The Middle East Journal of Anesthesiology is a publication of the Department of Anesthesiology of the American University of Beirut, founded in 1966 by Dr. Bernard Brandstater who coined its famous motto: “For some must watch, while some must sleep” (Hamlet-Act. III, Sc. ii). and gave it the symbol of the poppy flower (Papaver somniferum), it being the first cultivated flower in the Middle East which has given unique service to the suffering humanity for thousands of years. The Journal’s cover design depicts The Lebanese Cedar Tree, with’s Lebanon unique geographical location between East and West. Graphic designer Rabi Moukalled

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*Post tetanic count
*Second twitch


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WELCOME OUR NEW EDITOR-IN-CHIEF

The Editorial Board of the Middle East Journal of Anesthesiology is pleased to announce that Dr. George B. Bikhazi is the new Editor-in-Chief of the Middle East Journal of Anesthesiology. This comes in line with the appointment of Dr. Bikhazi as the new Chairman of Anesthesiology at the American University of Beirut - School of Medicine and Medical Center as of July 1st, 2014.

Dr. Bikhazi received his MD degree from the American University of Beirut in 1971. Following graduation he pursued his residency and fellowship at AUB and in the USA. In 1976, he was appointed assistant professor of anesthesia at University of Miami School of Medicine and the Director of Pediatric Anesthesia until 2001. During his stay at Miami, he was promoted to associate professor (1979) and professor (1991). Dr. Bikhazi joined the Department of Anesthesiology at St. Jude Children’s Research Hospital in Memphis, Tennessee in 2002 and later on became the Chief of the Division of Anesthesia until he returned to AUB as the Chairman of the Department of Anesthesiology in 2014.

Dr. Bikhazi is a member and has served on boards-committees of several professional organizations and societies (ASA, AMA, ASA Committee on Pediatric Anesthesia) and throughout his career has received numerous prestigious awards and recognitions (Fellow, American College of Anesthesiologists and Diplomat, American Board of Anesthesiologists). Furthermore, Dr. Bikhazi has published around 113 original articles, abstracts, and book chapters throughout his academic career. He delivered numerous lectures at major national and international scientific meetings.

The Editorial Board extends a warm welcome to Dr. Bikhazi and looks forward for fruitful years and bright future of the journal under his leadership.
SOMATIC AND AUTONOMIC UPREGULATION
IN THE QUADRIPLEGIC PATIENT

Patients with chronic spinal cord transection develop both somatic and autonomic denervation below the level of denervation. This can result in “up-regulation” of both the somatic and adrenergic receptors below the level of the cord transection, with a subsequent increased sensitivity to the chemical transmitter at both the neuromuscular junctions and the adrenergic receptors.

The number of postjunctional receptors can be influenced by the ambient concentration of the chemical transmitter. As a rule, there is an inverse relationship between the concentration of the transmitter and the number of its receptors. Alteration in the number of the receptors is referred to as either “up-regulation” or “down-regulation”. Patients with chronic spinal cord transection will develop both somatic and autonomic denervation, which can result in “up-regulation”, and hence a supersensitivity response at both the neuromuscular junction and the adrenergic vascular receptors.

Somatic denervation will be followed by extrajunctional spread of the receptors beyond the motor endplate into the whole muscle membrane, with a subsequent increased sensitivity to the chemical transmitter acetylcholine. A similar response will follow sympathetic denervation, resulting in extrajunctional spread of the adrenergic receptors, with a subsequent adrenergic supersensitivity to the chemical transmitter norepinephrine which can trigger the so-called “autonomic hyperreflexia”.

The “autonomic hyperreflexia” is not secondary to an increased secretion of the chemical transmitter norepinephrine, but rather to an increased sympathetic response of the expanding adrenergic receptors, resulting in severe hypertension, associated with reflex slowing of heart rate via the innervated carotid sinus baroreceptors. It has been shown that plasma catecholamines (epinephrine and norepinephrine) are subnormal in patients with cord transaction. During autonomic hyperreflexia, the level of norepinephrine increases, but still does not exceed the resting level of the control normal patients. These findings demonstrate that patients with chronic spinal cord transection have a subnormal sympathetic tone, even during an attack of autonomic hyperreflexia. These findings suggest the excessive reflex elevation of the blood pressure in patients with spinal cord transaction is not secondary to autonomic hyperreflexia, but is rather due to a denervation supersensitivity response of the adrenergic receptors to the released norepinephrine.

The somatic “up-regulation” will explain the marked hyperkalemia following the administration of succinylcholine to the quadriplegic patient. That is why, succinylcholine is contraindicated in the quadriplegic patient, while the nondepolarising relaxants may be safely administered whenever indicated.
The autonomic “up-regulation” will explain the marked vasopressor response to stimulation below the level of cord transection. The autonomic response consisting of severe hypertension associated with reflex bradycardia can follow bladder distension, uterine contractions during pregnancy and labor, as well as surgical stimulation. About 85 percent of patient with cord transection above T6 will exhibit the reflex, since vasodilation in the neurologically intact portion of the body is insufficient to offset the effects of vasoconstriction below the level of transection.

The vasopressor response can be decreased by the use of epidural meperidine or intrathecal morphine which act on the substantia gelatinosa in the spinal cord, blocking the response to nociceptive stimulation. The technique has been used to block the autonomic hyperreflexia in the quadriplegic patient undergoing delivery or surgery below the level of cord transection.

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

References

REVIEW ARTICLE

DIFFERENTIAL DIAGNOSIS OF DELAYED AWAKENING FROM GENERAL ANESTHESIA: A REVIEW

ELIZABETH A. M. FROST*

Abstract

With the general use of fast acting anesthetic agents, patients usually awaken quickly in the post operative period. However, sometimes recovery is protracted and the list of possible causes is long. Accurate diagnosis is key to institution of appropriate therapy.

Key Words: Anesthetic agents, delayed recovery, overdose, risk factors.

Definition

There is no single definition of what might constitute delayed awakening or emergence after general anesthesia. With the almost universal use of evanescent agents such as propofol and desflurane, patients generally awaken in a few minutes. Even after prolonged surgery and anesthesia a response to stimulation within 60-90 minutes should occur1. Consciousness implies “awake and aware of surroundings and identity” according to the Oxford English Dictionary. But consciousness is a continuum with varying depths. Coma, from the Greek, means a state of sleep and is defined medically as “a state of unresponsiveness from which the patient cannot be aroused”. Although the Glasgow Coma Scale (Table 1) was originally developed as a means to assess prognosis after head trauma, it has also been used to trend the level of consciousness although inconsistencies may occur2. Other scores have been developed including the Aldrete Score (Table 2)3 and the Postoperative Quality Recovery Scale (PQRS)3. Recognizing that recovery from anesthesia and possible long term effects of the perioperative experience are complex issues, this latter scale tracks multiple domains of recovery from immediate to long-term periods in patients of different ages, languages and cultures. In consists of 6 domains; physiologic, nociceptive, emotive, activities of daily living, cognitive and patient perspective4. Physiologic recovery was complete in 40% of patients by 40 minutes. In only 11% of patients was recovery complete in all domains by day 3. Thus the concept of awakening would seem to be more involved with far greater dimensions than assessing a patient as being “recovered” or “awakened” and judging the anesthetic effect as terminated. These added factors have been assessed in several studies by patient reported surveys addressing functional quality of recovery5-9. Patient reports are an important approach in assessing recovery, but other crucial aspects are in areas perhaps influenced by anesthesia that may not rise to the patient’s consciousness. For example the topic of cognitive recovery especially after cardiac and even non cardiac surgery is rarely assessed. This questions as to whether recovery as a measure

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of the quality of anesthesia care should be targeted for not only identification but also for improvement\textsuperscript{10-16}.

