial opioids are required at all for efficacious peripartum analgesia. The reasons are multiple. Firstly, buprenorphine has very strong affinity to opioid receptors and hence fentanyl (the most commonly used neuraxial opioid in obstetric analgesia-anesthesia) may not be able to displace buprenorphine from these blocked receptors (Fig. 4). Secondly, fentanyl has high lipophilicity and hence cranial spread of this medication is very limited, making neuraxial fentanyl ineffective in countering supraspinal analgesic needs of BMT patients. Thirdly, there is no data in BMT patients for the use of neuraxial hydromorphone which is less potent (1/10th) than fentanyl, but has more cranial spread due to its hydrophilicity, and is rarely used in obstetric analgesia-anesthesia because of delayed onset of analgesic action as well as respiratory depression. Fourthly, supraspinal analgesic requirements may be variable and receptors in BMT patients may be insensitive to regular doses of parenteral opioid supplementation because of long half life of buprenorphine and its strong affinity to opioid receptors (spinal and supraspinal). Fifthly, the superfluous concentrations of neuraxial fentanyl molecules that are not able to displace buprenorphine molecules from anti-nociceptive receptors may then be acting on unoccupied pro-nociceptive receptors via excitatory neuropeptides and spinal dynorphin and/or descending pathway facilitation, similar to the proposed mechanisms/theories that are used to explain opioid induced hyperalgesia. Finally, the superfluous concentrations of some buprenorphine molecules that are actually displaced by neuraxial fentanyl from the low affinity sites in the spinal cord are free to act upon the orphanin FQ/nociceptin/ opioid receptor-like 1 receptor system with full agonism that consequently in itself attenuates the generalized (supraspinal and spinal) anti-nociceptive efficacy of buprenorphine.

The percentage (3-37%) of buprenorphine molecules displaced by fentanyl is dependent on the concentrations of the pre-existent buprenorphine (0.5-2 nmol/liter) in the body. Consequently, the number of these displaced molecules of buprenorphine may be very small when the patient is on high to very high buprenorphine dose (8-32 mg/day). Therefore, this opioid receptor-like receptor agonism, that is unique to buprenorphine compared to fentanyl, may be minimal.

Although lacking statistical significance, our results suggest that it may be better to avoid neuraxial opioids for peripartum analgesia in BMT patients because a larger dose of peripartum rescue analgesics were required when they had received concomitant neuraxial opioids in peripartum period; in contrast to a former study, our retrospective analysis of nineteen patients shows the clinical trend for more rescue analgesics in both vaginal delivery as well as elective CS patients when they had received neuraxial opioids (Tables 1-2). Therefore, in our opinion, a suggested peripartum management for BMT patients would be: (a) to continue maintenance doses of buprenorphine, (b) effective epidural or intrathecal catheter placement for peripartum pain, (c) utilization of higher than usual concentrations of local anesthetic solutions to accommodate the absence of neuraxial opioids and to prevent overt sensitization of ascending pain pathways, (d) liberal use of non-steroidal inflammatory agents in postoperative periods for inflammatory cervical, perineal and incisional pain, (e) aggressive management with transversus abdominis plane block supplementation for post-cesarean incisional pain, and (f) “Last resort” supplementation with parenteral opioids with different receptor selectivity, or alpha-2 agonists and N-methyl-D-aspartate antagonists for non-resolving pain.

Pre-emptive sensory blockade with higher doses of epidural bupivacaine may prevent the sensitization of the pro-nociceptive pain pathways in the opioid dependent peripartum patients who are highly susceptible to opioid-induced hyperalgesia that may be precipitated in peripartum patients who are highly susceptible to opioid-induced hyperalgesia that may be precipitated in peri-operative setting or is worsened with the use of peri-operative opioids (intrathecal opioids as well as parenteral opioids). This explanation for higher requirements of parenteral opioids and poor pain control with neuraxial opioids in BMT patients has ample support in medical literature as acute opioid induced hyperalgesia. Though
these earlier reports theorized pro-nociceptive role of intrathecal opioids even in opioid-naïve patients, the mechanism holds true (and may be to a greater degree) for opioid dependent patients receiving neuraxial opioids. Similar to higher analgesic potency and efficacy of neuraxial opioids as compared to parenteral opioids, it is logical to assume and theorize that hyperalgesic potency and efficacy of neuraxial opioids will be higher than parenteral opioids; this may particularly hold true when the anti-nociceptive receptors have been strongly occupied by pre-existent buprenorphine in BMT patients.

This study has limitations. The number of patients was very low (n = 19) and hence the study was underpowered. It was a retrospective analysis. Biochemical and molecular evidence cannot be offered for neuraxial opioid-related hyperalgesia theory in BMT patients with this small retrospective analysis. Larger randomized prospective trials are required but are needed to be done as multi-center multi-national trials due to paucity of pregnant BMT patients.

Conclusions

As the study was underpowered (n = 19), future adequately powered studies are required to conclude for-or-against the use of neuraxial opioids in BMT patients; and pro-nociceptive activation by neuraxial opioids may be worth investigating to improve our understanding of peri-partum pain management of BMT patients.

Acknowledgements

The authors are deeply indebted to the appreciative efforts of Ms. Connie Tourangeau, Pharmacist, and Mr. Xavier Bell, Field Engineer, Department of Pharmacy, Main Operating Room Complex, Harper Hospital, Detroit Medical Center, Detroit, Michigan, United States in regards to their retrospective enlisting of the inpatients who had received buprenorphine according to inpatients’ pharmacy’s database.
MARKED VARIABILITY IN PERI-PARTUM ANESTHETIC MANAGEMENT OF PATIENTS ON BUPRENORPHINE MAINTENANCE THERAPY (BMT): CAN THERE BE AN UNDERLYING ACUTE OPIOID INDUCED HYPERALGESIA PRECIPITATED BY NEURAXIAL OPIOIDS IN BMT PATIENTS?

References

COMPARISON LARYGEAL MASK AIRWAY WITH THE ENDOTRACHEAL TUBE FOR THE EXTERNAL DACRYOCYSTORHIONOSTOMY SURGERY. A RANDOMIZED CLINICAL TRIAL

MOHAMMAD HOSSEIN EGHBAL*, MOHAMMAD ALI SAHMEDDINI**

Abstract

Background: General anesthesia (GA) is considered the gold standard for external dacryocystorhinostomy (DCR) surgery. There are few reports about laryngeal mask airway (LMA) use in DCR surgery. The aim of this study was to compare the use of endotracheal intubation (ETT) vs LMA for airway management during DCR surgery.

Methods: Ninety patients were randomized to two groups. In the group C, ETT and in the group L, classic LMA was used to maintain and protect the airway during the procedure. Hemodynamic data before, after intubation or LMA insertion and after skin incisions were recorded. Coughing and straining at the end of anesthesia and postoperative nausea and vomiting (PONV) were recorded.

Results: In the group L, the mean arterial pressure and the heart rate after LMA insertion and after the skin incisions were significantly lower than the group C (p <0.05). Furthermore, incidence of coughing, straining at the end of anesthesia and PONV was lower in the group L than the group C (p <0.05).

Conclusion: LMA can be used in external DCR, to decrease the hemodynamic changes, to decrease coughing, straining at the end of anesthesia and the incidence of PONV.

Keywords: Dacryocystorhinostomy. Laryngeal Masks. Postoperative Nausea and Vomiting

Introduction

Surgeons usually prefer to perform external dacryocystorhinostomy (DCR) procedure under general anesthesia (GA)1-3 with the anesthesiologists using oral endotracheal intubation (ETT) for airway management4-7. Although ETT serves as a standard protective device against blood aspiration, marked hemodynamic response including hypertension, tachycardia and arrhythmias often follows direct laryngoscopy and tracheal intubation8. This response can be harmful, especially in the old patients with coexisting heart disease9.
At the end of external DCR surgery a smooth extubation is indicated because coughing and straining will result in increased bleeding from the nose. Also during DCR surgery, blood usually enters the stomach and as such postoperative nausea and vomiting (PONV) are common complications following this surgery.

Laryngeal mask airway (LMA) allows the support of a patent airway with some benefits. Insertion of an LMA doesn’t require laryngoscopy and thus eliminate all its associated complications. Also, the incidence of coughing on emergence has been shown to be lower with the LMA than with the ETT secondary to lack of tracheal stimulation. Furthermore, previous studies showed that the incidence of postoperative nausea and vomiting (PONV) to be lower with LMA versus ETT.

There is little data regarding the use of laryngeal mask during external DCR surgery. The aim of this study is to assess the effects of using an LMA for external DCR surgery on blood pressure and heart rate at the start of surgery, the incidence of coughing on emergence and the incidence of postoperative nausea and vomiting.

Methods

After the approval of our institutional ethics committee and attaining written informed consent, ninety patients with ASA I-II, scheduled for elective external DCR because of nasolacrimal duct obstruction were randomized into two groups: Group C (Classical group, received ETT) and Group L (received LMA). Patients were excluded from the study if they had history of (1) any pathology in gastrointestinal tract (2) motion sickness or received antiemetic drugs for the last 2 weeks (3) chronic obstructive lung disease or asthma (4) bleeding diathesis or on anticoagulants and (4) with extreme obesity (body-mass index >40 Kg/m²).

Patients in both groups received midazolam (0.03 mg/kg) and fentanyl (2 μg/kg) intravenously. Then anesthesia was induced intravenously with thiopental (4-5 mg/kg) and atracurium (0.6 mg/kg) was used to facilitate oral tracheal intubation in the group C or classic laryngeal mask airway (LMA) insertion in the group L (Fig. 1). Anesthesia was maintained with isoflurane (1.20 vol %) in a 50% oxygen-N2O mixture. Lung ventilation was mechanically controlled throughout the surgery and for prevention of gastric insufflation in patients who had LMA, tidal volume was set at 5 ml/Kg and peak airway pressure (PAP) was set at 18 cm H₂O.

The heart rate (HR) and mean arterial blood pressure (BP) of patients in both groups before induction of anesthesia, 5 minutes after oral tracheal

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**Fig. 1**  
Flowchart of the patients according to the consort guidelines
intubation in group C or 5 min after laryngeal mask insertion in group L, and 5 minutes after surgical incisions in both groups were recorded.

At the end of surgery and when the patients became fully awake, the LMA or ETT was removed and the incidences of coughing or straining, if any, were recorded. Then the patients were transferred to the post anesthesia care unit and the postoperative nausea and vomiting episode was recorded until 24 hours after surgery. The incidence of PONV was recorded according to the patients complaints as follow: 0 = no nausea or vomiting; 1 = nausea only; 2 = retching or and vomiting. Vomiting was defined as the forceful expulsion of gastric contents from the mouth nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.

Statistical analysis

The primary outcome of study was 20% decrease in the MAP following the use of LMA instead of ETT. According to variance 27and mean difference10 in the MAP, a sample size of at least 40 patients in each group was considered sufficient to detect a 5% difference (α = 0.05, β = 0.8). However another 10% was added to sample size of each group to compensate for drop outs and finally, 45 patients in each group (total of 90 pts) was calculated as being appropriate. Statistical analyses were performed with SPSS version 14.0 software (SPSS, Inc., Chicago, IL, USA). All values were presented as means ± SD and P< 0.05 was considered significant in all statistical tests.

Student's t-test was used for analysis of baseline characteristics of both groups and Chi-square test was used for analysis of categorical data. Repeated analysis of variance was used repeated measures of BP and HR. All comparisons were two-tailed. P-values < 0.05 were considered statistically significant.

Results

Three patients were excluded from group L due to displacement of LMA (Fig. 1). No significant differences in baseline mean arterial pressure and baseline heart rate were noted between the two groups (P = 0.15, P = 0.24 respectively) (Fig. 2 and Fig. 3). However, at 5 min after intubation and 5 min after incision the mean arterial blood pressure and heart rate were significantly higher in the group C than in group L (P = 0.002, P = 0.001 respectively) (Fig. 2 and Fig. 3).

### Table 1

<table>
<thead>
<tr>
<th>Patients’ Characteristics (mean +/- SD)</th>
<th>Group C (N =45 )</th>
<th>Group L (N =42 )</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year)</td>
<td>49.32 ± 3.81</td>
<td>52.32 ± 1.49</td>
<td>0.91</td>
</tr>
<tr>
<td>Weight(Kg)</td>
<td>69.67 ± 4.19</td>
<td>70.34 ± 3.92</td>
<td>0.70</td>
</tr>
<tr>
<td>Body-Mass Index</td>
<td>25.11 ± 1.31</td>
<td>26.78 ± 1.92</td>
<td>0.87</td>
</tr>
<tr>
<td>Gender(F/M)</td>
<td>25/20</td>
<td>27/18</td>
<td>0.69</td>
</tr>
<tr>
<td>Operation duration (min)</td>
<td>45.89 ± 7.81</td>
<td>48.67 ± 5.61</td>
<td>0.54</td>
</tr>
</tbody>
</table>

The incidence of coughing and straining in group L was 3% and significantly lower than in group C (64.44%; P = 0.0001). The incidences of postoperative nausea and vomiting were lower in group L than in group C (P = 0.001) (Table 2).

### Table 2

| Incidence of postoperative nausea and vomiting (PONV) in the group C and group L |
|-------------------------------|-------------------------------|------------------|
| Variables                      | Group C (N=45)               | Group L (N=42)   |
| Nausea, No. (%)                | 21(46.6%)                    | 10 (23.8%)       |
| Vomiting, No. (%)              | 15(33.3)                     | 6(14.2%)         |
| Total PONV, No. (%)            | 36(79.9%)                    | 16(38%)          |

Discussion

The present study showed that use of classic LMA during GA for external DCR surgery is associated with less significant hemodynamic response as compared to oral endotracheal tube and may result in lesser coughing, straining at the end of anesthesia and less postoperative nausea and vomiting.

In 2008 Makuloluwa reported a case series about
the use of the classic LMA during endoscopic DCR and suggested the use of the classic LMA during anesthesia for endo-DCR decreased complications associated with the use of the ETT which include laryngospasm, aspiration and significant bleeding with straining and coughing following extubation\(^1\). These complications can produce considerable morbidity in the patients following GA for DCR\(^1\). However this report just was a case series but our study was a clinical trial with the more patients that compared the classic LMA with the ETT during GA for external DCR, these are considered as the positive points of our study.

Waleed Riad et al. published an article regarding anesthesia for external DCR and wrote the use of endotracheal intubation and pharyngeal pack are remained an important place during GA for DCR\(^6\). However they confirmed that to decrease the bleeding during surgery, the patients’ blood pressure should be

\(\text{Mean arterial blood pressure (mmHg) in both groups}\)

At 5 min after intubation and 5 min after incision the mean arterial blood pressure (MAP) were significantly higher in the ETT group than in the LMA (\(p < 0.05\)).

\(\text{Heart rate in the both groups}\)

At 5 min after intubation and 5 min after incision, heart rate was significantly higher in the ETT group than in the LMA (\(p < 0.05\)).
maintain 20% lower than normal value and to decrease nose bleeding at the end of surgery, a smooth extubation without coughing and straining is necessary. They also noted that postoperative nausea and vomiting is a common problem after DCR surgery that could be decrease by the use of pharyngeal pack\(^6\).

Multiple clinical studies showed that hemodynamic changes are less during the LMA placement than during tracheal intubation\(^{16,17,18}\) also, in the current study the mean arterial pressure and heart rate in the LMA group lower than the ETT group during the surgery. Regarding coughing and straining at end of surgery, Jeff E et al. and Tanaka A et al. in their studies showed that the incidence of coughing and straining are much less during removal of the LMA than during tracheal extubation\(^{19,20}\). The present study showed that incidence of coughing and straining are much less during removal of the LMA than during tracheal extubation and like other studies this could decreased nose bleeding at end of surgery.

Piltcher et al. like Waleed Riad in their study showed the effect of pharyngeal pack in the prevention postoperative nausea and vomiting by preventing blood enter the stomach during nasal and sinus surgery\(^21\), but Erkalp K et al. showed in their study that pharyngeal pack during nasal surgery increases postoperative morbidity by leading to the development of painful oral \textit{aphthous} lesions or sore throat\(^22\). In the present study, laryngeal mask worked like pharyngeal pack and effective in the prevention of entering blood to the esophaguse and stomach and decreasing PONV, without the usual complications of pharyngeal pack.