**Incidence**

In otherwise healthy patients who have undergone relatively short operative procedures the incidence of delayed awakening is practically zero and its occurrence usually relates to some underlying but undiagnosed condition or medical error.

<table>
<thead>
<tr>
<th>Category</th>
<th>Best Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye opening</td>
<td>4</td>
</tr>
<tr>
<td>To speech</td>
<td>3</td>
</tr>
<tr>
<td>To pain</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Oral</td>
<td>5</td>
</tr>
<tr>
<td>Irritable</td>
<td>4</td>
</tr>
<tr>
<td>Cries to pain</td>
<td>3</td>
</tr>
<tr>
<td>Moans</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Follows commands</td>
<td>6</td>
</tr>
<tr>
<td>Localizes to pain</td>
<td>5</td>
</tr>
<tr>
<td>Withdraws to pain</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal flexion</td>
<td>3</td>
</tr>
<tr>
<td>Abnormal extension</td>
<td>2</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1

Glasgow Coma Scale. A score of >12 indicates return of consciousness in most patients and <8 indicates coma. The scale is also used as a trend monitor.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description of patient</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity level</td>
<td>Moves all extremities voluntarily/on command</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Moves 2 extremities</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Cannot move extremities</td>
<td>0</td>
</tr>
<tr>
<td>Respiration</td>
<td>Breaths deeply and coughs freely</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Is dyspnic, with shallow, limited breathing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Is apneic</td>
<td>0</td>
</tr>
<tr>
<td>Circulation (blood pressure)</td>
<td>Is 20 mm Hg &gt; preanesthetic level</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Is 20 to 50 mm Hg &gt; preanesthetic level</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Is 50 mm Hg &gt; preanesthetic level</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Is fully awake</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Is arousable on calling</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Is not responding</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Requires supplemental oxygen to maintain level &gt;90%</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Has level &gt;90% with oxygen supplementation</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2

The commonly used Aldrete score is broad based. A value of 9 is required for discharge from the postanesthetic care unit (PACU).

**Causes**

Drug effect: Too much drug may have been given or the patient is very susceptible or drug interaction has occurred.

Duration and type of anesthetic. Speed of emergence is inversely related to blood gas solubility and directly related to alveolar ventilation. Other factors include total tissue uptake of the drug (depends on solubility), duration of anesthesia and average
Potentiation by other drugs: Premedication with other sedatives such as benzodiazepines or alcohol increases central nervous system depression.

Neuromuscular blockade: Although these patients may not be unconscious, prolonged muscle paralysis may be almost indistinguishable from delayed awakening.  

Table 3

Many factors may result in delayed awakening, roughly divided into 4 factors although clearly there is considerable overlap

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Drug Factors</th>
<th>Surgical Factors</th>
<th>Metabolic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremes of age</td>
<td>Dosage/hypoxia/hypotension</td>
<td>Long surgery and anesthesia</td>
<td>Hypo/hyper glycemia</td>
</tr>
<tr>
<td>Genetic variation</td>
<td>Absorption/distribution</td>
<td>Muscle relaxant use</td>
<td>Hypo/hyper natremia</td>
</tr>
<tr>
<td>Body habitus</td>
<td>Metabolism</td>
<td>Regional techniques with sedation</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>Excretion</td>
<td>Decreased pain and stimulation</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>Drug interactions</td>
<td>Intracranial surgery</td>
<td>Hepatic/renal failure</td>
</tr>
<tr>
<td>Cognitive dysfunction</td>
<td>Local anesthetic toxicity</td>
<td></td>
<td>Central anticholinergic syndrome</td>
</tr>
<tr>
<td>Seizures</td>
<td>Fluid overload</td>
<td></td>
<td>Acidosis</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td>Coagulation defects</td>
</tr>
</tbody>
</table>
cognitive dysfunction\textsuperscript{25,26} Two large-scale clinical studies are currently underway to explore these issues. The PANDA study is a large-scale, multisite, ambidirectional sibling-matched cohort study in the USA. The GAS study will compare the neurodevelopmental outcome between sevoflurane anaesthesia and regional anaesthesia, in infants undergoing inguinal hernia repair. Results from these studies may not be known for 1-2 decades\textsuperscript{27}.

A common cause of delayed return to consciousness in children is hypothermia. Because of their relatively large body area compared to weight, heat loss is greater than in adults. Hence drug metabolism is delayed\textsuperscript{28}.

**Genetic factors**

Unexpected responses such as prolonged somnolence following the administration of specific anaesthetics are most commonly associated with a genetic defect of the metabolic pathway either of a given agent or its receptor. Most anesthetic agents are metabolized in the liver by the cytochrome P450 superfamily enzymes (CYPs) and phase II drug-metabolizing enzymes (glutathione S-transferases (GSTs), sulphotransferases (SULTs), UDP-glucuronosyltransferases (UGTs) and NAD (P) H:quinone oxidoreductase (NQO1))\textsuperscript{28}. Polymorphic changes in GABRG 2 receptor can adversely affect the expected rapid reversal of propofol anesthesia\textsuperscript{28}. Unanticipated drug reactions are a common and important complication of drug therapy both in adults and in children. It is becoming increasingly apparent that genetically controlled variations in drug disposition and response are important determinants of unexpected events for many important adverse events associated with drug therapy\textsuperscript{29}.

Pharmacogenetic differences appear to play major roles in predicting adverse effects, especially of opioids\textsuperscript{30}. A subset of genes appears to modulate the proteins involved in pain perception pathways, metabolism of analgesics (pharmacokinetics), and transport and receptor signaling (pharmacodynamic). Adult genetic studies have limited direct applicability, as children’s genetic predispositions to analgesic response are influenced by different factors and contain developmental and behavioral components as well as altered sensitivity to analgesics and variation in gene-expression patterns. While the entire science of pharmacogenetics is still in its infancy, it is growing rapidly. Undoubtedly in the not too distant future, it will be possible to plan a precise, tailored anesthetic.

**Body Habitus**

Males with a higher percentage of fat have a tendency to delayed awakening after propofol anesthesia, an effect that is not seen in women\textsuperscript{31} With the exception of neuromuscular antagonists, lean body weight is the optimal dosing scale for most drugs used in anaesthesia especially opioids and anaesthetic induction agents\textsuperscript{32}. A diagnosis of obstructive sleep apnea with an increased incidence of fat deposits in the pharynx and chest wall coupled with increased oxygen utilization and carbon dioxide production places the morbidly obese patient at risk for adverse respiratory events secondary to anesthetic agents, thus altering the pharmacodynamic properties of these drugs.

Cardiac output increases with obesity and thus these individuals require administration of higher drug doses to attain the same peak-plasma concentration than would be required for a standard-size person. Lean body weight (LBW) correlates highly with increased cardiac output, more so than fat mass\textsuperscript{33}. Clearance for most drugs increases nonlinearly with total body weight but linearly with LBW. Thus morbid obesity, which implies mainly increased fat mass, has no clinically significant impact on the uptake of the inhalation anesthetics isoflurane, sevoflurane, and desflurane in routine clinical practice. Total body weight dosing of neuromuscular blocking agents may result in a prolonged effect although other studies have found different results\textsuperscript{32,33}. However, in a study of 56 obese patients undergoing craniotomy Bilotta et al found desflurane-based anesthesia allowed earlier postoperative cognitive recovery and reversal to normocapnia and normal pH\textsuperscript{34}.

Propofol and remifentanil infusions have been used for spinal fusion, especially in obese individuals, when evoked potential monitoring was required. However, this combination has been shown to delay
awakening. Addition of dexmedetomidine reduces the dose requirements of propofol and remifentanil allowing faster wake up.

**Co-morbidities**

Preexisting cardiac and pulmonary disease require adjustments in anesthetic dosages to prevent overdose and postoperative somnolence. Significant lung disease decreases the ability to wash out inhaled agents as the speed of emergence relates directly to alveolar ventilation. Similarly, congestive cardiac failure and decreased cardiac output prolong somnolence.

Both hyper and hypo glycemia may induce coma. Patients with hyperglycemia have usually been diagnosed as type II diabetics. A sugar infusion may have been inadvertently given or the patient may have recently eaten a carbohydrate meal. Dexamethasone and long duration of surgery (stress response) can also significantly increase hyperglycemia. Hypoglycemic patients are more likely to be juvenile or insulin dependent diabetics. Postoperative hypoglycemia most frequently results from starvation, or excessive insulin, especially in patients with end stage renal disease. Causes of hyper/hypoglycemia are shown in Table 4.

**Table 4**

<table>
<thead>
<tr>
<th>HYPERGLYCEMIA</th>
<th>HYPOGLYCEMIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoacidosis/pancreatitis</td>
<td>Starvation</td>
</tr>
<tr>
<td>Hyperosmolar non ketotic coma</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>Liver failure</td>
</tr>
<tr>
<td>Failure to take antiglycemic medications</td>
<td>Children</td>
</tr>
<tr>
<td>Steroids</td>
<td>Hypoadrenalism</td>
</tr>
<tr>
<td>Insulin resistance (Cushing, acromegaly)</td>
<td>Endocrine tumors</td>
</tr>
</tbody>
</table>

**Obstructive sleep apnea (OSA)**

Patients with OSA have several anatomical and functional factors that contribute to airway compromise. Obesity, body mass index (BMI) ≥ 30 kg/m², with enlarged neck circumference (males ≥ 17 inches; females ≥ 16 inches) are often present. Other anatomical abnormalities include nasal polyps, septal deviation, lingual tonsils, large adenoids, retrognathia, or tumors of the naso-oro-hypo-pharynx.

Following anesthesia and surgery and for several days thereafter, sleep architecture is largely disturbed in most patients but more so in patients with OSA who already have altered architecture sleep patterns as a consequence of the disease. Most patients do not experience the deeper planes of non rapid eye movement (NREM) sleep or REM sleep for the first three postoperative days. “REM rebound” then follows as a “catch-up” on missed REM sleep phase. During REM rebound, nightmares may trigger a sympathetic surge, causing dysrhythmias, and myocardial ischemia. Also, during REM sleep, the increase in upper airway resistance, coupled with generalized atonia and airway obstruction, may lead to severe hypoxemia. The residual effects of anesthetic agents and neuromuscular blocking agents that tend to have a more profound effect on the upper airway muscles than on ventilatory muscles, further contribute to respiratory obstruction. Benzodiazepines as well as opioids (especially methadone) may cause central followed by obstructive apneic events. Thus, profound/prolonged upper airway muscle weakness may be present despite adequate spontaneous ventilation by the patient. Thus patients with OSA are at considerable risk of cardiorespiratory complications after surgery and during a period when analgesia may be maintained principally with opiates.

**Cognitive Dysfunction**

Structural disorders of cerebral nervous system such as increase in intracranial pressure, brain ischemia, and psychological disorders may all cause postoperative somnolence. For example, patients with Parkinson’s disease are more prone to postoperative confusion and hallucinations. Inhalational anaesthetic agents have complex effects on brain dopamine concentrations, inhibiting synaptic reuptake of dopamine, thereby increasing the extracellular concentration and affecting both spontaneous and depolarization-evoked
dopamine release\textsuperscript{40-42}, changes that occur at clinically relevant concentrations. Hypotension is a concern due to hypovolemia, norepinephrine depletion, autonomic dysfunction and the co-administration of other medications. Patients taking bromocriptine or pergolide are prone to excessive vasodilation further exacerbating hypotension.

Patients who are depressed and taking monoamine oxidase inhibitors (MAO) or selective serotonin reuptake inhibitors (SSRI) may experience severe drug interactions with intravenous agents that can result in hyper/hypotension and postoperative coma, up to a full blown serotinergic syndrome. Other agents that can result in drug interactions include St John’s Wort, ginseng, lithium, ondansetron, metoclopramide, codeine, fentanyl, oxycodone among many others. Severe symptoms include tachycardia and shock. Temperature may rise to above 41.1 °C (106.0 °F) in life-threatening cases. Other abnormalities include metabolic acidosis, rhabdomyolysis, seizures, renal failure, and disseminated intravascular coagulation; these effects usually arising as a consequence of hyperthermia\textsuperscript{43}.

Patients with Down syndrome or mental retardation may be particularly susceptible to delayed awakening. Risk factors included age <21 years, males and those given > 0.032mg/kg midazolam especially when administered together with propofol\textsuperscript{44}. Intravenous sedation for dental patients with disabilities, particularly those with cerebral palsy increases the risk of hypoxia and delayed recovery of > 60 minutes is expected.