This study had some limitations, first we should used reinforced LMA instead of the classic LMA in our study, reinforced LMA has a flexible tube which permit the anesthesiist to tape the tube away from the operative field especially in head and neck surgery so decrease the incidence of LMA displacement in the event of movement of head and neck during surgery. Second, the surgical filed and surgeon satisfaction with the ETT or LMA should be evaluated and compared. Therefore, more studies are recommended to use reinforced LMA during anesthesia and to compare surgeon satisfaction about surgical filed during surgery with the ETT or reinforced LMA.

In conclusion, LMA can be used instead of ETT in external DCR in the patients in whom insertion of LMA is not contraindicated, in order to decrease the incidence of hemodynamic changes during insertion, decrease the incidence of coughing and straining at the end of surgery and decrease the incidence of PONV.
References

THEOPHYLLINE VERSUS ACETAMINOPHEN
IN THE TREATMENT OF POST-DURAL PUNCTURE HEADACHE (PDPH)

ALIREZA MAHOORI*, EBRAHIM HASSANI*, HEYDAR NOROOZINIA*,
NEGIN JAVAHERI**, SANAZ HATAMI**

Abstract

Background: Post-dural puncture headache (PDPH) is the most frequent complication of procedures associated with dural puncture for spinal anesthesia or following accidental dural puncture during epidural anesthesia. Since invasive treatments have known complications, pharmacologic management may be preferable. The aim of this study was to evaluate and compare the efficacy of theophylline and Acetaminophen in treatment of PDPH.

Methods: In this single-blind randomized clinical trial, 60 patients with Class I physical status according to ASA classification system, who suffered from PDPH were enrolled. Patients in Theophylline group were received theophylline tablet 250 mg three times per day, and in the other group acetaminophen 500 mg three times per day was administered. Pain intensity was assessed 2, 6, and 12 hour after drug administration using 0-10 cm Visual Analog Scale.

Results: The main VAS values is significantly lower in theophylline group in comparison with the acetaminophen group at 2 (5 ± 1.57 vs. 5.97 ± 1.27), 6 (3.43 ± 1.73 vs. 4.33 ± 1.49), and 12 (2.67 ± 2.35 vs. 4.24 ± 1.97) hours after drug administration (p <0.05). No adverse effects were reported.

Discussion: Theophylline is a safe and effective treatment for PDPH. It may be tried in PDPH patients before using any invasive technique. Further investigations studying other Methylxanthines are recommended as well.

Key words: Theophylline; Lumbar puncture; Headache; Acetaminophen

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Introduction

Neuroaxial blocking has numerous advantages over general anesthesia. Being safe, low required dose of drugs, lower cost for patients, no risk of pulmonary aspirations, no age limits are some benefits of neuroaxial blocking. However, some complications have been reported for spinal anesthesia. Post-dural puncture headache (PDPH) is the most frequent complication of these procedures, which is attributed mostly to the excessive leak of cerebrospinal fluid (CSF) from the puncture point leading to intracranial hypotension, associated with a resultant cerebral vasodilatation. The incidence of PDPH was reported to be 1-30%, with 0%-14.5% incidence rate when small needles are used.

Several invasive and non-invasive treatments were suggested for management of PDPH, including medical therapy with non-steroidal analgesics, morphine, casyntropin or invasive procedures such as blood patch or caudal normal saline injection. A medical therapy with theophylline has been suggested, but the recommendations mostly were not evidence-based. Feuerstein et al conducted a preliminary study in 1986 on 11 patients with post-dural puncture headache and compared per oral treatment with theophylline versus placebo. They found theophylline to be effective in treating PDPH, however because of the small sample size; the findings were not completely reliable. In 2008, Ergun et al compared the efficacy of intravenous theophylline treatment for PDPH, versus placebo and claimed that intravenous theophylline infusion is effective for decreasing the painfulness of PDPH.

Although more than a quarter of a century has passed since the introduction of theophylline as a treatment for PDPH, surprisingly few studies have focused on this treatment and its efficacy up until now. In this randomized controlled trial, we aimed to investigate and compare the efficacy of oral theophylline therapy versus acetaminophen for the treatment of PDPH.

Methods

This study was implemented with the approval of Scientific & Ethical Review Boards of Urmia University of Medical Sciences (UMSU), Urmia, Iran. In this single-blind randomized clinical trial, sixty patients with ages between 30-50 years who were candidate of various surgical procedures under spinal anesthesia were enrolled. The patients had a Class I physical status according to the classification system of American Society of Anesthesiology (ASA). All the subjects have experienced PDPH according to the definition of International classification of headache disorders (ICDH-II) prior to recruiting or randomization within groups. Participants were randomly recruited into two Intervention and control groups each consisted of 30 patients. According to the power analysis, 54 patients were enough to have a 90% chance of detecting, as significant at the 5% level, an increase in the PDPH remission rate from 20% in the acetaminophen group to 60% success rate in the theophylline group. A total of 60 were entered to this two-treatment parallel-design study. The power of study for detecting the 0.9 difference in means of VAS scores between groups at a two-sided 0.05 significance level will be 92%. All the patients signed an informed consent form prior to participation in the study. For randomized recruitment computer software was used. The patients with central nervous disorders, hypertension, ischemic heart disease, cardiac arrhythmias, hyperthyroidism, age higher than 60 years old and past history of migraine headaches were excluded from the study.

The patients in the intervention group received a tablet of 250 mg Theophylline (the therapeutic dose of theophylline which usually associates with no complication), every eight hours, whilst the cases in the control group were treated with Acetaminophen tablets (500mg) every eight hours (TDS administration to ascertain the blindness of subjects in both study groups). The definition of international classification of headache disorders (ICDH-II) was used to identify post-dural puncture headache (PDPH) cases. For measuring the severity of headache, we applied visual analog scale (VAS), which is a psychometric response scale for measuring subjective characteristics.

The pain scale consisted of a 10 cm horizontal line marked from 0 (denoting no pain) to 10 (denoting worst possible imaginable pain). If headache exists, its intensity was recorded within the continuous spectrum.
of this scale. In the 2nd, 6th and 12th hours after the administration of drug, the intensity of headache was evaluated and registered again. Except the anti-headache treatment, other therapies (including fluids and drugs) were similar in patient of both groups. Data were analyzed by independent t-test and chi-square test among two groups using SPSS statistical software ver16 (Chicago, IL). P-value <0.05 was considered statistically significant.

Results

Sixty consecutive patients who met the inclusion criteria were included in the study. Demographic characteristics such as age, gender, and baseline headache intensity were similar between the groups (Table 1).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Theophylline group (N = 30)</th>
<th>Acetaminophen group (N = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean ± SD)</td>
<td>40.06 ± 5.95</td>
<td>40.00 ± 6.43</td>
<td>0.6</td>
</tr>
<tr>
<td>Sex (Male/ Female)</td>
<td>19/11</td>
<td>22/8</td>
<td>0.4</td>
</tr>
<tr>
<td>Baseline pain</td>
<td>5.46 ± 1.33</td>
<td>5.96 ± 1.20</td>
<td>0.13</td>
</tr>
</tbody>
</table>

The visual analogue scale scores on 2nd, 6th, 12th hours after treatment were significantly lower (P < 0.05) in the Theophylline group compared to the Acetaminophen group (Table 2).

<table>
<thead>
<tr>
<th>Headache intensity</th>
<th>Theophylline group (N = 30)</th>
<th>Acetaminophen group (N = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hrs after treatment</td>
<td>5.00 ± 1.57</td>
<td>5.97 ± 1.27</td>
<td>0.01</td>
</tr>
<tr>
<td>6 hrs after treatment</td>
<td>3.43 ± 1.73</td>
<td>4.33 ± 1.49</td>
<td>0.03</td>
</tr>
<tr>
<td>12 hrs after treatment</td>
<td>2.67 ± 2.35</td>
<td>4.24 ± 1.97</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Both theophylline and acetaminophen were well tolerated and no adverse events (such as nausea, diarrhea, dizziness, lightheadedness or tachycardia) were reported in both groups. Also no patient requested to be withdrawn from the study.

Discussion

Several studies proposed the potential role of theophylline in treating PDPH, but only two trials were investigated its efficacy until now. In this study the intensity of pain was significantly lower in the group treated with oral theophylline compared to the group treated with Acetaminophen 2 hours, 6 hours and 12 hours after receiving medical treatment. The patients have not reported any adverse effect due to treatment with theophylline (no nausea, diarrhea, dizziness, lightheadedness or tachycardia).

Similar to our findings, both of the studies which are implemented by Feuerstein et al and Ergun et al, have reported the theophylline to have beneficial effect in treating PDPH in comparison with the placebo. However because of the limited sample size in the study of Feuerstein et al, we can only consider it as a pilot study. The study protocol was different in study of Ergun et al compared to ours. In Ergun’s study, theophylline was administered intravenous, but we have studied the efficacy of oral theophylline therapy in treatment of PDPH. The other difference is related to the use of Acetaminophen, as a simple analgesic in our study instead of using placebo. The findings of this study are in favor of the superiority of theophylline therapy over Acetaminophen in treating PDPH.

Intravenous aminophylline reduced the number of participants affected by PDPH of any severity after a lumbar puncture when compared to no intervention in patients undergoing elective caesarean section. However based on the results of Zajac et al, prophylactic administration of aminophylline did not influence the incidence of PDPH.

Methylated xanthines and their derivates are from the pharmacologic group of nonselective phosphodiesterase inhibitors, which leading to the relaxation of bronchial smooth muscles (bronchodilatation) as well as cerebral vasoconstriction. It seems that the vasoconstriction through blocking adenosine receptors is the main mechanism of theophylline or aminophylline in treating the PDPH. Also it supposed to induce CSF production by stimulating Na-K pumps.

A limitation for this study was the limited number of patients who were compatible with our
inclusion (PDPH & ASA grade I) and exclusion criteria (especially the exclusion of patients with any history of hypertension, ischemic heart disease or migraine headache). The difference among the half life of acetaminophen with theophylline, at least theoretically, could be a limitation for the findings of this study.

Several studies proposed the potential role of theophylline in treating PDPH, but only two trials were investigated its efficacy until now. In this study the intensity of pain was significantly lower in the group treated with oral theophylline compared to the group treated with Acetaminophen 2 hours, 6 hours and 12 hours after receiving medical treatment. The patients have not reported any adverse effect due to treatment with theophylline (no nausea, diarrhea, dizziness, lightheadedness or tachycardia).

Since we have enrolled only patients with class I physical status according to ASA classification system to our trial, implementation of further studies on the use of theophylline or aminophylline in the treatment of PDPH in other patient groups is suggested.

**Conclusion**

According to the findings of this study, the authors recommend the use of theophylline in treating the post-dural puncture headache. Theophylline revealed to be a safe and effective medical therapy in the cases that invasive therapy is not necessarily indicated.

There was no conflict of interests in this study.

References

RATE AND PATTERN OF ANTIBIOTIC RESISTANCE IN MICROBIOLOGICAL CULTURES OF SEPSIS PATIENTS IN A LOW-MIDDLE-INCOME COUNTRY’S ICU

OTGON BATAAR*, CHULUUNCHIMEG KHUDERCHULUUN*,
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Abstract

Background: In this prospective, observational study, the rate of antibiotic resistance in cultures sampled from sepsis patients was determined in an intensive care unit of a low-middle income country.

Methods: Critically ill patients suffering from bacterial sepsis were eligible for enrollment. Aside from demographic, disease-related and sepsis-specific parameters, the type of microbiological sample and cultured microorganism as well as the resistance pattern (extensively resistant bacteria, multi-drug resistant bacteria) were documented. Descriptive statistical methods, parametric and non-parametric tests were used.

Results: 215 sepsis patients were included. 193 of the 410 cultured organisms (47.1%) showed antibiotic resistance [extensively resistant bacteria, n = 90 (11%); multi-drug resistant bacteria, n = 103 (25.1%)]. 51.6% of the patients were infected by ≥1 resistant bacteria. Bacteria with an exceptionally high rate of antibiotic resistance were Acinetobacter baumannii (90%), Enterobacter spp (60%) and coagulase-negative Staphylococci (60%). Patients infected with resistant bacteria more often received inadequate empirical antibiotic therapy (36.9 vs. 13.5%, p <0.001), required mechanical ventilation (66.7 vs. 42.3%, p <0.001) and renal replacement therapy (28.8 vs. 9.6%, p <0.001) more frequently, and had a longer stay in the intensive care unit [5 (3-9.5) vs. 5 (2-8)%, p <0.001] than patients with sepsis due to non-resistant bacteria. There was a trend towards a higher mortality in patients with resistant bacteria (43.2 vs. 31.7%, p = 0.09).

Conclusion: Resistant bacteria were detected in up to 50% of microbiological samples from critically ill sepsis patients in the intensive care unit of a low-middle-income country. Antibiotic resistance appears to be a relevant problem of sepsis management in a resource-limited setting.

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** Department of Anesthesiology, Perioperative Medicine and General Intensive Care Medicine, Salzburg General Hospital and Paracelsus Private Medical University, Salzburg/Austria.

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Introduction

While sepsis receives most attention in the medical literature and public in high-income countries, the majority of worldwide deaths due to sepsis occur in middle- and low-income countries. Reasons for this are multiple, ranging from the additional burden of tropical infectious diseases, low hygienic standards, a high prevalence of HIV/AIDS and tuberculosis as well as resource-limited health care systems with insufficient infection prevention and management facilities.

Independent of the causative pathogen of sepsis, timely and adequate empirical antibiotic therapy is crucial for survival. Antibiotic resistance is an important factor influencing the adequacy of both empirical and targeted antibiotic therapy. The rate of antibiotic resistance drastically varies for different bacteria and between geographic regions. Due to uncontrolled antibiotic use, availability of only a restricted amount of antibiotic agents, particularly high antibiotic resistance rates have been observed in resource-limited healthcare systems. So far, only scarce data on the incidence and clinical relevance of antibiotic resistance patterns in critically ill sepsis patients treated in middle-and low-income countries have been published.

In this prospective observational study, the rate of antibiotic resistance in cultures sampled from critically ill sepsis patients was determined in an intensive care unit of a low-middle income country. Furthermore, the influence of antibiotic resistance on clinical outcome was assessed. We hypothesized that antibiotic resistance was frequent and relevantly affected clinical outcome in this study population.

Methods

This analysis was designed as a prospective observational study. During the time from Jan 1, 2011 until Aug 31, 2012, the study was conducted in an eight bed multidisciplinary intensive care unit of a tertiary university teaching hospital in Ulaanbaatar, the capital city of Mongolia. The study protocol was approved by the Ethics Committee of the Central State University Hospital/Mongolian Medical University (protocol number, 83/4 24 June 2010). Considering that only anonymous data were collected, no blood or tissue samples were taken and the patients’ management was not changed by the study. Written informed consent was waived.

Description of the Study Setting

The study setting is an intensive care unit typical for many low-middle-income countries with part-time intensivist staffing, possibilities to provide basic organ support (mechanical ventilation and intermittent hemodialysis for renal replacement) but with restricted and inconsistent supply of drugs and disposable materials. The hospital-based microbiological laboratory processes 100-120 microbiological sample tests per day. During the study period, the principal method used for bacterial cultures and determination of antibiotic resistance was API strip, ATB strip and the disc diffusion method, respectively. The laboratory is limited by only a restricted number of staff as well as intermittent shortages of material resources.

Patients

Critically ill patients who suffered from bacterial sepsis, confirmed by a positive microbiological culture, were eligible for study enrollment. Exclusion criteria were: sepsis without microbiological confirmation, lack of an antibiogram, sepsis due to viral or fungal infection, infections with mycobacteria (n = 31 during the study period), and patient age <18 years. Patients suffering from viral, fungal or mycobacterial infection were excluded because no testing for antimicrobial resistance of these organisms could be performed in the study hospital during the observation period.

Data

The following data were collected in each study patient: age, gender, the McCabe classification, admission diagnosis, the Simplified Acute Physiology Score II, type of infection, presence of severe sepsis or septic shock, presence of multiple organ dysfunction, adequacy of empirical antibiotic therapy, availability of adequate antibiotic agent(s), need for mechanical
ventilation or renal replacement therapy, intensive care unit length of stay and mortality. The type of microbiological sample and cultured microorganism as well as the resistance pattern were documented for each positive culture.