\textbf{Seizures}

Seizures are not uncommon after brain injury, including after surgical intervention. A post ictal state may well mimic unconsciousness. Anti epileptic drugs are well known to reduce neuromuscular blocking agent responsiveness when given chronically but not acutely\textsuperscript{45-47}. Sahoo et al reported on a case of a patient with a long term seizure history who was not currently taking any antiseizure medication and was paralyzed for over 3 hours following rocuronium 40mg and a loading dose of phenytoin 20mg.kg\textsuperscript{47}.

\textbf{Stroke}

Stroke is not common after anesthesia although several risk factors such as hypertension, smoking, diabetes, obesity among others increase susceptibility. Stroke may occur following carotid endarterectomy when an atheromatous plaque has been dislodged of after cardiac surgery due to the embolization of small clots or air. Occasionally this complication can be detected intraoperatively by cerebral oximetry. However, usually the first sign is a delayed return to cognitive function. Diagnosis depends on signs and radiologic studies. Neurologic consult should be sought immediately and an interventionalist consulted if time allows for intravenous administration of recombinant tissue plasminogen activator (usually within 4-6 hours of the event). Occasionally in patients who have had a stroke in the past but recovered, paralysis of the previously affected limb may appear. This complication usually reverses within a few hours.

\textbf{Drug Factors}

The most common cause of delayed return to consciousness relates to residual drug effects Due to the many patient variables as noted above, it is not surprising that a drug given at one dose may be satisfactory for one patient but not for another.

\textbf{Overdose}

The dose may have been excessive or the patient elderly or of small size. If vaporizers are not calibrated correctly, higher dose than believed of inhaled agents may be delivered, especially if end tidal drug concentrations are not measured. Drug metabolism is delayed by renal or hepatic failure and in hypothermic patients. Sensitivity to some drugs is recognized, for example in patients with myasthenia gravis non-depolarizing muscle relaxants have a long duration of action. Preoperative oral midazolam while it may cause delayed awakening in geriatric patients was not predictive of delayed emergence in adolescents or preadolescents unless there was detectable preoperative sedation\textsuperscript{48}.  
Inhaled Agents

The speed of emergence from inhaled agents directly relates to alveolar ventilation and hypoventilation may delay emergence. The less soluble the agent, the more rapid the elimination. Thus awakening is fastest with desflurane and nitrous oxide. After prolonged surgery and anesthetic administration, tissue uptake, which relates to drug solubility becomes a factor.

Intravenous Agents

Recovery is determined chiefly by redistribution from blood and brain into muscle and fat. Awakening after propofol is fast because of rapid hepatic metabolism and no accumulation. Pentothal is redistributed quickly but elimination by oxidative metabolism in the liver is slow and the drug has a long elimination half life of 3.4 to 22 hours. Up to 30% of the dose may remain in the body for up to 24 hours if repeat doses have been given or it is administered as an infusion. Advanced age or renal or hepatic disease can prolong drug action of agents dependent on hepatic metabolism or renal excretion. One report notes miscalculation combined with advanced age and cardiac disease as a cause of continued somnolence in an 86 year old patient receiving an intravenous lidocaine infusion for dysrythmia.

Neuromuscular Blocking Agents

Residual paralysis is not delayed awakening but unresponsiveness may be perceived as such.

Causes include, overdose, incomplete reversal, syringe swap when additional dosing may have been given rather than the reversal agents, infiltration of the intravenous cannula or in patients following succinylcholine administration who may have plasma cholinesterase deficiency. Repeated doses of succinylcholine may result in dual block. Causes of succinylcholine apnea are listed in table 4. Mivacurium is also metabolized by plasma cholinesterase and can have prolonged effects in susceptible individuals.

Table 4
Several factors may contribute to prolonged apnea after succinylcholine administration.

<table>
<thead>
<tr>
<th>Genetic</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma cholinesterase deficiency</td>
<td>Hepatorenal disease</td>
</tr>
<tr>
<td>Myotonic dystrophy</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>(Malignant hyperthermia)</td>
<td>Thyrotoxicosis</td>
</tr>
<tr>
<td>Mitochondrial myopathies</td>
<td>Cardiac failure</td>
</tr>
<tr>
<td></td>
<td>Drug interactions(</td>
</tr>
<tr>
<td></td>
<td>ecotoipate, neostigmine,</td>
</tr>
<tr>
<td></td>
<td>fertilizers)</td>
</tr>
</tbody>
</table>

Potentiation by other drugs

Prior ingestion of sedative premedication such as benzodiazepines, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors and some herbal preparations like St Johns Wort or alcohol potentiates the central nervous system depressant effects of anesthetic and analgesic drugs and may delay emergence from anesthesia. The effects of non depolarizing muscle relaxants may be increased by drugs such as amino glycosides, lithium, calcium channel antagonists, and diuretics.

Local Anesthetic Toxicity

Repeated dose of local anesthetic agents especially into very vascular areas may result in toxicity that may manifest from somnolence to seizures to cardiac arrest. Management requires cardiopulmonary support and lipid emulsion infusion.

Fluid Overload

Crystalloids migrate from the vascular space quickly after infusion to dependent and soft tissue spaces such as the airway, gut wall and lungs. Pulmonary edema after lung surgery correlates with large fluid administration (12-15% incidence). Ten% of patients receiving >6l fluid over 24 hours had respiratory failure. Hypoxia and hypercarbia are common due to cardiac failure.

Surgical Factors

As noted above long surgery is associated with...
delayed return to consciousness.

Procedures most likely to be associated with postoperative somnolence are neurosurgical interventions. Comparison of patients undergoing spinal or intracranial surgery indicated that those who underwent craniotomy for removal of large mass lesions awoke more slowly than patients who had spinal procedures or only small lesion. Incident rupture of an arteriovenous malformation may cause intracerebral hemorrhage and delay awakening. Acute intracranial hemorrhage has also been described after ventriculo-peritoneal shunt placement.

Patients with dystonia undergoing deep brain stimulation may have an almost 70% incidence of delayed emergence, related to excessive anesthetic potentiation of the low output pallidial state in dystonia which may depress the pallido-thalamo-cortical-circuitry or depression of the ventral pallidal inputs to the septo-hippocampal system.

The beach chair position has been associated with decreased cerebral perfusion and cerebral ischemia. Recommendations are that blood pressure should be measured at the level of the auricle and some form of cerebral monitoring be used such as entropy or cerebral oximetry.

**Metabolic Factors**

Many of these factors are already mentioned above as also being part of patient characteristics.

Other causes include:

1. Epileptic drugs reduce neuroblocking agents responsiveness when given chronically but not acutely.
2. Hypo- hyperglycemia, electrolyte, acid-base disorders and hypothermia may cause delayed emergence from anesthesia. Hypokalemia is induced by low potassium intake, excessive excretion from gastrointestinal (GI) and kidneys (diuretics).
3. Hypothyroidism may be diagnosed for the first time by delayed awakening.

**Rare Causes of delayed return to consciousness**

**Hypokalemia**

Rayazi et al reported 2 cases of delayed awakening associated with low potassium levels due perhaps to hyperventilation. They recommended serum potassium evaluation as part of determining the differential diagnosis.

**Child Abuse**

Ott et al reported a case of a child who underwent meatoplasty in what appeared to be a straight forward anesthetic. The child was very slow to recover and eventually died. Autopsy showed very high chlorpromazine levels, the drug apparently administered by her mother during the hospitalization.

**Dandy Walker Malformation**

De Santis et al described an incidental diagnosis of Dandy Walker malformation (DWM) in a 73 year old adult following coronary artery surgery complicated by delayed awakening. DWM is a rare posterior fossa malformation defined by hypoplasia and upward rotation of the cerebellar vermis. The patient remained intubated for 6 days.

**Brainstem Paralysis**

After local perioperative bupivacaine wound infiltration in 2 adolescent patients who underwent foramen magnum decompression for Arnold Chiari malformation delayed awakening was attributed to absent brainstem reflexes caused by the local anesthetic. A similar case of absent brain stem reflexes due to a field block with bupivacaine was described by Fuzaylov et al in an infant.

**Intravenous Infiltration**

Infiltration of an intravenous infusion of remifentanil was noted shortly after induction in a 30 year old male. A 2nd vein was cannulated and the anesthetic continued with remifentanil and sevoflurane for the short duration of the microlaryngoscopy. A
few minutes after extubation, the patient developed respiratory arrest, responsive to naloxone. He remained somnolent for the next 5 hours. No other abnormalities were detected and the cause was determined to be subcutaneous remifentanil accumulation.

**Hunter Syndrome**

Hunter syndrome, one of the mucopolysaccharide storage diseases, is known to complicate anesthetic and airway management. Following an apparently uneventful intraoperative course including isoflurane, nitrous oxide and fentanyl recovery was delayed in a patient with severe manifestations of the disorder for almost 2 hours until naloxone was given68.

**Diagnosis**

As causes of delayed awakening are multifactorial, an accurate diagnosis must be made.

1. Past history should be reviewed, especially as regards drug ingestion, including herbal therapies such as St Johns Wort.
2. Ensure all agents are turned off.
3. The anesthetic record should be reviewed as regards concentration and dosages of drugs and duration.
4. Amount of fluid administration should be reviewed as excess fluid may gravitate to the lungs, causing decreased oxygen exchange and hypercarbia and hypoxia.
5. Vital signs should indicate cardiopulmonary stability.
6. Temperature should be close to normal.
7. Hypo and hyperventilation should be excluded by blood gas analyses.
8. Metabolic acidosis should be excluded.
9. Residual muscular paralysis should be excluded by train of four monitoring and head lift of >5 seconds.
10. Neurologic examination should include pupil examination, symmetric motor movements, presence of a gag or cough.
11. CT scan, neurologic/neurosurgical consultation is indicated if other causes have been excluded.
12. In difficult cases, there should be no delay in requesting help.

**Treatment**

Therapy depends on the cause. Nevertheless in the initial assessment of the patient who is not recovering as expected in the PACU, several steps must be followed:

1. Give oxygen to treat hypoxia.
2. Give naloxone and/or flumazenil to reverse an overdose of narcotics or benzodiazepines.
3. Reverse effects of non depolarizing muscle relaxants.
4. Give intravenous aminophylline to antagonize the effects of sedative and analgesic drugs, including propofol69.
5. Correct any airway difficulties including jaw life, insertion of an airway, reintubation, application of continuous positive airway pressure.
6. Establish blood pressure at appropriate levels for the patient with vasopressor if necessary.
7. Warm the patient to a temperature of 36-37 degrees.
9. Perform a complete blood count and give blood if indicated.
10. Obtain a 12 lead electrocardiogram and appropriate consults.
11. Order a CT scan and request a neurological consult.

**Concluding Statement**

The causes of delayed awakening after anesthesia are often multifactorial and governed by patient, drug, surgical and metabolic factors. Drug overdose and interactions, especially with neuromuscular blocking
agents, are among the most common causes. Metabolic abnormalities often do not present with the usual signs and symptoms in a patient who is anesthetized. Organic cause of unresponsiveness may have long lasting sequelae and thus early diagnosis and treatment are imperative. On rare occasions, dissociative states may present first as extended periods of unconsciousness without other identifiable causes.


45. RICHARD A, GIBAUD F, GIBAUD DC, ET AL: Cisatracurium-induced neuromuscular blockade is affected by chronic phenytoin or carbamazepine treatment in neurosurgical patients. Anesth Analg; 2005, 100:538-44.


Abstract

**Background:** Ideal anesthetic technique for renal allograft recipients should provide hemodynamic stability, optimum graft reperfusion and adequate analgesia. Balanced anesthesia is preferred because renal nociception is conducted multi-segmentally and chronically ill ESRD patients have labile psychological profile. Present study compared the efficacy of dexmedetomidine with fentanyl administered via intravenous and epidural route before induction of general anesthesia.

**Methods:** Prospective, double blind randomized study, recruited sixty hemo-dynamically stable ESRD adults, 18-55 years, scheduled for elective live related renal transplantation. Patients randomly received intravenous dexmedetomidine 0.5 µg/kg followed by epidural dexmedetomidine 0.5 µg/kg alongwith 5ml;0.25% ropivacaine or intravenous fentanyl 1 µg/kg followed by epiduralfentanyl 1 µg/kg alongwith 5ml;0.25% ropivacaine. All patients received standardized general anaesthesia and continuous epidural ropivacaine 0.25%; 4-8 ml/hr. Preoperative sedation, peri-operative haemodynamics, end tidal anaesthetic agent requirement, peri-operative fluid requirement, need for vasopressors, blood loss and early graft function was assessed.

**Results:** 80% patients receiving intravenous dexmedetomidine did not require rescue midazolam for achieving satisfactory sedation before induction of general anaesthesia. Dexmedetomidine significantly reduced propofol and end tidal inhalational agents requirement and need for rescue analgesics. Early renal graft function (onset time of diuresis after declamping, 24 hours urine output and serum creatinine levels) was comparable. There were no adverse sequelae.