Definitions

Sepsis, severe sepsis and septic shock were defined according to the most recent ACCP/SCCM criteria. Multiple organ dysfunction was defined as the presence of two or more organ dysfunctions as defined by an organ Sequential Organ Failure Assessment Score count of two or higher. The pattern of antibiotic resistance was defined as suggested by the joint initiative of the European Centre for Disease Prevention and Control as well as the Centers for Disease Control and Prevention. Accordingly, resistant bacteria were grouped into extensively resistant and multidrug-resistant bacteria. Extensive drug resistance was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories. Multidrug resistance was defined as non-susceptibility to at least one agent in three or more antimicrobial categories. For five bacteria [Staphylococcus aureus, Enterococcus spp, Enterbacteriaceae (other than Salmonella and Shigella), Pseudomonas aeruginosa and Acinetobacter spp] pre-defined resistance profiles and antibiotic susceptibility categories were applied. For all other bacteria, those antibiotic categories intrinsically active against the bacterium and for which resistance testing was available were considered. Resistance or non-susceptibility was defined using breakpoint criteria as suggested by the Clinical Laboratory Standards Institute.

We did not apply the definition of pandrug-resistance, since not all antibiotic agents which are commonly tested in high-income countries to define pandrug-resistant bacteria, were available and tested in the study laboratory.

Statistical Analysis

The primary endpoint was to identify the rate of bacterial resistance per sample and critically ill sepsis patient. Secondary endpoints were to compare intensive care unit mortality, adequacy of empirical antibiotic therapy, need for mechanical organ support, presence of multiple organ dysfunction and length of stay in the intensive care unit between study patients with and without resistant bacteria.

Following plausibility testing, study variables were tested for normality distribution using the Shapiro Wilk’s test. Descriptive statistics were applied to identify the rate of bacterial resistance. Comparisons of study variables between patients with and without resistant bacterial infections were performed using the Student’s t- (continuous normally distributed variables) or the Mann-Whitney U-test (continuous, non-normally distributed variables) as well as the Fisher’s Exact test (categorical data), as appropriate. P-values <0.05 were considered to indicate statistical significance. Data are given as median values with interquartile ranges, if not otherwise indicated.

Results

During the study period, 1,284 patients were admitted to the study intensive care unit. Two-hundred-fifteen of these had no exclusion criteria present and suffered from sepsis confirmed by 410 positive microbiological cultures. Table 1 presents details of the study population. Hundred-ninety-three of the 410 cultured organisms (47.1%) revealed antibiotic resistance.
extensively resistant bacteria, similar inter-group differences were observed between patients with extensively resistant bacteria as well as between patients with multidrug-resistant bacteria.

**Discussion**

In this prospective observational study, approximately half of the microbiological cultures sampled from critically ill sepsis patients in a Mongolian intensive care unit revealed resistant resistance. Characteristics of microbiological samples with resistance patterns are given in Table 2. Resistant bacteria were mostly observed in clusters during the study period (Fig. 1).

Sepsis patients infected with resistant bacteria more often received inadequate empirical antibiotic therapy, required mechanical ventilation and renal replacement more frequently, suffered from multiple organ dysfunction more often and had a longer stay in the intensive care unit than patients with sepsis due to non-resistant bacteria. Except for a lacking difference in the presence of multiple organ dysfunction and the length of intensive care unit stay in patients with extensively resistant bacteria, similar inter-group differences were observed between patients with and without extensively resistant bacteria as well as between patients with and without multidrug-resistant bacteria.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>215</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51 (37-67)</td>
</tr>
<tr>
<td>Male gender n (%)</td>
<td>104 (48.4)</td>
</tr>
<tr>
<td>McCabe Classification n (%)</td>
<td>70 (32.6)</td>
</tr>
<tr>
<td>1</td>
<td>92 (42.8)</td>
</tr>
<tr>
<td>2</td>
<td>49 (22.8)</td>
</tr>
<tr>
<td>3</td>
<td>4 (1.9)</td>
</tr>
<tr>
<td>Admission Diagnosis n (%)</td>
<td>89 (41.4)</td>
</tr>
<tr>
<td>Medical</td>
<td>83 (38.6)</td>
</tr>
<tr>
<td>Surgical</td>
<td>13 (6)</td>
</tr>
<tr>
<td>Neurological</td>
<td>6 (2.8)</td>
</tr>
<tr>
<td>Traumatological</td>
<td>24 (11.2)</td>
</tr>
<tr>
<td>Other</td>
<td>41 (33-50)</td>
</tr>
<tr>
<td>Type of Infection n (%)</td>
<td>161 (74.9)</td>
</tr>
<tr>
<td>Community-acquired</td>
<td>54 (25.1)</td>
</tr>
<tr>
<td>Severe Sepsis n (%)</td>
<td>64 (29.8)</td>
</tr>
<tr>
<td>Septic Shock n (%)</td>
<td>104 (48.4)</td>
</tr>
<tr>
<td>Multiple Organ Failure n (%)</td>
<td>73 (34)</td>
</tr>
<tr>
<td>Mechanical Ventilation n (%)</td>
<td>118 (54.9)</td>
</tr>
<tr>
<td>Renal Replacement Therapy n (%)</td>
<td>81 (37.7)</td>
</tr>
<tr>
<td>Intensive Care Unit Length of Stay days</td>
<td>6 (3-10)</td>
</tr>
<tr>
<td>Intensive Care Unit Mortality n (%)</td>
<td>81 (37.7)</td>
</tr>
</tbody>
</table>

Data are presented as median values with interquartile range, if not otherwise indicated.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Characteristics of Microbiological Samples and Resistance Patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>410</td>
</tr>
<tr>
<td>Samples per patient n</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>Type of sample n (%)</td>
<td>Sputum 136 (33.2)</td>
</tr>
<tr>
<td>Urine</td>
<td>78 (19)</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>36 (8.8)</td>
</tr>
<tr>
<td>Catheter tip</td>
<td>32 (7.8)</td>
</tr>
<tr>
<td>Wound swab</td>
<td>31 (7.6)</td>
</tr>
<tr>
<td>Other</td>
<td>97 (23.7)</td>
</tr>
<tr>
<td>Microorganisms n (%)</td>
<td>Staphylococcus aureus 111 (27.1)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>71 (17.3)</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>65 (15.9)</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>30 (7.3)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>28 (6.8)</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>22 (5.4)</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>21 (5.1)</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>19 (4.6)</td>
</tr>
<tr>
<td>Other</td>
<td>43 (10.5)</td>
</tr>
<tr>
<td>Drug-Resistance per Patient n (%)</td>
<td>Extensive Drug Resistance 49 (22.8)</td>
</tr>
<tr>
<td>Multi-Drug Resistance</td>
<td>62 (28.8)</td>
</tr>
<tr>
<td>Drug-Resistance per Sample n (%)</td>
<td>193 (47.1)</td>
</tr>
<tr>
<td>Extensive Drug Resistance</td>
<td>90 (22)</td>
</tr>
<tr>
<td>Multi-Drug Resistance</td>
<td>103 (25.1)</td>
</tr>
<tr>
<td>Drug-Resistance per Microorganism n (%)</td>
<td>Acinetobacter baumannii 27 (90)</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>39 (60)</td>
</tr>
<tr>
<td>Coagulase-negative Staphylococcus</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>10 (52.6)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>14 (50)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>33 (46.5)</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>9 (42.9)</td>
</tr>
</tbody>
</table>
bacteria. Extensively resistant bacteria were observed in 22% and multidrug-resistant bacteria in 25.1% of microbiological cultures, respectively. In total, 51.6% of the study patients were infected by one or more resistant bacteria. Bacteria with an exceptionally high rate of antibiotic resistance (≥60%) were Acinetobacter baumannii, Enterobacter spp and coagulase-negative Staphylococci. Sepsis patients infected with resistant bacteria received inadequate empirical antibiotic therapy, mechanical ventilation, renal replacement therapy more frequently and suffered from multiple organ dysfunction more often than sepsis patients without resistant bacteria. The length of stay in the intensive care unit was longer in sepsis patients with resistant bacteria but the mortality rate in the intensive care unit did not significantly differ between groups despite a trend towards a higher fatality rate in sepsis patients infected with resistant bacteria.

A 47.1% rate of resistant bacteria in microbiological cultures sampled from sepsis patients is high. Even when taking extensively resistant bacteria not into account, a 25.1% rate of multidrug-resistant bacteria is striking both from a clinical point of view and in comparison with reports of intensive care units in high-income countries11,12. Since the microbiological laboratory of the study hospital did not routinely test resistance against all antibiotic agents active against the cultured bacterium in their antibiograms due to resource limitations, the true rate of antibiotic resistance is likely to be underestimated and the rate of pan-drug resistance could not be evaluated. Our results need to be further relativized when considering that frequently resistant microbes causing sepsis in Mongolia such as mycobacteria and fungi were not analyzed in this study for reasons stated above. Compared to other middle- and low-income settings, our study showed similar results as reported by other authors12-16. So far, however, none of these studies specifically evaluated the rate of resistant bacteria in critically ill sepsis patients.

Particularly high resistance rates with 50% or more of the cultures being resistant were found for five specific bacteria, four of which were gram-negative. Almost all cultures of Acinetobacter baumannii revealed antibiotic resistance. This is particularly relevant for our setting, since Acinetobacter baumannii was detected in 7.3% of all study samples. Extremely high resistance rates of Acinetobacter spp have been reported in the literature17,18 and are explained by the bacterium’s ability to mutate rapidly and spontaneously during therapy19. Similar observations were made in other low-and middle-income settings as well as high-income countries for Enterobacter spp, Klebsiella spp and Pseudomonas aeruginosa20-22.

Reasons for the high resistance rate observed in this population cannot be determined by our results. Other authors have suggested that irrational use of a restricted selection of antibiotics, even in patients with no infectious disease, plays an important causative role3. In most middle- and low-income countries over-the-counter availability of antibiotic agents with widespread unprescribed use is a key problem23. This is also the case in Mongolia24. In addition, common use of antibiotics for non-medical reasons contributes to an
extent that has not yet been quantified and analyzed in these settings.

Fig. 1 shows that most samples culturing resistant bacteria were detected in clusters during the study period. Although this can partly be explained by the fact that repeated samples were taken in sepsis patients with resistant bacteria, it may also indicate that patient-to-patient transmission within the study ICU could have played a role. Hand hygiene is a crucial measure to prevent patient-to-patient transmission of infectious pathogens and is notoriously under-respected in resource-limited health care systems. Hand hygiene is a crucial measure to prevent patient-to-patient transmission of infectious pathogens and is notoriously under-respected in resource-limited health care systems.25,26

In our study population, sepsis patients infected with resistant bacteria had a higher morbidity as reflected by a more frequent need for mechanical ventilation and renal replacement therapy as well as more frequent multiple organ dysfunction. One reason for this observation could be the higher rate of inadequate empirical antibiotic therapy in these patients. Inadequate empirical antibiotic therapy has repeatedly been identified as a relevant risk factor for increased morbidity and mortality in critically ill sepsis patients. Despite these data on an increased fatality rate in case of inappropriate empirical antibiotic therapy, we observed a trend but no significant difference in intensive care unit mortality between sepsis patients with and without resistant bacteria. Including 215 patients, our sample size was too small to detect a significant mortality difference. Indeed, a post hoc power analysis suggests that a beta-level of merely 41% was achieved to detect an absolute 11.5% mortality difference at an alpha-level of 5%. While studies from high-income countries report controversial data on the mortality effects of resistant bacteria in sepsis, there are almost no data on this aspect from resource-limited settings. However, as our data indicate the association between resistant bacteria and mortality may be different in resource-limited settings. While antibiotic agents active against resistant bacteria are routinely available in high-income countries, this is typically not true for middle- and low-income settings where the majority of new generation and back-up antibiotics are not or only inconsistently available. Therefore, unlike in high-income countries, infection with resistant bacteria in middle- and low-income countries is likely to be equivalent to inadequate antibiotic therapy and thus likely to negatively affect patient outcome. Accordingly, in eight of our study patients infected with resistant bacteria the adequate antibiotic agent was not available. Seven of these patients died during their stay in the intensive care unit.

Our study suffers from relevant limitations that need to be taken into account when interpreting its results. First, due to the unavailability of laboratory resources, no specifications of antibiotic resistance could be performed. Thus, we cannot report on the incidence of key resistance factors such as production of extended spectrum or other beta-lactamases (e.g. AmpC or metallo-beta-lactamase-1). Neither could we test for antibiotic resistance genes as well as presence of certain enzymes characterizing resistant bacterial strains. In addition, both mycobacteria and fungi, which frequently exhibit resistance in resource-limited settings, were not included in our analysis. Finally, it was impossible to evaluate the true pathogenic relevance of all microbiological samples. Therefore, it we cannot exclude that a certain number of resistant bacteria which were cultured in this study population rather reflected colonization than true infection.

In conclusion, resistant bacteria were detected in up to 50% of microbiological samples from critically ill sepsis patients in the intensive care unit of a low-middle-income country. Antibiotic resistance appears to be a relevant problem of sepsis management in a resource-limited setting.
References


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RESEARCH EXPERIENCE, INTEREST AND PERCEIVED BARRIERS OF CLINICAL STAFF WORKING AT THE INTENSIVE CARE DEPARTMENT OF A TERTIARY CARE ACADEMIC HOSPITAL IN SAUDI ARABIA

HASAN M. AL-DORZI*, BRINTHA NAIDU**, SHAKEEL KHOKHAR***, DAVID WHITE****, YASEEN M. ARABI*****

Abstract

Background: Promoting clinical research is important considering the shortage of clinical investigators and the increasing need for large multicenter studies. Participation of clinical staff in research is crucial to achieve this goal. Our objective was to assess the research experience and interest of clinical staff working at a tertiary-care intensive care unit (ICU) and explore the perceived research barriers.

Methods: A written survey was administered to 185 multidisciplinary ICU staff at a 900-bed tertiary-care academic hospital in Riyadh. It consisted of questions/statements on previous research experience, interests and barriers. Responses were either Yes/No answers or graded according to the 5-point Likert scale.

Results: Most (62.8%) staff responded (age = 33.9 ±7.2 years, 69.6% females, 76.0% nurses, 10.4% physicians, clinical experience = 7.6 ±6.8 years). Fifty (40%) respondents participated in clinical research (physicians 69.2%, nurses 37.9% and respiratory therapists 25%, p =0.052 ), 42 (33.6%) of them in the current ICU but only 11.2% presented in-person their research projects at national/international meetings. Most respondents (86.2%) believed that participation in research would enhance their career. There was no differences in research tasks clinical staff were willing to perform except for writing manuscripts with physicians (69.2%) and respiratory therapists (58.3%) more willing than nurses (29.5%), p =0.03. Perceived research barriers were lack of time (76.8%), of financial compensation (58.4%) and of encouragement (48.8%).

Conclusions: The majority of clinical staff working at a tertiary-care ICU of an academic hospital was interested in conducting research but the lack of time, financial compensation and encouragement were perceived as significant barriers.

Key words: Critical care, Critical care nursing, Education, Biomedical research
Introduction

Globalization of clinical research, a recently growing phenomenon, requires expanding the pool of clinical researchers in developing countries, whose contribution to clinical research remains low in proportion to their population. An illustration of that is the number of studies registered in the clinicaltrials.gov website in 2011. There were 894 clinical trials from 13 Middle-Eastern countries, 2,007 clinical trials from 6 South-Asian Countries, 6,835 clinical trials from France, 8,755 clinical trials from Canada, and 57,066 clinical trials from the United States. This is probably related to multiple factors that include inadequate knowledge of clinical research processes, deficient training and specialization in this field and lack of support from healthcare institutions, private industry and governments leading to shortage of qualified clinical investigators. In Saudi Arabia, the healthcare system has been rapidly developing in the last few decades. As it relates to “Intensive Care Speciality” at our institution, this has been associated with an increase in clinical research performance. Reflective of that is the gradual growth of clinical research, which started by performing observational studies and developed to conduct investigator-led clinical trials and then participation in renowned international multicenter trials.

The objectives of this survey were to determine research experience, interest and perceived barriers to conduct research for clinical staff working in the Intensive Care Department of a tertiary-care academic center in Saudi Arabia.

Methods

The study was approved by the Institutional Review Board. This was a survey that was conducted at the Intensive Care Department of a tertiary-care academic hospital, in Riyadh, Saudi Arabia. The hospital was a 900-bed teaching tertiary care center and had been accredited by the Joint Commission International since 2006. The staff came from more than 50 nationalities including Saudi Arabia, Australia, South Africa, Philippines, India, Pakistan, Malaysia, and other Middle Eastern countries. The hospital was established in 1983 and became affiliated with King Saud Bin Abdulaziz University for Health Sciences, which was established in 2005, and with King Abdullah International Medical Research Center, which was founded in 2007. Selected hospital staff were given academic titles with promotion dependent partly on research performance and publication. The Intensive Care department covered a 21-bed medical/surgical closed intensive care unit (ICU) that treated a heterogeneous group of patients including trauma patients, a 14-bed intermediate care unit and an 8-bed neuro-critical care unit. At the time of the survey, the department was staffed with 12 North American board-certified critical care physicians and 10 registrars for 24 hours per days, 7 days a week, and provided training to critical care fellows and rotating residents from different specialties. Additionally, there were 150 nurses, many of whom had critical care training and some were undergoing postgraduate studies, 40 respiratory therapists (RTs) and two clinical pharmacists. All staff were primarily hired to perform clinical work.

The initial draft of the survey was designed by the director of the departmental clinical research program. The draft was then revised after obtaining feedback from two charge nurses and one registrar. It was later finalized after review by the Department Chair. The final survey was made up of 35 items that covered the following: demographic information, training background, previous research experiences, research interests and barriers. In addition, participants were asked to rate their knowledge of nine different research skills, including generation of study proposals, data collection and management and statistical analysis, as lacking, adequate, good or excellent. Otherwise, responses were mostly either Yes/No answers or graded according to the 5-point Likert scale. At the end of survey, respondents were asked to write down perceived barriers other than those stated and to register their names if they were willing to participate in clinical research in the department. Surveys were distributed in paper form to all available staff in November 2008 and to staff that joined thereafter in November 2010. Multiple reminders were sent to all staff to complete surveys, but participation was voluntary.

Statistical analysis was done using SPSS version
17.0 software (SPSS, Chicago, Ill). Continuous variables were reported as means with standard deviation and categorical variables as absolute and relative frequencies. The Chi-squared test was used to assess the difference between categorical variables and the student t-test was used for the analysis of differences in the means of continuous variables.

Results

General characteristics of respondents

One hundred eighty five surveys were distributed and 125 were returned (response rate of 62.8%). The characteristics of respondents are presented in Table 1.

Research experience and interests

The vast majority of respondents (95.2%) agreed that clinical research is important in critical care and 50 respondents (40%) indicated that they have participated in such research in the past (69.2% of physicians, 37.9% of nurses and 25% of RTs, p = 0.052). Only 14 (11.2%) respondents indicated that they have presented their research project in person at national or international meetings (no difference among physicians, nurses and RTs, p = 0.18). A significant number of respondents (n = 42, 33.6%) indicated that they have participated in research while working in the department (no difference among the 3 disciplines, p = 0.56). Ninety nine (87.2%) respondents thought that the department was a good platform for research and 90 (75.6%) were interested in conducting research in the department in the future. Only 8.8% of respondents were not interested in performing research at all. Most respondents (86.2%) believed that participating in research will enhance their future career.

Clinical staff rating of knowledge of different research topics

Table 2 describes clinical staff rating of their knowledge of nine different research topics. Significant number of respondents lack knowledge in most research topics. Of note is that more than two thirds of them thought that they are able to collect and manage data and almost one half reported that they knew how

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td><strong>Characteristics of respondents</strong></td>
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<tr>
<td><strong>Respondents (N = 125)</strong></td>
</tr>
<tr>
<td>Age (years), mean ± SD</td>
</tr>
<tr>
<td>Female gender, N (%)</td>
</tr>
<tr>
<td>Professional status, N (%)</td>
</tr>
<tr>
<td>Physicians</td>
</tr>
<tr>
<td>Nurses</td>
</tr>
<tr>
<td>Respiratory therapists</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td>Nationalities, N (%)</td>
</tr>
<tr>
<td>Saudi</td>
</tr>
<tr>
<td>Filipino</td>
</tr>
<tr>
<td>South African</td>
</tr>
<tr>
<td>Malaysian</td>
</tr>
<tr>
<td>Australian</td>
</tr>
<tr>
<td>Other nationalities (N = 17)</td>
</tr>
<tr>
<td>Clinical work experience (years), mean ± SD</td>
</tr>
<tr>
<td>Previous work at a hospital that conducted research, N (%)</td>
</tr>
<tr>
<td>Current work (years), mean ± SD</td>
</tr>
</tbody>
</table>
to perform statistical analysis. Knowledge to write and submit manuscripts and to present research results as posters seemed to be more lacking than other research activities. There was no statistical difference in the rating of physicians, nurses and RTs regarding all the nine research topics.

Fig. 1 describes the research activities that the respondents were willing to perform in the future. Of note is that most (77%) respondents were willing to perform data collection. There was no difference in the type of research activities among physicians, nurses and RTs except for writing abstracts and manuscripts as physicians (69.2%) and RTs (58.3%) were more willing to do that than nurses (29.5%), p = 0.03.

**Research barriers**

Fig. 2 describes the factors perceived by different clinical staff to hinder performance of research. Physicians, nurses and RTs agreed that lack of time and of compensation were important factors with no statistically significant differences among the groups (p-values of 0.30 and 0.52, respectively). All RTs, 62.6% of nurses and 30.8% of physicians thought that lack of encouragement was also an important factor (p < 0.001 among the three groups). Other barriers stated by respondents included lack of training in research and presence of only one biostatistician in the department.

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### Table 2

<table>
<thead>
<tr>
<th></th>
<th>Lacking N (%)</th>
<th>Adequate N (%)</th>
<th>Good N (%)</th>
<th>Excellent N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research ethics</td>
<td>37 (29.6)</td>
<td>48 (38.4)</td>
<td>30 (24.0)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Conducting literature review</td>
<td>38 (30.4)</td>
<td>45 (36.0)</td>
<td>45 (23.2)</td>
<td>5 (4.0)</td>
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<td>45 (36.0)</td>
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<td>2 (1.6)</td>
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<td>22 (17.6)</td>
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<td>Writing abstracts and manuscripts</td>
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<td>42 (33.6)</td>
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<td>34 (27.2)</td>
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<td>Presentation of research work (oral or poster presentation)</td>
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<td>36 (28.8)</td>
<td>24 (19.2)</td>
<td>4 (3.2)</td>
</tr>
</tbody>
</table>

**Fig. 1**

Research activities that clinical staff of a tertiary-care intensive care unit were willing to perform

**Fig. 2**

Barriers to participation in clinical research as perceived by the clinical staff of a tertiary-care intensive care unit
Discussion

This study evaluated research experience, interest and barriers of clinical staff working in the Intensive Care Department of a tertiary-care hospital in Saudi Arabia and found that a minority of physician, nursing and respiratory care staff had prior research experience while the majority of staff in these three disciplines showed high interest in participating in research in the future. In addition, these healthcare providers indicated that they needed education on various research areas and perceived the lack of financial support, time and encouragement as important research barriers.

We found a high interest in performing research among clinical ICU staff primarily hired to perform clinical work. This was likely, at least in part, due to the belief that it would enhance their future career. Research accomplishments and publications are frequently used to gain promotion and improve academic status. A survey of 139 medicine departments chairs in the United States and Canada found that performance of clinical research, in particular the journals in which publications appeared, the number of peer reviewed publications and presentation of research in national meetings, was an important criterion for promotion of clinical educators. This seemed to be more important for promotion committee chairpersons. As our institution developed over time to be a more academic center, conducting research and publication were crucial to obtain academic titles in the university and for subsequent promotion.

Promoting clinical research is important especially with the existence of worldwide shortage in clinical investigators and clinician scientists, even in developed countries. In the United States, the percentage of physicians engaged in research decreased steadily from a peak of 4.6% in 1985 to 1.8% in 2003. This was related to both the growth of the pool of practicing physicians and the decline of the number of physician-scientists, due to multiple reasons that included debt owed by medical graduates forcing them to go into the more financially rewarding clinical practice, lengthy clinical training, scarcity of research mentors, difficulty attaining research grants and uncertainties about promotion in academic hospitals. These reasons may not be all applicable in other countries, such as Saudi Arabia, as the education and healthcare systems might be different. However, the same problem of clinical investigator shortage is present and surely more severe, making the expansion of researchers’ pool more urgent. Although 33.6% of our clinical staff participated in research, only 11.2% presented their research at national or international meetings, suggesting that the number of principal investigators was modest.

To solve the problem of clinical investigator shortage, Western countries resorted to multifaceted approach. Research was promoted by the foundation of MD/PhD dual degrees, research fellowships and various clinician-investigator programs and by the incorporation of research in specialty and subspecialty residency programs. Short and focused research courses can also boost research knowledge and experience. Sherman et al. found that pediatric residents who participated in a formal education process on the topic of informed consent in their residency education program positively affected residents’ knowledge and attitudes about the processes and issues involving informed consent. In a controlled before-and-after study, Löwe et al. investigated the effectiveness of a one-year resident clinical research training program that included a weekly class in clinical research methods, completion of a research project and mentorship found that those who went through the training program had better methodological knowledge and that higher proportion of them were writing journal articles (87% vs. 36%) than those who did not. Our survey was conducted in preparation for a departmental research course and aimed at identifying clinical staff who were interested in clinical research and the research areas they would like to learn about. This was added to our institution’s efforts to enhance research culture by offering several postgraduate courses and workshops in various clinical research topics, such as bioethics, regulatory requirements and research methodology, and by encouraging staff to conduct clinical research as accomplishments in this field added positively to their annual evaluation, which was required for contract extensions/rehiring.

In this survey, significant number of clinical staff alleged adequate knowledge in many research areas. Surprisingly, more than 50% of respondents reported
adequate or more than adequate knowledge in many research skills. A survey at two Swiss teaching hospitals in which participants (n = 409) rated their ability to perform 26 research-related activities, found that the proportion of respondents who were able to perform a specific activity was 33.2% on average and that the most important factors determining skill levels were current time commitment to research, past experience, and formal training. Our survey did not specifically address the knowledge issue as the Swiss study did, but we believe that in the current study clinical staff might have overestimated their ability to perform certain research activities and that their responses reflected their perceptions and attitudes about clinical research.

To facilitate participation of clinical staff in research, barriers should be identified and addressed. In our survey, most ICU staff believed that lack of financial support and the closely linked lack of time were important factors that hindered participation in clinical research. A Canadian study conducted to identify barriers perceived by junior clinician-scientists found that the financial aspect was important. A review of seven studies that evaluated the disincentives to academic medicine found that lower financial rewards were the most frequently cited factor. To address this issue, the National Institute of Health in the United States increased research funding and established multiple awards for clinical researchers such as the K23 for new investigators in patient-oriented research and K24 for midcareer investigators and Clinical Research Repayment Program to repay educational debts for individuals who spent most of their time in clinical research. This financial problem may be further solved by providing healthcare providers with protected time for research, creating formal salary policies at organizational level, obtaining grant support and establish a clear path for both promotion and tenure. Our institution had recently gained ground in organizing and supporting clinical research. Previously, research projects were the results of individual efforts. More recently, research had received additional support from King Abdullah International Medical Research Center, which provided research grants, statistical support and research coordination, thus eliminating many of the barriers that were present before.

The current study has several limitations. These are primarily related to the survey methodology, specifically sampling and measurement. Not all staff responded, which may have led to the overrepresentation of those who had strong opinions about clinical research. However, the relatively high response rate probably reduced this voluntary response bias. The staff knowledge that participation in the survey was voluntary and had no effect on their evaluation should have reduced socially desirable responses.

In conclusion, this study found that the vast majority of clinical staff from multiple disciplines working at the Intensive Care Department of a tertiary-care academic hospital in Saudi Arabia were interested in conducting research and identified research areas that they need more education. These findings could result in targeted tutoring and training. Moreover, the lacks of time, of encouragement and of financial compensation were perceived as significant barriers to participation in clinical research. Finding the appropriate incentives and addressing perceived barriers are crucial to the success and maintenance of any research program.
References


DURAL PUNCTURE EPIDURAL ANALGESIA IS NOT SUPERIOR TO CONTINUOUS LABOR EPIDURAL ANALGESIA

Deepak Gupta*, Arvind Srirajakalidindi*, Vitaly Soskin**

Abstract

Background: Some anesthesiologists consider combined spinal epidural (CSE) analgesia as superior alternative to continuous labor epidural (CLE) analgesia. However, during CSE, even small doses of intrathecally administered local anesthetics with opioids induce almost instant analgesia that precludes the testing of epidural catheters as well as early appreciation of failed epidural catheters. To overcome the shortcomings of CSE analgesia, dural puncture epidural (DPE) analgesia had been devised.

Objectives: The goals for the present study were to test whether DPE technique would provide superior and safer labor analgesia as compared to CLE technique.

Materials and Methods: 131 ASA Class I, II and III pregnant patients who requested labor epidural analgesia consented for their participation in this prospective randomized study. Group A patients received CLE analgesia for labor pain. Group B patients received DPE analgesia for labor pain.

Results: After exclusion of nineteen patients, final comparative data was available for 112 patients only [Group A (n = 63) versus Group B (n = 49)]. Per our analysis, the only positive aspect for DPE analgesia as compared to CLE analgesia was that patients who received DPE analgesia reported lower incidence for immediate failures of labor analgesia (P = 0.04). However, there was higher incidence of paresthesias while performing successful dural punctures (P <0.0001). Pre-insertion epidural depth assessment with ultrasound (n = 112) correlated positively with the air-filled loss of resistance syringe technique (r = 0.88; P <0.0001).

Conclusion: DPE technique did not provide superior labor analgesia as compared to CLE technique. Technically, fewer immediate failures in labor analgesia but higher incidence of paresthesias were observed with DPE technique.

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Introduction

Presently, combined spinal epidural (CSE) analgesia is revered by many anesthesiologists at various labor and delivery centers as a potentially superior alternative to continuous labor epidural (CLE) analgesia. However, during CSE, even small doses of intrathecally administered local anesthetics with opioids can induce almost instant analgesia that precludes the testing of epidural catheters as well as early appreciation of failed epidural catheters.

To overcome the shortcomings of CSE analgesia, dural puncture epidural (DPE) analgesia had been devised. With DPE technique, after dural puncture with 25G spinal needle through 17G Tuohy needle, intrathecal analgesics are not administered. Therefore, DPE technique allows confirmation of epidural space as similar to CSE technique; however, testing for early epidural catheter failure is not delayed in DPE analgesia as the masking effects of intrathecal analgesics are avoided. It has been theorized that enhancement of labor analgesia by intrathecal transfer of epidural analgesics across the dural puncture occurs in both CSE and DPE techniques.

The aims for the present study were to test whether DPE technique can provide superior and safer labor analgesia as compared to CLE technique, and whether visual appreciation of intrathecal transfer of epidural analgesics would be feasible with ultrasound with the DPE technique.

Materials and Methods

After institutional review board approval, 131 ASA Class I, II and III pregnant patients at an academic university women’s hospital who requested labor epidural analgesia were included in this prospective randomized study. Patients’ written and informed consents were taken for their participation in the study. ASA class IV and V patients, patients with history of back surgery or central nervous system disease, and patients’ who refused to have dural puncture were excluded from the study. For lumbar ultrasound examinations, VENUE 40 ultrasound machine (GE Healthcare, Wauwatosa Wisconsin, United States) was used with curvilinear probe (Model 4C, 1.5-4.5 MHz, GE Healthcare, Wauwatosa, Wisconsin, United States). The study participants were randomized (via a computer generated program) into two groups:

Group A (CLE technique): Using transverse lumbar ultrasound at L2-L3 or L3-L4 interspaces, the depth of epidural space was assessed. Under sterile conditions and after local anesthetic infiltration, a 17 gauge Tuohy needle and loss of resistance technique with air was used to enter the epidural space. The actual depth of the epidural space was compared with the depth of the epidural space determined with the ultrasound. A 19 gauge epidural catheter was threaded through the needle with 5 cm of catheter left in the epidural space. Following a negative aspiration and a negative response to test dose (3 ml 1.5% lidocaine with 1:200,000 epinephrine), loading epidural dose of 0.125% bupivacaine with 10 mcg/ml fentanyl was administered in two incremental doses of 5 ml each. The ultrasound examination was performed in the sagittal orientation to assess any intrathecal movement of the epidural solution across the ultrasonic landmark of posterior ligament complex. After five minutes of continuous ultrasound observation, the epidural catheter was secured and attached to the continuous epidural infusion of the 10 ml/hr 0.125% bupivacaine with 2.5 mcg/ml fentanyl.