**Conclusion:** Dexmedetomidine-based anaesthetic regimen versus fentanyl-based anaesthesia provided appropriate anxiolysis and analgesia for conducting invasive procedures and subsequent epidural administration of these agents reduced anaesthetic requirement and prolonged postoperative analgesia without compromising hemodynamics and respiratory parameters. Further dose finding studies can be conducted in kidney transplant recipients.
enhance graft reperfusion and provide good postoperative pain relief\textsuperscript{1-3}. Every effort is made to choose the right techniques as well as pharmacological agents which facilitate proper functioning of the newly transplanted organ\textsuperscript{4,5}. Combined general and regional anesthesia has been preferred considering that renal nociception is conducted multi-segmentally and chronically ill ESRD patients have labile psychological profile\textsuperscript{6,7}. Epidural anesthesia provides dynamic pain relief, permits early extubation and a better response to the stress of anesthesia and surgery. However, large volumes of local anesthetics (LA) administered via neuraxial route can have deleterious hemodynamic consequences with associated risk of LA toxicity. Although, Ropivacaine has low risk of cardiovascular and central nervous system toxicity and a lesser propensity for motor blockade\textsuperscript{8}. Traditionally, opioids have been used as neuraxial adjuvants to reduce the dose of local anesthetics and improve the quality of peri-operative analgesia\textsuperscript{9}. However, there is always a possibility of urinary retention, nausea, vomiting, pruritis and respiratory depression with these agents\textsuperscript{10}. The incidence of motor blockade after epidural analgesia with amide local anesthetics (LA) and opioids is approximately 4-12%, which defeats the novel purpose of appropriate pain relief\textsuperscript{9}.

Dexmedetomidine, an $\alpha_2$-adrenergic agonist has sedative, anxiolytic, and anesthetic sparing properties. The anti-nociceptive properties of the drug has been demonstrated in various trials where it was administered via systemic, intrathecal, perineural or intra-articular routes\textsuperscript{11-15}. Compared to fentanyl, dexmedetomidine has been reported to induce sedation without affecting the respiratory status. However, efficacy of dexmedetomidine in renal transplant surgery has not been evaluated. Therefore, the present study was planned to compare dexmedetomidine and fentanyl administered via both intravenous and epidural route prior to induction of anesthesia.

Our hypothesis is that preinduction intravenous dexmedetomidine infusion will provide anxiolysis and analgesia for central venous line and epidural catheter insertions and its subsequent administration via epidural route alongwith ropivacaine will reduce intraoperative anesthetic requirement and prolong postoperative analgesia without compromising respiratory parameters in end-stage renal disease patients undergoing live-related kidney transplant surgery.

**Methods**

This prospective, double blind randomized trial, enrolled sixty ASA physical status II or III adults, either gender, 18-55 years suffering from end stage renal disease. Research ethics committee approval and informed written consent was taken. Patients with drug allergy, compensated/decompensated myocardial insufficiencies, coagulation abnormalities or accidental dural puncture were excluded. Premedication consisted of oral alprazolam 0.25 mg and ranitidine 150 mg administered the night before surgery. Preoperative monitoring included: electrocardiography (ECG), baseline heart rate, respiratory rate, noninvasive blood pressure (NIBP), arterial oxygen saturation (SpO$_2$), and bispectral index (BIS). The mean of first three recordings of hemodynamic parameters at 5 min interval taken after the patient was shifted to the operation theatre were considered as the baseline values. A 16 G cannula was secured in a peripheral vein normal and saline infusion was started at 2 ml/kg/hour. The limb with arterio-venous fistula was not used for peripheral venous access and invasive pressure monitoring.

Patients were randomized using computer generated permuted block into two groups (randomized blocks of 6 patients in a 1:1 ratio using sealed envelopes). Group F patients (n=30) received 1 µg/kg fentanyl infusion diluted to 20ml intravenous fluid over 10 minutes before induction of anesthesia and 1 µg/kg fentanyl in combination with 5ml of 0.25% ropivacaine (total volume 8ml ) via epidural route after insertion of epidural catheter. Group D patients (n = 30) received 0.5 µg/kg dexmedetomidine infusion diluted to 20 ml intravenous solution over 10 minutes before induction of anesthesia and 1 µg/kg fentanyl in combination with 5ml of 0.25% ropivacaine by epidural route (total volume 8 ml).

A 20 G arterial canula was inserted in the radial artery under local infiltration for continuous blood pressure monitoring. A double lumen central venous catheter was inserted in to internal jugular
under local infiltration. Subsequently, under aseptic precaution 18G epidural catheter was placed in T12-L1 space with patient in left lateral position. Correct placement of catheter was confirmed by injecting epidural test dose (3ml 2% lignocaine with adrenaline 5µg/ml). The epidural study solutions were prepared by an uninvolved anesthesiologist according to written instructions on sealed envelopes. The solution (8ml) was infused over 10 minutes via epidural route. This was followed by maintenance infusion of 0.2% ropivacaine at 4ml-8ml/hr administered epidurally.

Hypotension was defined as systolic blood pressure (SBP) < 90 mmHg or a greater than 20% drop in mean arterial pressure (MAP) and managed with intravenous fluid administration to maintain CVP 12-15 mmHg. If MAP remained low despite adequate fluid infusion, vasoconstrictor (mephenteramine 3-6 mg intravenous boluses) or ionotropic support was instituted to maintain hemodynamic parameters within 20% of the baseline values.

General anesthetic technique consisted of intravenous propofol, atracurium and a mixture of O2, N2O and isoflurane titrated to BIS value between 40-60. Endotracheal intubation was facilitated by IV atracurium 0.5 mg/kg when TOF count was zero. After intubation, intermittent positive pressure ventilation was commenced with a mixture of 50% nitrous oxide in oxygen and isoflurane, using a closed circuit with a circle absorber. Ventilation was adjusted to maintain end-tidal carbon dioxide (EtCO2) between 35-40mm Hg. A TOF count of 2 or more was an indication for giving atracurium 0.1mg/kg IV. Total dose of atracurium consumption was noted. In all the patients, CVP was gradually build up to 15 mmHg by crystalloids up to 50 ml/kg and colloids (2-4 ml/kg; 20% albumin) until revascularization. Intravenous frusemide 2 mg/kg, hydrocortisone 10 mg/kg and 20% mannitol 2 ml/kg was given to all patients before reperfusion of grafted kidney. Target hemodynamics of mean BP > 85 mmHg, systolic BP > 135 mm of Hg and CVP of 12-15 mm of Hg were maintained during and after declamping. Blood transfusion was considered according to hemodynamic parameters, estimated blood loss and serum hemoglobin levels.

In case of poor graft function (no urine output) fluid administration was restricted. The total dose of vasoconstrictors/ ionotropes used to maintain perioperative hemodynamics were noted. Intravenous ondansetron (0.1 mg/kg) was administered half an hour before the expected time of completion of the surgery. At end of surgery patient was reversed with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg)/ glycopyrolate (0.01 mg/kg) and extubated on meeting the standard criteria for extubation. They were shifted to post renal transplant care unit as per the institutional protocol where hourly hemodynamic parameters were recorded for 24 hrs. For postoperative pain relief, 4-8 ml/hr of 0.2% ropivacaine infusion was used. If VAS was >4, first rescue analgesic with intravenous tramadol 50 mg was used. For the patients not relieved with IV tramadol morphine 3mg was given.