Group B (DPE technique): Similar to Group A, transverse lumbar ultrasound examination was used to assess the depth of epidural space and this was compared with the actual depth of epidural space as identified with air-filled loss of resistance syringe. The 25 gauge Pencan needle was introduced through the Tuohy needle to make an intentional dural puncture. Subsequently, after intrathecal space was identified by the free CSF flow, the Pencan needle was removed without giving any medications intrathecally and a 19 gauge epidural catheter was threaded through the needle with 5 cm of catheter left in the epidural space. Following a negative aspiration and a negative test dose (3 ml 1.5% lidocaine with 1:200,000 epinephrine), loading epidural dose of 0.125% bupivacaine with 10 mcg/ml fentanyl was administered in two incremental doses of 5 ml each. The ultrasound examination was performed in the sagittal orientation to assess...
any intrathecal movement of the epidural solution across the ultrasonic landmark of posterior ligament complex. After five minutes of continuous ultrasound observation, the catheter was secured and attached to the continuous epidural infusion of the 10 ml/hr 0.125% bupivacaine with 2.5mcg/ml fentanyl.

The following observations were recorded: (a) pre-procedure: participant’s age, height and weight, (b) intra-procedure: the time taken for epidural placement, depth of epidural space (by ultrasound), number of skin insertion attempts at the epidural placement, number of changes in the orientation of the epidural needle to find epidural space, intrathecal flow of epidural solution as assessed on ultrasound examination, and any complications including but not limited to inadvertent dural puncture with Tuohy needle, intravascular catheter placement, paresthesias and immediate headaches, (c) post-procedure (initial 2 hours after procedure): incidence of failure of epidural analgesia, epidural boluses or augmentation of the rate of continuous epidural infusion, and any rescue ephedrine doses for hypotension secondary to neuraxial blockade, and (d) post-procedure (day 1): any headaches, backaches, neck-aches, or other adverse events, any persistent paresthesias, and participant’s satisfaction scores with ease of epidural placement and with adequacy of epidural analgesia. All of the above data were collected for both groups, and then analyzed and compared between the two groups.

For statistical analysis, initial calculation of adequate sample size\(^{18}\) was 134 subjects [power (1-beta) = 0.95; alpha error = 0.05] with medium effect (0.3) as predicted difference between the successes of the two analgesia methods (CLE and DPE). However, due to exclusion of withdrawn cases, the secondary statistical calculation ensured that even for power (1-beta) of 0.8 and alpha error of 0.05 with predicted difference as a medium effect (0.3), the minimum sample size required was 82 subjects (41 subjects in each group). ANOVA Single factor was used for comparison between the means and variance of the continuous data. Chi-Square test and a two tailed Fisher exact test were used to compare sample size based proportions. A P-value of <0.05 was considered significant.

### Results

A total of 131 patients consented for participation in the study. Two patients were excluded as they delivered within 30 minutes after consenting for study and two pre-term patients were excluded as they were discharged home after failed progression of cervical dilatation. Out of remaining 127 patients, 15 patients in Group B were excluded because dural punctures were not successful. Hence, final comparative data was available for 112 patients only [Group A (n = 63) versus Group B (n = 49)] (Tables 1-4). There was no significant difference in the demographics of the two patient-groups (Table 1). Per our analysis (Table 3), patients who had received DPE analgesia reported lower incidence for immediate failures of labor analgesia (P = 0.04) [Chi-Square Test; power (1-beta) = 0.53]. Additionally, less time was required by the anesthesia-operators to perform DPE (P = 0.03) (Table 1) possibly because the difficult and unsuccessful dural punctures got excluded from the final comparison (n = 15). In regards to adverse effects (Tables 2-4), there was higher incidence of paresthesias while performing successful dural

### Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td>Demographic Characteristics of the Study Patients who underwent Labor Analgesia</td>
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<tr>
<td>Age (yrs)</td>
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<tr>
<td>Body Mass Index (Kg/m(^2))</td>
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<tr>
<td>Time taken for Epidural Placement (min)</td>
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M.E.J. ANESTH 22 (3), 2013
Table 2

Intra-procedure Characteristics of the Study Patients who underwent Labor Analgesia

<table>
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<tr>
<th></th>
<th>Group A Continuous Labor Epidural (n = 63)</th>
<th>Group B Dural Puncture Epidural (n = 49)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Ultrasound evidence of Epidural Medications Flow</td>
<td>2 (n = 10) (20%)</td>
<td>0 (n = 10) (0%)</td>
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<tr>
<td>Ultrasound Evidence of Scoliosis</td>
<td>4 (6%)</td>
<td>8 (16%)</td>
<td>0.09</td>
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<tr>
<td>Number of Skin Attempts</td>
<td>1.60 ± 0.89</td>
<td>1.35 ± 0.63</td>
<td>0.09</td>
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<tr>
<td>Number of Needle Orientation Changes during Placement</td>
<td>1.21 ± 1.39</td>
<td>0.61 ± 1.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Incidence of Accidental Wet tap</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Incidence of Intravascular Placement of Epidural Catheter</td>
<td>2 (3%)</td>
<td>5 (10%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Incidence of Paresthesias during Epidural Placement</td>
<td>1 (2%)</td>
<td>14 (29%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patient Satisfaction Numerical Rating Scale for Epidural Placement</td>
<td>8.10 ± 2.86</td>
<td>8.08 ± 2.57</td>
<td>0.98</td>
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</table>

punctures (P <0.0001) (Table 2). Due to the novelty of ultrasound assessment for epidural medication flow to intrathecal space, only two visualizations of epidural medications’ flow were observed among the first twenty cases [Group A: first ten cases; Group B: first ten cases] wherein it was attempted (Table 2). However, pre-insertion epidural depth assessment with ultrasound (n = 112) correlated positively with the air-filled loss of resistance syringe technique (r = 0.88; P<0.0001) (see Fig. 1).

Discussion

There has been limited evidence related to DPE. Leach and Smith (1988) reported a case of inadvertent dural puncture and radiologically confirmed subarachnoid spread of epidural solution. Suzuki et al (1996) showed that DPE with 26G spinal needle increases caudal (not cranial) spread of epidural analgesia. However, Thomas et al (2005) did not report any improvements over CLE when DPE was performed with 27G spinal needle. More recently, Cappiello et al'
DURAL PUNCTURE EPIDURAL ANALGESIA IS NOT SUPERIOR TO CONTINUOUS LABOR EPIDURAL ANALGESIA

(2008) conducted randomized controlled trial for DPE with 25G spinal needle and concluded improvement in sacral spread and faster onset of pain relief for DPE analgesia. However our results with 25G spinal needle-induced intentional dural puncture suggest that DPE analgesia was not superior to CLE analgesia in our parturient patient population.

There were some differences in our study design (a possible explanation for the variant results) as compared to previous three studies5-7. In the first study, Suzuki et al5 had performed dural punctures in only 20 patients and observed that the caudal spread of epidural analgesia after the initial epidural bolus (15 ml 2% mepivacaine) was significantly more than analgesia observed in control group (n = 20) at 15 minutes and 20 minutes after the injection; however they did not document whether this advantage in caudal spread was still applicable when they repeated 10 ml 2% mepivacaine bolus at 60 minutes intervals. The mean duration of their surgical procedures was approximately two hours5; and our perfect success rates of DPE analgesia in the first two hours after epidural placement compared to 92% success rate with CLE analgesia (Table 3) similarly reflect that DPE analgesia related perfect initial success rates can be related to the caudal and intrathecal spread of initial epidural boluses. This advantage of absence of early failures of epidural analgesia did not transform into a significant difference in overall patients' satisfaction scores between our two groups of patients (Table 4) questioning how long dural hole remains patent or how long intrathecal-epidural pressure gradient allows intrathecal transfer of epidural medications. Therefore we would recommend caution in employing DPE for labor analgesia because compared to CLE analgesia, DPE analgesia had both significantly higher incidence of intra-procedure complication (paresthesias) as well as insignificant but clinically appreciable higher incidence of delayed complications (postpartum headaches and neck-aches) (Table 4).

In the second study, Thomas et al6 had utilized 27G spinal needle for DPE in 125 patients and observed that dural punctures were not successful (no CSF return observed in spinal needle) in 18 patients (14%). Analogously, we observed that dural punctures failed in 15 patients (23%) of our DPE analgesia group. Though Thomas et al6 had bigger sample size (CLE: n = 123; DPE: n = 107) for final analysis as compared to our study (CLE: n = 63; DPE: n = 49), incidence of intravascular placement of epidural catheters (CLE group: 6%; DPE group: 10%)6 were comparable to our study (CLE group: 3%; DPE group: 10%) (Table 2). As compared to our perfect success rates of DPE analgesia in the first two hours precluding the need for epidural replacements (Table 3), epidural replacement rates were 9% with DPE according to Thomas et al6. However, as compared to their observed incidence of 9% for intra-procedure paresthesias with DPE6, we observed 29% incidence of intra-procedure paresthesias with DPE. In summary, Thomas et al6 had suggested that 27G spinal needle induced dural puncture may be too small for epidural medications to transfer across intrathecally and this may be the explanation for their higher epidural replacement rates

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Table 3
Early Complications in the Study Patients who underwent Labor Analgesia

<table>
<thead>
<tr>
<th></th>
<th>Group A Continuous Labor Epidural (n = 63)</th>
<th>Group B Dural Puncture Epidural (n = 49)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of Headache immediately after Epidural Placement</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Incidence of Failure of Epidural Analgesia within 2 hrs</td>
<td>5 (8%)</td>
<td>0 (0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Incidence of Additional Epidural Boluses within 2 hrs</td>
<td>10 (16%)</td>
<td>5 (10%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Incidence of Augmentation of Epidural Infusion Rate within 2 hrs</td>
<td>4 (6%)</td>
<td>3 (6%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Incidence of Administration of Ephedrine Rescues for Hypotension within 2 hrs</td>
<td>5 (8%)</td>
<td>4 (8%)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

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compared to our perfect success rates with 25G spinal needle induced DPE analgesia.

In the third study, Cappiello et al' (CLE: n = 40; DPE: n = 39) observed that 85% patients reported visual analogue scores <10 mm on 100-mm scale at 20 minutes after DPE (with 25G spinal needle induced dural puncture) compared to only 65% patients with CLE (reflecting faster onset of analgesia). Although the sacral spread as denoted by first sacral spinal segment blockade was not significantly different at 20 minutes with DPE7, the sacral spread was significantly better with DPE (92% patients) at any time during labor compared to only 70% patients achieving sacral spread to first sacral spinal segment with CLE7. However the sacral spread beyond first sacral spinal segment was not different with DPE (77% patients) or CLE (65% patients) at any given time point during the study7. Epidural catheter replacement rates were higher (DPE: 3%; CLE: 13%)7 than our study. Though Cappiello et al7 had observed 31% instrumental vaginal deliveries with DPE as compared to 13% with CLE, we did not collect data reflecting the incidence of instrumentation during vaginal deliveries in our patients. However cesarean section rates observed by Cappiello et al7 were higher (CLE: 25%; DPE: 31%) as compared to our observations (CLE: 16%; DPE: 20%).

Lumbar ultrasound imaging performed in the transverse plane has been reported to accurately estimate epidural space depth for facilitating the appropriate catheter placement for neuraxial labor analgesia. This pre-insertion screening ultrasound has been investigated in non-obese parturients19 as well as obese parturients20. Additionally, it was our hypothesis during our study design that visual appreciation of intrathecal transfer of epidurally administered medications may be feasible with lumbar ultrasound and may become a great addition to obstetric anesthesiologists’ armamentarium. Although our results showed good correlation between ultrasound assessment of epidural space depth and air-filled loss of resistance syringe technique (Figure 1), we were not able to appreciate the ultrasonographic visualization of epidural medication flow (within the epidural space or across the dural puncture into the intrathecal space). This failure may be related to the novelty of visualizing medication flow in epidural and intrathecal spaces; however our failure may not deter future researchers from refining the technique to visualize neuraxial medication flow with lumbar ultrasound.

With DPE technique, dural puncture precipitated

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Delayed Complications in the Study Patients who underwent Labor Analgesia</th>
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<tbody>
<tr>
<td></td>
<td>Group A Continuous Labor Epidural (n = 63)</td>
</tr>
<tr>
<td>Incidence of Epidural Boluses during Pushing in Labor</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>Incidence of Conversion to Cesarean Section</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>Incidence of Failure of Epidural Anesthesia Intraoperatively</td>
<td>3 (n = 10) (30%)</td>
</tr>
<tr>
<td>Incidence of Failure of Epidural Analgesia Postoperatively</td>
<td>3 (n = 10) (30%)</td>
</tr>
<tr>
<td>Patient Satisfaction Numerical Rating Scale for Epidural Analgesia</td>
<td>8.68 ± 2.74</td>
</tr>
<tr>
<td>Incidence of Postpartum Headaches</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Incidence of Postpartum Backaches</td>
<td>37 (59%)</td>
</tr>
<tr>
<td>Incidence of Postpartum Neck-aches</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Incidence of Persistent Postpartum Paresthesia</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
high incidence of intra-procedure paresthesias possibly due to dural tenting by Tuohy needle and subsequent potential fluid waves in the subarachnoid space that might have been minimally compressed (posteriorly) by the tented duramater. However, persistent paresthesias, 24hrs after the procedure, occurred in only one patient. These immediate (intra-procedure) paresthesias may also be explained by the dural puncture needle’s proximity to the cauda equina nerve roots because tented duramater might have reduced the anteroposterior diameter of subarachnoid space (free space for cauda equina nerve roots) at the site of subsequent dural puncture. Although long term sequelae of these paresthesias are not known, these paresthesias may deem DPE technique as unwarranted when per our results, DPE technique does not provide superior analgesia compared to CLE technique.

Our study had few limitations. Even though DPE analgesia was not superior to CLE analgesia, high satisfaction scores of the parturients may have been confounded by post-partum elation that might have interfered with patients' overall appreciation of differences, if any, between the analgesia achieved with DPE technique vs. CLE technique. Though headaches and neck-aches were more common with DPE technique (Table 4), they may not have reached level of significance [power (1-beta) of our results: 0.23 for headaches; 0.35 for neck-aches] due to overall very low incidence of these adverse effects. Therefore, per our results, DPE technique may appear to have a very limited role (as a confirmation test only) when accessing difficult epidural space wherein air-filled loss of resistance syringe technique is not providing good depth appreciation and lumbar ultrasound imaging of epidural space is not accessible or appreciable by the obstetric anesthesiologist.

### Conclusion

DPE technique did not provide superior labor analgesia as compared to CLE technique. Technically, fewer immediate failures in labor analgesia but higher incidence of paresthesias were observed with DPE technique. Due to novelty of ultrasound examination for epidural medication flow, visualization of intrathecal transfer of epidural analgesics was not appreciated in the present study.
References

MINIMAL/UNDERREPORTED BUT DEFINITE RISK OF DEATH/BODILY HARM THREATS (DBHTS) TO PAIN PRACTITIONERS: RESULTS OF NATIONWIDE SURVEY FROM UNITED STATES

DeePaK Gupt*a, RAMI BZEIH**, WALID OSTA*

Abstract

Background: Many physicians have experienced or will experience patient who acts threateningly towards them at least once in their careers. However, there have been no studies to gauge the incidence rate and severity of patients’ and/or patients’ families’ violence towards pain physicians.

Objectives: This nationwide survey was completed to evaluate the incidence of death/bodily harm threats (DBHTs) against pain physicians.

Methods: A questionnaire along with online assent form was uploaded on SurveyMonkey Online Portal. The uploaded survey web-link was sent to pain fellowship programs in the United States so that pain physicians and pain fellows can respond to this survey. The respondents were expected to anonymously complete the survey containing various questions relating to confrontational patients’ experiences, how these experiences affected them, how those situations were handled, and how the respondents would act differently in the future secondary to their victimization by the confrontational patients.

Results: The response rate to the nationwide survey was extremely low (5.2% of anticipated numbers), most likely secondary to underreporting. Out of total 26 respondents across the United States, seven respondents reported receiving DBHTs (incidence of 27%). The median number of absolute DBHTs received in lifetime by these seven respondents was three (range being 1 to 21-30).

Conclusion: There is minimal/underreported but definite risk of DBHTs for pain practitioners and the improved reporting, awareness and discussions can help pain physician community to formulate efficacious strategies to the prevention and management of future DBHTs.

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Introduction

Patients’ aggression towards physicians and other health care workers is a well documented occurrence in the field of medicine. Many physicians have experienced or will experience patient who acts threateningly towards them at least once in their careers. Surveys have found that 25% of physicians have encountered aggression from their patients'. For obvious reasons, practitioners of pain medicine are apparently at higher propensity for being victims of violence. However, there have been no studies to gauge the incidence rate and severity of patients’ and/or patients’ families’ violence towards pain physicians. Therefore, this nationwide survey was completed to evaluate the incidence of death/bodily harm threats (DBHTs) against pain physicians, to understand the nature of this violence towards pain physicians, to gain insight on how the violent situations were handled by the victimized physicians, and to eventually propose and/or realize the best methods to resolve aggressive confrontational pain patients and their families inclusive of both immediate and long term management.

Methods

After institutional review board approval, the questionnaire (Appendix A) along with online assent form was uploaded on SurveyMonkey Online Portal (SurveyMonkey Palo Alto, California, United States). The uploaded survey web-link was sent to all pain fellowship programs in the United States. The email addresses for the contact persons for these programs were accessed from their free information posted on their departmental websites. The individual pain fellowship program coordinators were asked to send the survey web-link, if deemed appropriate, to their programs’ pain physicians and pain fellows. Subsequently, these respondents were expected to anonymously complete the survey containing various questions relating to confrontational patients’ experiences, how these experiences affected them, how those situations were handled, and how the respondents would act differently in the future secondary to their victimization by the confrontational patients. The questionnaire included three types of questions that allowed dichotomous responses, multiple responses or open-ended responses. The survey also collected respondents’ information regarding gender, age, years of experience, and whether or not the respondent had received prior training specific to handling confrontational patients. Additionally, the respondents were asked to provide confrontational patients’/families’ characteristics including age, gender and if patients/families had known history of violence and/or psychiatric illnesses. It was anticipated that the time taken to complete the survey would have been less than twenty minutes. The survey web-link was open only for twelve weeks with one email reminder sent to the pain fellowship coordinators at the end of six weeks for improving the response rate to survey.

Statistical Analysis

Based on the scope of the survey we had anticipated at least 500 measurable survey responses and subsequent detailed regression analysis. However, due to underreporting by survey respondents, we had to limit statistical evaluations to Chi-squared tests, Fisher Exact test and one-way ANOVA for data analysis and \( p <0.05 \) was considered significant.

Results

The response rate to the nationwide survey was extremely low (5.2% of anticipated numbers), most likely secondary to underreporting. Out of total 26 respondents across the United States (Figure 1), seven respondents reported receiving DBHTs (incidence of 27%). The demographics of the respondents who denied receiving or who reported receiving DBHTs were insignificantly different (Table 1). Though these seven respondents reported DBHTs’ frequency as once in a month (29%), once in a year (57%) or once in lifetime (14%), the median number of absolute DBHTs received in lifetime by these seven respondents was three (range being 1 to 21-30). However detailed objective description in terms of survey-questionnaire's completion for DBHTs was completed for eight out of total ten threat descriptions reported
by these seven respondents. The age of respondents at the time of receiving DBHTs (n = 10) was 39.8 ± 6.76 years. DBHTs were evenly distributed in two time periods: five each in 1994-2000 period and 2008-2012 period. The respondents were primarily practicing in academic pain practice setting (60%) when they received DBHTs; other pain practice settings with incidence of DBHTs were personal office setting (30%) and private group practice (10%). Similarly, the respondents practicing with equal weightage to both interventional and medication based pain management (80%) more commonly received DBHTs as compared to respondents practicing primarily interventional pain management (10%) or primarily medication based pain management (10%). The perpetrators of DBHTs were primarily in the age group 31-40 years (60%); other age groups were 21-30 years (10%) and 41-50 years (30%). Male perpetrators (80%) outnumbered female perpetrators (20%). Patients themselves represented the major perpetrators of DBHTs threatening either on their own (70%) or along with their families (20%). DBHTs almost always happened in the outpatient setting (90%) with remaining 10% in inpatient setting. DBHTs were delivered face-to-face (60%), through third person (30%) and anonymously (10%) with three perpetrators vividly describing the intended execution methods of DBHTs as "handgun in purse; loud and threatening stance", "gun to your head", and "if I (the patient) go down, I am taking so and so with me". The respondents were not aware (60%) whether the perpetrators were on psychiatric medications at the time of DBHTs. Majority of respondents (60%) denied the presence of warning (premonitory) signs of violence before DBHTs. Neither of the ten DBHTs had sexual overtones nor these DBHTs were actually executed by the perpetrators. Further descriptions were completed for only eight DBHTs and these descriptions included perpetrator's personal reasoning for DBHTs, respondents' perceptive reasoning for receiving DBHTs (Table 2), respondents' actions in response to these DBHTs with long term effects of DBHTs on the respondents (Table 3). The respondents also suggested various interventions’ preventive role (if any) against future DBHTs (Table 4).

Discussion

At the time of initiating the survey, the working hypothesis was that pain physicians are exposed to confrontational/violent patient populations who are suffering from underlying unrelenting physical conditions; and the interplay of opioid medication failure or abuse, poor rapport with pain management...
### Table 1

**Demographics of Respondents of Survey about Death/Bodily Harm Threats (DBHTs) incidence**

<table>
<thead>
<tr>
<th>Experience of Practicing Pain Medicine (in years)</th>
<th>Respondents who denied receiving any DBHTs (n = 19)</th>
<th>Respondents who reported receiving any DBHTs (n = 7)</th>
<th>P Value (significant if &lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD: 9.1 ±10.7</td>
<td>Mean ±SD: 10.4 ±8.3</td>
<td>Median: 4; Mode: 1 Range: (0-33)</td>
<td>Median: 7; Mode: 15 Range: (2-25)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respondent's Sex</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>6 (32%)</td>
<td>2 (29%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Males</td>
<td>13 (68%)</td>
<td>5 (71%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respondent's Medical Residency's Specialty</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesiology</td>
<td>17 (89%)</td>
<td>6 (86%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Physical Medicine and Rehabilitation</td>
<td>2 (11%)</td>
<td>1 (14%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior Education for Confrontational/Violent Patients</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (11%)</td>
<td>1 (14%)</td>
<td>0.63</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2

**Reasons for Death/Bodily Harm Threats (DBHTs)**

<table>
<thead>
<tr>
<th>Perpetrator's Reasons for Perpetrating DBHTs (n = 8)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor Pain Control</td>
<td>7 (88%)</td>
<td></td>
</tr>
<tr>
<td>Loss of Function</td>
<td>1 (13%)</td>
<td></td>
</tr>
<tr>
<td>Worsening of Other Symptoms</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Distrust for the Physician</td>
<td>3 (38%)</td>
<td></td>
</tr>
</tbody>
</table>

*Others: wanting opioid medication*

<table>
<thead>
<tr>
<th>Physician's Perceptive Reason for Receiving DBHTs (n = 8)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor Pain Control</td>
<td>3 (38%)</td>
<td></td>
</tr>
<tr>
<td>Loss of Function</td>
<td>1 (13%)</td>
<td></td>
</tr>
<tr>
<td>Worsening of Other Symptoms</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Poor Rapport</td>
<td>2 (25%)</td>
<td></td>
</tr>
<tr>
<td>Opioid Diversion</td>
<td>1 (13%)</td>
<td></td>
</tr>
<tr>
<td>Opioid Dependence</td>
<td>2 (25%)</td>
<td></td>
</tr>
<tr>
<td>Opioid Abuse</td>
<td>5 (63%)</td>
<td></td>
</tr>
<tr>
<td>Opioid Tolerance</td>
<td>1 (13%)</td>
<td></td>
</tr>
<tr>
<td>Litigation Potential of Physician</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Less Options for Pain Doctor Shopping</td>
<td>2 (25%)</td>
<td></td>
</tr>
</tbody>
</table>

*Others: None*
MINIMAL/UNDERREPORTED BUT DEFINITE RISK OF DEATH/BODILY HARM THREATS (DBHTS) TO PAIN PRACTITIONERS: RESULTS OF NATIONWIDE SURVEY FROM UNITED STATES

Table 3
Post-hoc scenarios of Death/Bodily Harm Threats (DBHTs)

<table>
<thead>
<tr>
<th>Physician's Response to DBHTs (n = 8)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Threat Ignored</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Law Enforcement Agency Involved</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Only Hospital Security Involved</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Patient's Discharge from Practice</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Litigation against the Perpetrator</td>
<td>0</td>
</tr>
<tr>
<td>Compliance with the Perpetrator's Demands</td>
<td>0</td>
</tr>
</tbody>
</table>

Others: "documented in patient chart and discussed with primary team that we would not continue as consultant team; considered buying Kevlar vests for myself and staff"

<table>
<thead>
<tr>
<th>Effect of Receiving DBHTs on Physician (n = 8)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No Effect</td>
<td>3 (38%)</td>
</tr>
<tr>
<td>Increased Anxiety and Hyper-vigilance</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Changed Ways of Pain Practice</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Changed Place of Pain Practice</td>
<td>0</td>
</tr>
<tr>
<td>Changed City of Pain Practice</td>
<td>0</td>
</tr>
<tr>
<td>More Complacence to Patients' Demands</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Initiated Patients' Criminal Background Check</td>
<td>0</td>
</tr>
<tr>
<td>More Stringent in Pain Management Plans</td>
<td>3 (38%)</td>
</tr>
<tr>
<td>Stopped Practicing Pain Medicine</td>
<td>0</td>
</tr>
</tbody>
</table>

Others: "My secretary quit due to family threats," Eventually left the practice, although not directly related to this episode"

Table 4
Preemption against Death/Bodily Harm Threats (DBHTs)

<table>
<thead>
<tr>
<th>Preventive Role (if any) against Future DBHTs (n = 8)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unavoidable and Unpredictable</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Better Pain and Symptom Control</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Better Patient-Family-Physician Rapport</td>
<td>0</td>
</tr>
<tr>
<td>Vigilance to Warning Signs of Violence</td>
<td>0</td>
</tr>
<tr>
<td>Increased Private Security</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Criminal Background Check for New Patients</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Coordination with Law Enforcement Agencies</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Improvement in Opioid Dispensing Practices</td>
<td>3 (38%)</td>
</tr>
<tr>
<td>Continuing Medical Education of Difficult Patient Encounters</td>
<td>0</td>
</tr>
</tbody>
</table>

Others: "More thorough chart review and discussion with primary team prior to meeting patient. They wanted us to be the bad guys" and in that sense they succeeded. I discussed this with them afterwards. "Tighter control on new patients. It was clear this patient was only seeking opioids and we had no intention of providing them."

M.E.J. ANESTH 22 (3), 2013
The second observation of this survey was that even though the respondents varied from 0-33 years into their pain practice, the ten DBHTs reported in the survey were received in the first ten years of respondents’ pain practice with most common occurrence in the third year of their pain practice. However, paradoxically, the respondents who denied receiving DBHTs were primarily in their first couple of years of pain practice (Table 1: Median 4 years and Mode 1 year). Additionally, there was general lack of prior training among the respondents for dealing with confrontational/violent patients/families scenarios. Although 88% of the total respondents (n =26 ) never received the training, the respondents (n = 10) who had received DBHTs did not think that continuing medical education of difficult patient encounters have any role in preventing future DBHTs. However, the physicians who are naïve to DBHTs can be prevented from lingering trauma of victimization to DBHTs by improved pain management practices as suggested by the respondents (Table 4) without forgetting the values of continuing medical education about the difficult patient scenarios serving as a potential tool to create awareness among pain physicians’ population.

The third observation of this survey was middle aged male patients outnumbering others as perpetrators of DBHTs with three out of ten perpetrators (30%) giving vivid utterances involving gun-related violence which reflects that DBHTs even if assumingly minimal needs serious attention of pain medicine. The present survey could not come to any conclusion about warning signs related to pre-existant psychiatric illnesses or history of violence in the perpetrators but their existential role in DBHTs in general cannot be overlooked. Moreover, the society in general has implicit interests in ensuring conscientious prevention and appropriate management of DBHTs against pain practitioners because pain practitioners are one of the major prescribers of controlled substances (opioids) and their complacent attitudes developing from the incidence of DBHTs can worsen the existing critical socioeconomic issues related to opioid abuse, dependence and diversion.
The fourth observation of this survey was that perpetrators and physicians did not agree in regards to reasoning behind the DBHTs with perpetrators relating it to poor pain control (88%) and physicians relating it to opioid abuse (63%). This reflects that patients might not be able to personally recognize their evolution in opioid abuse that may have been secondary to prescription medications. Contrarily, the pain physicians' population prejudiced to opioid abuse as underlying cause for DBHTs might overlook poor pain control or opioid tolerance as the underlying causes in the event of aggressive future pain patients who are threatening their physicians.

The final observation of this survey was that even though DBHTs were ignored half-of-the-times with physicians denying any effect on them three-eighths-of-the-times, the post-hoc acts and effects of DBHTs on the rest of the respondents to the tune of staff quitting the pain practice eventually (Table 3) warrants that awareness, open discussions and preventative strategies among the pain physicians community should be instigated for future safety of pain practitioners and evolution of vigilant pain management policy making that is neither complacent to opioid abusers/diverters nor harmful to patients who are genuinely suffering from poor pain control. The preventative strategies as suggested in the survey (Table 4) may not include a comprehensive list and is a reflection of five respondents reporting eight DBHTs in detail (by completing the whole survey questionnaire). However, these strategies can be a good start to explore the final institution-specific population-adjusted universal guidelines for the pain practitioners across the country to prevent future DBHTs and their aftermaths. The United States is the global leader in consumption of prescribed opioids and hence, the pain practitioners here have the additional responsibility to reflect and manage their pain practice related difficult scenarios (that include the incidence of DBHTs) so that globally pain medicine practice is neither considered a high-risk medical subspecialty (and thus preventing the intelligent new crop of global physicians embracing this subspecialty) nor akin to misjudging the definite risk of DBHTs indigenous only to the United States by eventually sweeping the issue of local awareness about DBHTs under the rug.

**Conclusion**

In summary, there is minimal/underreported but definite risk of DBHTs for pain practitioners and the improved reporting, awareness and discussions can help pain physician community to formulate efficacious strategies to the prevention and management of future DBHTs.

**Acknowledgment**

The authors sincerely appreciate with gratitude the input and support of Milos Marjanovic MD, David H Rustom MD and Carl Hinshaw MD, Detroit Medical Center/Wayne State University, Detroit, Michigan, United States.