The level of sedation was assessed by the Modified Observers Assessment of Alertness/ Sedation Score (OAA/S)\(^6\). The intensity of pain (assessed by a linear Visual Analog Scale)\(^7\) and BIS values were noted every 5 minutes till the induction of anesthesia. Dose of intravenous propofol needed for loss of consciousness was also noted.

**Statistical Analysis**

ANOVA with post-hoc significance, Chi-square test and Fisher’s exact test were used as appropriate. Value of \(P<0.05\) was considered significant and \(P<0.001\) as highly significant. The sample size was calculated based on previous study\(^7\) employing epidural anesthesia with local anesthetic for renal transplant surgery. To detect a 50% decrease in the incidence of rescue analgesic requirement a minimum of 28 patients per group were required to ensure adequate power of the study with \(\alpha\) of 0.05 (confidence interval 95%) and \(\beta\) of 0.1 (power of 90%).

**Results**

The demographic profile of both groups was comparable (Table 1). The baseline hemodynamic parameters were comparable in both the groups.
### Table 1
The demographic profile of all the patients

<table>
<thead>
<tr>
<th>THE DEMOGRAPHIC Data</th>
<th>GROUP D (n=30)</th>
<th>GROUP F (n=30)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs)</td>
<td>34.33±9.77</td>
<td>35.80±10.35</td>
<td>0.579</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.10±7.298</td>
<td>160.93±7.315</td>
<td>0.539</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>55.04±7.55</td>
<td>53.08±9.05</td>
<td>0.366</td>
</tr>
<tr>
<td>Gender (M:F)*</td>
<td>25:5</td>
<td>22:8</td>
<td>0.387</td>
</tr>
<tr>
<td>Wt Before HD</td>
<td>56.58±7.76</td>
<td>54.58±9.04</td>
<td>0.362</td>
</tr>
<tr>
<td>Wt After HD</td>
<td>55.04±7.55</td>
<td>53.08±9.05</td>
<td>0.366</td>
</tr>
<tr>
<td>Preoperative Creatinine (mg/dl)</td>
<td>6.13 ± 1.74</td>
<td>6.74 ± 1.16</td>
<td>0.15</td>
</tr>
<tr>
<td>Preoperative GFR (ml/min)</td>
<td>11.93 ± 5.51</td>
<td>9.93 ± 1.99</td>
<td>0.14</td>
</tr>
</tbody>
</table>

### Table 2
Perioperative characteristics of the patients of both the groups

<table>
<thead>
<tr>
<th>PERIOPERATIVE CHARACTERISTICS</th>
<th>GROUP D (n=30)</th>
<th>GROUP F (n=30)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm ischemia time (min)</td>
<td>24.50±3.149</td>
<td>23.50±2.991</td>
<td>0.212</td>
</tr>
<tr>
<td>Cold ischemia time (min)</td>
<td>82.53±7.026</td>
<td>79.97±9.223</td>
<td>0.230</td>
</tr>
<tr>
<td>Time of onset of diuresis declamping (min)</td>
<td>5.44 ± 1.40</td>
<td>5.53 ± 1.53</td>
<td>0.972</td>
</tr>
<tr>
<td>Total dose of Propofol for induction (mg)</td>
<td>64.00±12.205</td>
<td>82.50±19.77</td>
<td>0.000*</td>
</tr>
<tr>
<td>Total dose of Atracurium (mg)</td>
<td>84.00±13.15</td>
<td>89.50±11.91</td>
<td>0.095</td>
</tr>
<tr>
<td>Total dose of Fentanyl (µg)</td>
<td>60.80 ± 9.54</td>
<td>92.00 ± 21.21</td>
<td>0.01*</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>255.00±56.24</td>
<td>263.33±54.03</td>
<td>0.561</td>
</tr>
<tr>
<td>Crystalloids (ml/kg)</td>
<td>2500.00±435.494</td>
<td>2513±450.178</td>
<td>0.905</td>
</tr>
<tr>
<td>Albumin (ml/kg)</td>
<td>198.33±20.692</td>
<td>186.67±34.575</td>
<td>0.118</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>121.33±10.41</td>
<td>125.33±11.66</td>
<td>0.279</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>191.33±13.83</td>
<td>190.67±12.61</td>
<td>0.458</td>
</tr>
<tr>
<td>Time to 1st Rescue analgesia</td>
<td>13(10-16)</td>
<td>4(3-5)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Post op Tramadol (mg)</td>
<td>11.67±21.50</td>
<td>50.00±22.74</td>
<td>0.000*</td>
</tr>
<tr>
<td>Post op Morphine (mg)</td>
<td>0.30±0.915</td>
<td>5.30±8.991</td>
<td>0.004*</td>
</tr>
<tr>
<td>Post surgery Urea (mg/dl)</td>
<td>60.07±19.59</td>
<td>72.91±33.34</td>
<td>0.075</td>
</tr>
<tr>
<td>Post surgery Creatinine (mg/dl)</td>
<td>3.71±1.38</td>
<td>4.84±2.305</td>
<td>0.060</td>
</tr>
<tr>
<td>Post operative Nausea</td>
<td>5 (16%)</td>
<td>4 (13%)</td>
<td>0.784</td>
</tr>
<tr>
<td>Postoperative Vomiting</td>
<td>4 (13%)</td>
<td>3 (10%)</td>
<td>0.673</td>
</tr>
<tr>
<td>Postsurgerery Shivering</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Postsurgery Headache</td>
<td>1 (3.3%)</td>
<td>0</td>
<td>0.554</td>
</tr>
</tbody>
</table>
Score noted at 5 minutes interval for 30 minutes after giving the intravenous drug in both the groups. OAAS of 4 was achieved in 25 patients in Group D after 10 minutes. However, in Group F only 4 patients achieved OAAS of 4. The Rest of the patients required injection of midazolam (1 mg iv). Between groups OAA/S was significantly better in group D versus group F (p<0.05).

Induction dose of propofol for hypnosis and achieving BIS value 40 – 60, was significantly lower in Group D as compared to Group F (p<0.05). EtAA requirement was significantly lower in Group D as compared to Group F (p<0.05).

A total 27 patients in Group F received injection tramadol as compared to only 8 patients in Group D for VAS > 4. In Group F, 18 patients received injection morphine as second rescue analgesic versus 4 patients in Group D (p<0.05).Time for maintaining adequate analgesia without the need for tramadol was significantly longer in group D.

Early graft function was assessed by onset of diuresis after declamping, hourly urine output, serum creatinine levels and glomerular filtration rate (GFR) estimation in the first 24 hours. Values were comparable in both the groups (p > 0.05). Both the groups did not differ in terms of post operative nausea, vomiting, shivering and headache. Patients in both the groups received epidural infusion of 0.2% of ropivacaine at the rate of 4-8ml/hr in the post operative period. The epidural catheter was removed when VAS was consistently less than 4 for 12 hours. All the patients were discharged from the transplant unit on the 6th or 7th postoperative day. There were no readmissions.