**Appendix A**

Survey Questionnaire [Incidence of Death/Bodily Harm Threats (DBHTs) to Pain Practitioners]

1. Are you a Pain Physician or Pain Medicine Fellow?
   a. Yes
   b. No
2. Which state do you presently practice?
   a. Name of State
3. Which year did you first start practicing pain medicine as Pain Fellow/Physician after completing your residency?
   a. 19--/20--
4. What is your sex?
   a. Male
   b. Female
5. In which specialty did you do your medical residency?
   a. Anesthesiology
   b. Physical Medicine and Rehabilitation
   c. Neurology
   d. Psychiatry
   e. Others
6. Before starting your pain practice as a Fellow/Physician, were you given education/training regarding management of confrontational/violent person?
a. Yes
b. No

7. Have you ever received a death/bodily harm from a pain patient/patient’s family?
   a. Yes
   b. No

8. How often have you received a death/bodily harm from a pain patient/patient’s family?
   a. Once in lifetime
   b. Once in a year
   c. Once in a month
   d. Once in a week
   e. More than once in a week

9. How many (TOTAL) death/bodily harm threats have you ever received from pain patients/ patients’ families?
   a. Number

In Next Few Pages, We Will Inquire about ONLY FIRST FIVE Threats Received by You
10. What was your age (in years) when you received this death/bodily harm threat from a pain patient/patient’s family?
    a. Age in years
11. Which year did you receive this death/bodily harm threat from a pain patient/patient’s family?
    a. 19--/20--
12. What type of pain practice setting were you part of at the time of this death/bodily harm threat?
    a. Academic Setting
    b. Private Group Practice
    c. Personal Office Setting
13. What form of pain medicine were you primarily practicing at the time of this death/bodily harm threat?
    a. Primarily Interventional Pain Management
    b. Primarily Medication Based Pain Management
    c. Equal Weight-age to Abovementioned Two
14. What was the age group of the person who threatened you?
    a. 0-10 yrs
    b. 11-20 yrs
    c. 21-30 yrs
    d. 31-40 yrs
    e. 41-50 yrs
    f. 51-60 yrs
    g. 61-70 yrs
    h. 71-80 yrs
    i. 81-90 yrs
    j. 91-100 yrs
    k. >100 yrs
15. What was the sex of the person who threatened you?
   a. Male
   b. Female
16. Who was the threatening person?
    a. Patient
    b. Patient’s Family
    c. Both
17. Where did you come in contact with this person who threatened you?
    a. Inpatient setting
    b. Outpatient setting
    c. Intensive Care Unit Setting
    d. Palliative Care/Hospice Setting
    e. Emergency Department
    f. Peri-operative Setting
18. How was this death/bodily harm threat delivered to you? (Multiple Answers allowed)
    a. Anonymous
    b. In person (face to face)
    c. Through third person
    d. On phone
    e. By Email
    f. By Regular Mail
    g. By Fax
    h. Any other Method
19. Was any specific killing/bodily harm method described in this death/bodily harm threat?
    a. Yes
    b. No
20. Was the person who threatened you on psychiatric medications?
    a. Yes
    b. No
    c. Don’t Know
21. Were there any warning signs (like history of violence) before the actual death/bodily harm threat?
    a. Yes
b. No

c. Don’t Know

22. Were there sexual overtones in this death/bodily harm threat?
   a. Yes
   b. No

23. What was the reason ACCORDING TO THE THREATENING PERSON for this death/bodily harm threat? (Multiple Answers Allowed)
   a. Poor Pain Control
   b. Loss of Function
   c. Worsening of other symptoms
   d. Distrust for the physician
   e. Others

24. What was the reason ACCORDING TO YOU for this death/bodily harm threat? (Multiple Answers Allowed)
   a. Poor Pain Control
   b. Loss of Function
   c. Worsening of other symptoms
   d. Poor Rapport
   e. Person/Family were apparently diverters
   f. Opioid dependence
   g. Opioid abuse
   h. Opioid tolerance
   i. Litigation potential
   j. Less options for Pain Doctor Shopping
   k. Others

25. Was this threat for bodily harm executed by the threatening person?
   a. Yes
   b. No

26. What happened to you when the bodily harm was executed? (Multiple Answers allowed)
   a. No medical attention was required
   b. First Aid was sufficient
   c. You were hospitalized
   d. You were in intensive care unit
   e. You required long term physical rehabilitation
   f. You required long term psychological rehabilitation

27. How did you handle this death/bodily harm threat? (Multiple Answers allowed)
   a. Ignored the Threat
   b. Involved Law Enforcement Agencies
   c. Involved Hospital Security only
   d. Discharged the person from your care
   e. Filed a lawsuit against the person
   f. Complied with the person’s demands for medication/treatments
   g. Other

28. How did this death/bodily harm threat affect you? (Multiple Answers allowed)
   a. Did not affect you
   b. You became anxious and hyper-vigilant for yourself and your family
   c. You changed your ways of pain practice (interventional versus medication based)
   d. You changed your place of pain practice
   e. You changed your city of pain practice
   f. You became more complacent to patients’ demands
   g. You started doing criminal background checkup of the patients
   h. You became more strict with your pain management plans
   i. You stopped practicing pain medicine
   j. Other

29. How could you have prevented this event? (Multiple Answers allowed)
   a. Unavoidable and Unpredictable
   b. Better pain and symptom control in patients
   c. Better patient-family-physician rapport
   d. Being more vigilant to warning signs showed by the person towards violence
   e. Increasing the private security for your pain practice
   f. Criminal background checkup for all new pain patients
   g. Coordinating and Follow up with law enforcement agencies regarding medication diversion
   h. Improved practices in opioid dispensing
   i. Continuing medical education/ training for management of difficult patient encounters
   j. Others

30. Did you receive any other death/bodily harm threat?
   a. Yes
   b. No

31. Thank You
References


CASE REPORTS

AVOIDING ECMO IN A PATIENT WITH “PUMP” LUNG POST-CARDIOPULMONARY BYPASS

MUOI A. TRINH*†, HIMANI V. BHATT**, MENACHEM M. WEINER*

Abstract

As newer anesthesia ventilators are developed their capabilities are becoming more similar to intensive care unit (ICU) ventilators. However, in situations where there is severe decrease in lung compliance, an ICU ventilator may be superior in its ability to regulate inspiratory flow improving both ventilation and oxygenation. We present a case where an ICU ventilator was brought to the operating room and used in the treatment of ARDS post-cardiopulmonary bypass and ultimately allowed us to avoid extracorporeal membrane oxygenation (ECMO) therapy.

Case report

A 68-year-old man with developmental delay, chronic obstructive pulmonary disease, coronary artery disease and mitral, aortic and tricuspid insufficiency presented for a 3-vessel coronary artery bypass grafting, tricuspid annuloplasty, aortic valve replacement and mitral valve repair. Pre-operative echocardiography demonstrated dilated heart chambers with mild biventricular systolic dysfunction (left ventricular ejection fraction 50%), severe aortic insufficiency and severe mitral insufficiency. A pre-anesthetic-induction radial arterial line was placed and general anesthesia was induced using midazolam, fentanyl, etomidate and vecuronium. The patient was easily intubated, placed on the ventilator (Dexta Omhed DAU) with peak airway pressure of 14 mm Hg. The initial arterial blood gas showed pH 7.35, PaCO2 49, PaO2 482 on FiO2 of 100%. An 9 Fr introducer sheath and pulmonary artery catheter were placed. Aminocaproic acid was used as an anti-fibrinolytic agent. Bypass was initiated uneventfully and lasted for approximately 4 hours. Epinephrine and norepinephrine was started prior to separation from cardio-pulmonary bypass (CPB). As ventilation was re-initiated peak airway pressures exceeded 50 mm Hg and eventually became unreadable on assist control. Ventilation mode was changed to pressure control with settings of inspiratory pressure set at 40 mm Hg. However we were only able to deliver tidal volumes of 140 ml. The arterial blood gas showed pH 7.16, PaCO2 49, PaO2 36 on FiO2 100%. An intra-aortic balloon pump was also initiated for
severe right-heart failure. Despite these therapies, the patient remained difficult to ventilate and oxygenate. While the surgical staff considered extracorporeal membrane oxygenation (ECMO) as an intervention, an intensive care unit ventilator, a Nellcor Puritan Bennet 840, was brought into the OR and instituted using pressure control setting and high peep. The patient’s pulmonary status improved gradually with the arterial blood gas improving to pH 7.36, PaCO2 43, PaO2 126 (FiO2 100%) and hemodynamics stabilized. The patient received a tracheostomy on post-op day 7 and after a prolonged hospital course, he was transferred to a rehabilitation facility.

**Discussion**

After an extensive literature review, we believe that this is the first case report of using an ICU ventilator in the operating room (OR) to improve gas exchange in a patient immediately post CPB to avoid ECMO. ARDS, also known as “pump” lungs when it occurs post-CPB is a lung injury that is associated with significant arterial hypoxemia and diffuse infiltrates radiologically, in the absence of elevated left atrial pressures. It is thought to be a result of extensive exposure of blood to foreign materials in the bypass circuit, resulting in the activation of complement and release of inflammatory mediators1-3. Treatment of ARDS includes aggressive ventilation strategies to limit barotrauma and improve oxygenation. In severe ARDS however, ECMO therapy can be used to improve oxygenation and reduce ventilator associated lung injury2,4,5. In our case, the patient had a significant A-a gradient and hypercarbia despite aggressive ventilatory management on the traditional anesthesia ventilator and ECMO was being considered as the next therapy.

It is well documented that older anesthesia ventilators are inferior to ICU ventilators in terms of their ability to preserve tidal volume delivery with decreased compliance in test lung models when in pressure control mode. Tung et al demonstrated that at high respiratory rates, a Puritan Bennett 7200, ICU ventilator was able to maintain tidal volumes with test model of a lung with low compliance with a pressure control setting compared to the Datex-Ohmeda Asteva 5 anesthesia ventilator. Anesthesia ventilators necessarily have greater compliance as gases are recirculated requiring a larger circuit volume. ICU ventilators have less compliance in their system as gases are delivered directly from the wall source to patient. Thus, ICU ventilators may be more efficient at delivering tidal volumes in patients with poor pulmonary compliance, requiring high pressure control settings and relatively high respiratory rates. The Dexta-Omheda ADU ventilator is a modern bellows system ventilator used at our institution. Despite advances in anesthesia machine ventilators, we found in this case report that the ICU ventilator (Nellcor Puritan Bennett 840) was superior to the anesthesia ventilator in its ability to manage severe ARDS and instrumental in improving oxygenation and ventilation in our patient.

**References**

RADIOLOGY QUIZ

ABDUL-LATIF HAMDAN*, HENRI TRABULSI**, ELIE ALAM***

A 28 year old female, case of thalassemia minor, diagnosed 2 years ago with adenocarcinoma of the colon, presented to the emergency room with progressive neck pain, sudden onset of dysphonia and mild dyspnea. Patient had history of hemicolecotomy and had been started on chemotherapy (FOLFOX-5-FU and oxaliplatin) more than a year ago. She had reported upper extremity venous catheterization for the delivery of her chemotherapy. Patient was hemodynamically stable and had mild right neck swelling and tenderness anterior to the right sternocleidomastoid muscle, on perceptual evaluation she had a breathy voice. Flexible naso-pharyngo-laryngoscopy revealed a fixed right vocal fold in the paramedian position with incomplete closure during phonation. Computerized tomography of the neck and chest with intravenous contrast was ordered (Fig. 1.)

What is your diagnosis?

Diagnosis

Right Internal Jugular Vein Thrombosis

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Discussion

Vocal fold immobility is described as restricted movement of the vocal folds. Its true incidence may be hard to draw in view of the disparities in the work-up of inflicted subjects. The left side is usually more affected than the right side and elderly seem to be more at risk. The clinical presentation varies with the position of the cord and whether one or both sides are affected. A large percentage of patients with vocal fold fixation may be asymptomatic, whereas a few mandate emergency care. In cases of unilateral vocal fold paralysis, patients may present with change in voice quality often described as breathiness. Other phonatory symptoms include loss of power and range, inability to project the voice and fatigability. Respiratory discomfort and decrease in exercise tolerance are also common complaints. In cases of bilateral paralysis with the vocal cords in the midline, patients may have a normal voice but suffer from stridor and respiratory distress.

The evaluation of vocal fold impaired mobility begins with a detailed medical and vocal history, a thorough head and neck assessment, a fiberoptic and or telescopic laryngeal examination, and radiologic evaluation. Contrast-enhanced computed tomography of the head and neck region is usually ordered in order to span the region from the cerebral cortex, throughout the tenth nerve from the base of the skull to the chest. When fixation of the cricoarytenoid joint is suspected, laryngeal electromyography is recommended to differentiate mechanical fixation from neural immobility.

The etiology of vocal fold impaired mobility includes, neoplastic lesions, surgery, laryngeal manipulation, viral infections, and idiopathic causes. In a report by D. Myssiorek, surgery is still the leading cause of recurrent laryngeal nerve injury. The most common surgeries are thyroid and parathyroid surgery, carotid endarterectomies, skull base operation, chest surgery, and cervical spine surgeries using the anterior approach. Netterville et al found thyroid surgery to be the most common cause of iatrogenic recurrent laryngeal nerve injury with the incidence being higher when the nerve is not identified intra-operatively. In a large series of carotid endarterectomies, 2.5% were found to have post-operative vocal fold immobility. Similar rates have been reported following anterior approach to the cervical spine. Transient cranial neuropathy is also commonly described after skull base surgery, with the vagal nerve commonly affected. As for the neoplastic lesions, non-laryngeal tumors account up to 37% of cases of recurrent laryngeal nerve paralysis. These include neoplastic lesions of the thyroid gland, lungs, esophagus and mediastinum. Other causes include endotracheal intubation, viral etiologies and drug induced paralysis. Still up to 27% of cases of vocal fold impaired mobility remain listed as idiopathic.

No previous report has described internal jugular vein thrombosis as the cause of vocal fold impaired mobility. Based on an extensive literature review, this is the first case of internal jugular vein thrombosis presenting with sudden onset of dysphonia and mild dyspnea. The exact mechanism responsible for the impaired mobility of the vocal fold remains unknown. Possible etiologies include vagal nerve compression, thrombosis of the vasa nervosum, perineural inflammation and or viral neuropathy. These remain hypothetical etiologies because of lack of further investigation. Another possible etiology in our case is the repeated intravenous injections and catherizations that could have lead to thrombosis of the internal jugular vein.

Patient was admitted and started on anticoagulation. Two days later patient was reassessed and found to have significant improvement in her voice quality and breathing. Repeated fiberoptic naso-pharyngo-laryngoscopy revealed normal vocal fold mobility. The rapid improvement in the patient’s condition substantiates the fact that internal jugular vein thrombosis is most likely to be the etiology.
References

RETROGRADE INTUBATION IN THE PATIENT WITH CYSTIC TUMOR LOCATED AT THE BASE OF TONGUE

Feyzi Çelik*, Orhan Tokgöz*, Erdal Doğan*, Abdülmenap Gülzel*, Taner Çiftçi*, Adnan Tüfek*

Abstract

Retrograde intubation is one of the methods used to maintain an airway in the event of a difficult intubation. Retrograde intubation has been successfully carried out on patient for whom intubation was not possible with a direct laryngoscope and fiber optic bronchoscope. The central venous catheter needle and guide wire are the materials that are the most practical to prepare and access for the retrograde intubation. To conclude, In conclusion, retrograde intubation may be a good alternative to invasive airway management such as surgical tracheostomy for difficult or impossible intubations because it can be performed easily, quickly, and successfully.

Key words: retrograde intubation, difficult intubation

Introduction

The retrograde intubation (RI) method is one of the alternative techniques that are resorted to in situations where it is difficult to maintain a clear airway. Water first defined this technique in 1963. RI is mentioned in the American Anesthesiologists Association (ASA) guidelines as an invasive intubation technique that achieves an airway through the cricothyroid membrane or the cricotracheal ligament. This technique is recommended in situations where the vocal chords are not visible because of blood, secretions or anatomic deformities and when intubation attempts with a direct laryngoscope and fiber optic bronchoscope are unsuccessful.

Retrograde intubation is a complex, unfamiliar technique that requires practice. The part of entry for this technique is through the cricothyroid membrane or the cricotracheal ligament. Previous studies on cadavers showed that the cricotracheal ligament technique results in less damage to the vocal chords and has a higher rate of success.

In this report, we present the case of a patient with a severe oropharyngeal obstruction secondary to a cystic mass who successfully underwent retrograde intubation following failed intubations with flexible fiber optic bronchoscope.
Case Presentation

A 43 year old male patient presented to our hospital’s Ear, Nose and Throat clinic with difficulties in breathing and swallowing. A computerized cervical tomography revealed the presence of a cystic mass (Fig. 1) of approximately 3 × 5 cm at the base of his tongue that completely filled the oropharynx. The patient was scheduled for surgery to excise the cystic mass. The patient was informed that there might be difficulties for maintaining the airway and a written informed consent was obtained for the use of anesthesia. Before induction of anesthesia, preparations were made for intubation with flexible fiber optic bronchoscope (FOB). Topical anesthesia was done by spraying Xylocaine® on the nasal and oral passages. The nasal passage was dilated with the proper sized airways and after sedating the patient, an expert senior anesthesiologist tried intubation both nasally and orally by FOB. However, because of the large mass extending into the glottis region, the FOB could not be guided to the trachea after passing the mass. As such, retrograde intubation was deemed necessary.

Technic: A small folded towel was placed beneath the shoulders and the cricothyroid area was identified and cleaned. A short mid-line skin incision was made and an 18-gauge needle passed into the trachea in a slightly cephalad direction until a distinct ‘pop’ was elicited. The position was confirmed by easy aspiration of gas. The needle was angled to 45”, the position again confirmed and introducing wire was passed through the needle until tip was visualized into the oral cavity. The guide wire was held and put out from the oral cavity by the Magill forceps. An endotracheal tube was passed over the introducing wire. The guide wire was held taut at both the distal end and the proximal end and the tube was advanced towards the trachea. After it was be certain that endotracheal tube tip was in trachea, then guide wire was withdrawn completely from tube. The correct position of the tracheal tube was confirmed via capnographe and it was secured. No complications was encountered at any other stage of this procedure.

Discussion

One of the main responsibilities of anesthesiologists is to predict difficulties in intubation and ensure a safe airway. Difficult intubation is described in the ASA guide as a situation that requires more than 3 attempts to place an endotracheal tube with a conventional laryngoscopy or if this procedure takes more than 10 minutes to complete. According to the ASA algorithm, intubation with FOB is recommended as the first choice on conscious patients in difficult intubation scenarios. However its use is not widespread due to the cost of equipment and trained staff may not be readily available in many clinics. Also, supraglottic airway tools cannot be used because they might compromise on the field of surgery. Therefore, it should be considered that RI may be used in cases where endotracheal intubation is difficult but necessary.

In our patient, intubation was tried initially using FOB. However, due to the large mass at the base of the tongue blocking the oropharynx completely and the risk of rupturing the cyst the FOB manipulation was limited. Also since the distance to the glottis was short after the mass has been passed, the FOB was
moving towards the esophagus even though it was being guided to the trachea. Thus it was decided that RI would be more appropriate.

RI is an invasive technique that uses the seldinger technique by way of the cricothyroid membrane or cricotracheal ligament to achieve intubation. This technique is recommended not as a priority choice but as an alternative in situations where the visibility of the trachea is obstructed by blood, secretions or anatomical deformities and direct laryngoscopy and fiberoptic intubation attempts are unsuccessful. We used the CV catheter because it is cheaper and provided easily. Of course, all anesthesiologists are familiar to using CV catheter and its guide wire.

When the cricothyroid membrane is selected as the entry point during RI the proximity to the vocal chords can cause unwanted situations such as vocal cord damage. In a study where entries at the cricothyroid membrane and cricotracheal ligament were compared, vocal cord damage was more encountered in cricotracheal ligament entries. When the cricothyroid membrane is selected as the entry point into the trachea, since the area is relatively close to the vocal cords, unwanted situations in which the tube is shifted from its position while the guide wire is being removed from the endotracheal tube can happen.

Complications like emphysema, laryngeal oedema, intratracheal bleeding and subglottic stenosis are associated with retrograde intubation and are caused by the use of hard guiding devices. In order to avoid the damage caused to tissue by the hard guiding devices, softer devices like silk suture and epidural catheters can be used for guidance into the trachea. However, since these devices are not hard enough they often result in several unsuccessful attempts the need to retry and therefore lead to loss of valuable time unsuccessful attempts. In our patient whose oropharynx was completely blocked, we used the guide wire of a CV catheter.

In conclusion, as in our case, retrograde intubation may be good alternative to invasive airway management such as surgical tracheostomy for difficult or impossible intubations because it can be performed easily, quickly, and successfully.

Acknowledgements

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The Authors declare that they have no conflict of interest.
References

Abstract

We report a case in which the use of benzocaine spray to facilitate awake fiber optic intubation (FOI) in a patient with a difficult airway caused methemoglobinemia intraoperatively. Local benzocaine was sprayed to numb the patient’s airway for a total time of one second. Fifteen minutes later SpO2 decreased to 85% on the pulse oximeter. Arterial blood gas (ABG) showed a MetHb of 24.6% of total Hemoglobin. The patient was successfully treated with methylene blue intravenously and recovered uneventfully. Small amounts of local benzocaine sprayed to numb the airway can cause significant methemoglobinemia that requires immediate recognition and appropriate management.

Introduction

Benzocaine spray is commonly used to numb the airway for awake fiber optic intubations. It can cause significant methemoglobinemia, which usually occurs 15-20 minutes after its application, at that time the patient is usually under anesthesia covered with drapes. Many factors may drive the anesthesiologist away from promptly identifying methemoglobinemia which may delay treatment and have detrimental consequences on the patient. We report a case of methemoglobinemia under general anesthesia caused by benzocaine spray used for an awake fiberoptic intubation. We discuss diagnostic clues that help the anesthesiologist identify and manage methemoglobinemia as it occurs.

Case Report

A 32 year old female patient with a large facial arteriovenous malformation scheduled for face reconstruction, laser treatment of the soft palate and Botox injection. She had history of twelve facial surgeries, in ten of which she had awake fiber optic intubations (FOI) without any complications due to anticipated difficult airway with her facial deformity and decreased mouth opening. On the morning of surgery, her vital signs were stable and her physical exam was normal. We anticipated a difficult airway and decided to proceed with awake fiber optic intubation. To facilitate the awake FOI and ensure patient’s comfort we premedicated her with midazolam 2 mg IV, fentanyl 50...
megl IV, and glycopyrrlate 0.2 mg IV. To anesthetize the airway we used cotton tip swaps to apply viscous lidocaine on the tonsilar pillars, lidocaine nebulizer 120 mg, lidocaine atomizer 80 mg, and sprayed benzocaine 20% (Hurricane) for 1 second. Awake FOI went smoothly. Anesthesia was induced smoothly with IV propofol. Vital signs remained stable during induction with SpO2 around 97%. However, 15 minutes after induction we noticed bluish brown discoloration of the fingers and lips and SpO2 went down to 85%, other vital signs remained stable. We increased FIO2 to 100% and ensured adequate ventilation, however SpO2 remained 85%. An arterial blood gas (ABG) showed a pH 7.5, pCO2 31, pO2 608, HCO3 22.8 on 100% O2. However, despite a pO2 of 608, SpO2 was 85%, we suspected methemoglobinemia based on the saturation gap. A second ABG with co-oximetry showed a pH 7.49, pCO2 31, pO2 323, HCO3 23.4, THb 10.6, O2 Hb 74.5%, CoHb 0.3% and MetHb 24.6% on 100% O2. Based on the high MetHb level a diagnosis of methemoglobinemia was established. We treated the patient with methylene blue 2 mg/kg IV. SpO2 went up to 95%. ABG after methylene blue showed a pH 7.49, pCO2 31, pO2 299, HCO3 23, THb 10.1, O2 Hb 90.3%, CoHb 0.3% and Met Hb 9% on 100% O2. The patient remained stable throughout the procedure. At the end, she woke up and was extubated without complications. Her postoperative course was uneventful.

Discussion

Methemoglobin (MetHb) is an abnormal form of hemoglobin (Hb) that has a diminished capacity for carrying oxygen. It is produced when Hb is oxidized and an electron is removed from one of the iron atoms of the heme group causing the conversion of ferrous or Fe2+ iron to the ferric or Fe3+ state which diminishes the Hb molecule ability to bind O2 causing a functional anemia (Fig. 1). It also results in a left shift of the oxygen-hemoglobin dissociation curve. This, in turn, depending on the level of MetHb, may cause cellular hypoxia and, ultimately, death.

The red blood cells are continuously subjected to oxidative stressors that result in the formation of methemoglobin spontaneously in normal individuals at a rate of 0.5-3% of the available hemoglobin per day. Reduction of methemoglobin maintains a steady state level of methemoglobin of about 1% of total hemoglobin. There are 2 mechanisms by which erythrocytes reverse the effects of oxidation and the formation of MetHb. The most significant of these

![Fig. 1](image.png)
METHEMOGLOBINEMIA WITH THE USE OF BENZOCAINE SPRAY FOR AWAKE FIBEROPTIC INTUBATION

is via nicotine adenine dinucleotide methemoglobin reductase (NADH-MetHb reductase), also known as cytochrome-b5 reductase\(^2\). The second, and less physiologically significant, is via NADPH-MetHb reductase. This second pathway requires a cofactor or an electron acceptor such as methylene blue or flavin to carry out the reduction of MetHb to Hb (Fig. 2). Individuals with a deficiency of NADH-MetHb reductase have insufficient enzyme levels for reduction of methemoglobin to occur and develop hereditary methemoglobinemia. They are particularly susceptible to worsening methemoglobinemia in the presence of oxidizing agents.

Medications are the most common cause of MetHb in clinical practice, of these, local anesthetics (benzocaine and procaine), antibiotics (dapsone), and nitrites (nitroglycerin/nitric oxide) are the most common offenders.

Benzocaine is one of the most powerful oxidizing agents among local anesthetics, animal studies showed it has a more powerful oxidizing effect than lidocaine, and a dose response relationship has been demonstrated between benzocaine and methemoglobin. Since 1977, when the first case of benzocaine spray induced methemoglobinemia was reported\(^1\), approximately 200 cases have been documented in the literature. Benzocaine has been reported to cause methemoglobinemia when applied to infants as an ointment or a rectal suppository\(^4,5\) and when used topically to the perineal area\(^6\). It has also been associated with methemoglobinemia after its use as a lubricant on endotracheal, bronchoscopic, and esophageal tubes\(^7,8\). The particular preparation of benzocaine spray used in this case contained benzocaine 20% (Hurricane). It is most often used prior to procedures such as endotracheal intubation, upper gastrointestinal endoscopy and transesophageal echocardiography.

Clinical findings are the first clue for the anesthesiologist to suspect methemoglobenemia. Low SpO2 and cyanosis that fail to improve with increased inspired oxygen concentration, choclate-colored, brown, blue, or black blood that fails to change color when exposed to air, and a discrepancy between SpO2 and SaO2 on ABG (saturation gap). However, co-oximetry is the diagnostic test of choice. Limitations of traditional pulse oximetry, which can detect only 2 wave lengths of ultraviolet light: 660 and 960 nm, leads to an unreliable measure of oxygen saturation, as a result, co-oximetry detecting multiple ultraviolet wavelengths and all four types of hemoglobin should be used to measure an arterial blood gas and confirm the diagnosis of methemoglobinemia\(^9\).

Treatment starts with discontinuing the offending agent, in most cases methemoglobinemia resolves within 24-36 hours after the clearing of the residual benzocaine. General supportive measures (O2, close observation) are appropriate when methemoglobin level is less than 30%. In more severe cases, methylene blue in the dose of 1 to 2 mg/kg of 1% solution, slow IV push over 5 minutes, is the preferred treatment. Methylene blue, along with NADPH, serve as cofactor for the enzyme NADPH-MetHb reductase\(^4\). This reaction contributes minimally to the reduction of methemoglobin under normal, physiologic conditions. However, if the normal reductive pathways are overwhelmed, as in methemoglobinemia, this pathway becomes very important. Methylene blue will cause marked reduction in the methemoglobin concentration, usually by 50%, within 30 to 60 minutes. Administration can be repeated in 1 hour if symptoms do not resolve.
Conclusion

Benzocaine spray is commonly used to numb the airway before awake FOI, it is associated with the risk of causing methemoglobinemia even when used is small doses. We recommend avoiding the use of benzocaine spray before awake FOI. If used, the anesthesiologist should monitor the patient closely, look for signs of methemoglobinemia, and be prepared to treat it.

References

LETTER TO THE EDITOR

USE OF THE TUBE EXCHANGE CATHETER IN PATIENTS WITH A TRAUMATIZED AIRWAY

I read with interest the case report of Karci et al about the use of airway exchange catheter (AEC) in a patient with Down’s syndrome who suffered from severe suprasternal retraction and subcutaneous emphysema secondary to tracheal injury due to a foreign body, with a consequent tracheal rupture. The emphysema progressed rapidly following tracheal intubation and mechanical ventilation. Bronchoscopy was required for diagnosis and for removal of the foreign body, and for treatment of the suspected tracheal rupture. The AEC was inserted for tracheal extubation before bronchoscopy

During the tragic events in Lebanon 1975-1990, we came across many patients suffering from faciomaxillary injury. In some of these patients, the Cook TEC was used during direct laryngoscopy to facilitate tracheal intubation. Also, it was reintroduced via the tracheal tube lumen before extubation, to facilitate tracheal reintubation if indicated, and to maintain post operative oxygenation if required (Fig. 1).

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Emeritus Professor of Anesthesiology
American University of Beirut

Fig. 1
At the end of surgery, the exchange catheter was reintroduced via the tracheal tube lumen, and the trachea was extubated, while the exchange catheter was left in situ to maintain oxygenation, and to facilitate tracheal reintubation if required.

References

POST-OPERATIVE ALOPECIA AFTER ROBOTIC SURGERY IN STEEP TRENDENBURG POSITION: A RESTATED OBSERVATION OF PRESSURE ALOPECIA

Lakshman Gollapalli*, Peter Papapetrou*, Deepak Gupta*, Samir F Fuleihan*

Abstract

Postoperative alopecia is an uncommon complication and its outcome is aesthetically drastic. Although its mechanism has not been clearly elucidated, a proposed risk factor is steep Trendelenburg positioning (30-40 degrees) that is frequently used during robotic gynecologic surgeries. We report a case of postoperative alopecia in 53-year-old female patient who had undergone robotic-assisted laparoscopic hysterectomy and bilateral salpingoophorectomy with sacrocolpopexy and cystoscopy. Prevention of alopecia with proper head positioning, avoidance of mechanical compression by rigid objects and maintenance of intraoperative hemodynamics is of utmost importance for anesthesiologists.

Letter

Postoperative alopecia is an uncommon complication and its outcome is aesthetically drastic. Although its mechanism has not been clearly elucidated, a proposed risk factor is steep Trendelenburg positioning (30-40 degrees) that is frequently used during robotic gynecologic surgeries. Robotic procedures have several advantages like better visualization of surgical field and faster postoperative recovery. However, these procedures require positioning patient in steep Trendelenburg position for prolonged durations and are associated with complications like postoperative visual loss (POVL). Postoperative alopecia after robotic surgeries can be explained by a similar mechanism as first described and explained with observations of pressure alopecia after gynecologic surgeries in Trendelenburg position during 1960s.

We report a case of postoperative alopecia in 53-year-old female patient who had undergone robotic-assisted laparoscopic hysterectomy and bilateral salpingoophorectomy with sacrocolpopexy and cystoscopy. Prior to the procedure she had denied any signs/symptoms of hair loss or thinning. She had undergone general anesthesia with inhalational anesthetics' maintenance and peri-operative epidural analgesia in steep Trendelenburg position for the majority of the procedure (approximately five hours). She was extubated in the operating room, and was taken to the recovery area without any

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complications. On postoperative day 3, she reported to primary surgical team about 1.5 inch circular area of alopecia in occipital region (Fig. 1). She denied any other symptoms like headache or visual changes. Her alopecia was still persistent during 3-month follow up telephonic interviews.

Postoperative alopecia shares same risk factors with POVL. An increased risk of POVL has been shown in cases with steep Trendelenburg as well as prone positioning. Secondary to patient positioning, increased intraocular pressure and decreased ocular perfusion pressure lead to optic nerve ischemia and visual loss in non-ocular cases. Furthermore, intraoperative hypotension is another risk factor. A mechanism as similar to POVL can explain postoperative alopecia. Our patient had occipital alopecia wherein her head was in contact with adult-sized silicone-based donut head pad for prolonged duration in steep Trendelenburg position. Additional risk factor could have been inadvertent or unrecognized mechanical compression of scalp by electrocardiography (ECG) cable trunk yoke assembly that lies between ECG trunk cable and ECG lead set. This could have potentially caused hair follicle ischemia or venous engorgement secondary to scalp compression. This reduction in blood inflow as well as outflow might have contributed to her hair loss.

In 2012, Anesthesia Patient Safety Foundation (APSF) developed consensus conclusions regarding POVL. It was decided that during consent for surgery, anesthesiologists and/or surgeons should bring to patients' attention about risk of developing POVL specially in association with risk factors like prolonged surgery in prone position and robotic surgery in steep Trendelenburg position, increased blood loss and male gender. APSF also stated the methods to reduce risk of developing POVL by minimizing surgery's duration and keeping patient's head at or above the level of heart. As pathophysiologies of POVL and postoperative alopecia are apparently similar, the patients should also be made aware of risks of postoperative alopecia while anesthesia providers should be aware of its risk-reducing methods. In summary, preventing these two significant complications (POVL and pressure alopecia) with proper head positioning, avoidance of mechanical compression by rigid objects and maintenance of intraoperative hemodynamics are of utmost importance for anesthesiologists when providing anesthesia care to patients in steep Trendelenburg position.
References

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- References should be indicated by Arabic numerals in the text in the form of superscript and listed at the end of the paper in the order of their appearance. Please be accurate, giving the names of all authors and initials, the exact title, the correct abbreviation of the journal, year of publication, volume number and page numbers.

- The titles of journals should be abbreviated according to the style used in the list of Journals Indexed for MEDLINE.

Example: (1) from a journal (2) from a book.

10. Tables

Tables capture information concisely and display it efficiently: They also provide information at any desired level of details and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text.

- Type or print each table with double spacing on a separate sheet of paper.
- Number tables consecutively in the order of their first citation in the text.
- Supply a brief title for each.
- Place explanatory matter in footnotes, not in the heading.
- Explain all nonstandard abbreviations in footnotes.
- Identify statistical measures of variations, such as standard deviation and standard error of the mean.

11. Figures

- Figures should be submitted in JPEG or TIFF format with a minimum of 150 DPI in resolution.
- Colored data if requested by author is chargeable.
- If a figure has been published previously, acknowledge the original source and submit written permission from the copyrights holder to produce the figure.

Abbreviations and symbols:
- Use only standard abbreviations.
- Avoid abbreviations in the title of the manuscript.
- The spelled-out abbreviations followed by the abbreviation in parenthesis should be used in first mention.