Discussion

In the present study, combination of general anesthesia alongwith continuous epidural ropivacaine infusion was used for live-related renal transplant surgery. We also used a fixed dose of two different adjuvants ie fentanyl versus dexmedetomidine via intravenous and epidural routes prior to induction of general anaesthesia. Both these adjuvants alongwith standard anaesthesia, provided stable hemodynamics and optimum intraoperative analgesia. Considering frequent reports of labile hemodynamic profile of ESRD patients, fixed and relatively lower doses of these two study drugs were chosen. For the same reasons, variable rate local anesthetic epidural infusion was administered perioperatively ie 0.25% ropivacaine at 4-8 ml/hour to titrate MAP within 20% of the baseline values. Both the anesthetic regimens provided satisfactory anesthesia, but dexmedetomidine group proved to be a better alternative with less requirement of intraoperative anaesthetic agents and postoperative rescue analgesics.

ESRD patients frequently have marked swings in BP during surgery (±30%) and exaggerated responses to induction, laryngoscopy, intubation, declamping and extubation. This is because of preoperative dialysis induced dehydration, increased sensitivity to anesthetics and/or long-term usage of anti hypertensives. Therefore, a concern about haemodynamic instability has been raised when general anaesthesia is administered alongwith central neuraxial blockade. In previous studies, prophylactic low dose dopamine infusion has been used to maintain perfusion pressure of the grafted kidney. Bhosale et al reported 6% incidence of hypotension in their prospective study involving CSEA in renal transplant surgery. Dauri et al compared combined general and epidural anaesthesia with general anaesthesia. No case of hypotension was reported though the dopamine infusion rate required to maintain perfusion pressure was higher in the combined group. Akpek et al started dopamine infusion soon after the epidural drug was administered to maintain adequate perfusion pressures. This may be the reason that no case of hypotension was reported.

Literature reveals that high vasoressor support required for the maintainence of perioperative haemodynamics can adversely affect micro circulation of the grafted kidney. Therefore, it has been commented that vasoconstrictors with strong α-adrenergic effects, such as phenylephrine, should be drugs of last resort. Several animal models have also demonstrated that vessels in the transplanted organs are more sensitive to sympathomimetics. Therefore, it is worthwhile to find out ideal anesthetic regimens. Low dose epidural ropivacaine is being preferred because it is less cardiotoxic, provides better analgesia without motor blockade. Addition of neuraxial adjuvants like opioids and alpha-2 receptor agonists
further improve the quality of peri-operative analgesia due to sedative, anxiolytic, and local anesthetic sparing properties. Asano T et al. observed in an animal study that anti-nociceptive efficacy of epidural dexmedetomidine is approximately five times more compared to its systemic administration. Salgado P et al. found that epidural dexmedetomidine does not affect onset time or upper level of anesthesia (p > 0.05) moreover it prolongs block duration time (p < 0.05) and postoperative analgesia (p < 0.05), and also results in a more intense analgesia (p < 0.05). Superiority of epidural dexmedetomidine has been proved in an orthopedic study. These findings were confirmed in the present study in ESRD patients. Kasaba et al. observed that hypotensive effects of propofol are additive to epidural anesthesia, resulting in significant decrease in MAP. Ngwenyama N et al. has commented that concomitant use of intravenous dexmedetomidine in patients undergoing spinal fusion surgery reduced propofol infusion requirements with less effect on hemodynamics. We also observed that induction dose of propofol required in Group D was significantly lower as compared to Group F. Intraoperative EtAA requirement for maintaining BIS value within 40-60 was also lower in Group D.

All the graft recipients received adequate hydration to maintain CVP of 12-15mm of Hg. Intraoperative fluid requirements (crystalloid and colloid) to maintain CVP was comparable in both the groups. Carlier and Luciani et al. The authors have emphasize upon the importance of maximal hydration and maintenance of adequate haemodynamic parameters at the time of reperfusion for the development of early diuresis and prophylaxis of acute tubular necrosis in the immediate postoperative period. Kadieva et al. reported that maintenance of perfusion pressure by generous administration of intravenous fluids to permit adequate renal blood flow was more important than
perioperative dopamine infusion in achieving graft function and survival. During declamping there is a release of acid metabolites, prostaglandins, activated complements, cold perfusate of grafted kidney and myocardial depressant factor. After eclamping the MAP decreased in all the patients. However, the fall was not significant in both the groups. Akpek et al. in their prospective study comparing general anaesthesia and epidural anaesthesia for renal transplant recipients found no difference in the immediate postoperative graft function as determined by biochemical markers and DTPA scan. Early graft function was assessed by onset of diuresis after declamping, post operative serum creatinine and urine output estimation at hourly intervals for first twenty four hours. These parameters were comparable in both the study groups. Warm and cold ischaemic time and time of onset of diuresis was comparable in both the groups. The estimated blood loss didnot differ amongst groups. Postoperatively analgesia as assessed using visual analogue scale (VAS) scores revealed longer and better pain relief in Group D.

None of the patients had adverse effects related to the study drugs, anaesthetics used or surgery. Opioid related urinary retention, pruritis, or respiratory depression did not occur with the dose of fentanyl used. Undue bradycardia did not occur with the single dose dexmedetomidineadministered via parenteral and epidural route. None of the patients had any cardiovascular or neurological side effects due to local anaesthetics. There was no accidental dural puncture, There was no case of epidural hematoma, neurological deficits, hyperacute graft rejection, excessive bleeding, anuria, injury to bowel or other vascular structures.

Considering the paucity of published data in ESRD patients, we preferred to use fixed single dose of dexmedetomidine and infusion was not continued intraoperatively or postoperatively. Frumento et al found that dexmedetomidine infusion administered as a supplement to epidural analgesia induces diuresis in post-thoracotomy patients with normal preoperative renal function and undergoing fluid restriction. In the

Fig. 2

*Peri-operative Hemodynamics, Preoperative Sedation Scores Intra-operative Anesthetic Agent Requirement Data*
present study, single dose of dexmedetomine was used and no such beneficial effects were noticed. Further studies can be conducted in renal transplant recipients to demonstrate this effect of dexmedetomidine on the grafted kidney.

To conclude, dexmedetomidine-based anaesthetic regimen versus fentanyl-based anaesthesia provided appropriate anxiolysis and analgesia for conducting invasive procedures and subsequent epidural administration of these agents reduced anaesthetic requirement and prolonged postoperative analgesia without compromising hemodynamics and respiratory parameters. Further dose finding studies can be conducted in kidney transplant recipients.

Fig. 3
Postoperative Pain VAS scores
References


Summary

**Background:** The most common peripheral nerve blocks used in umbilical hernia repair are rectus sheath block and regional block (caudal block).

Ultrasound guidance of peripheral nerve blocks has reduced the number of complications and improved the quality of blocks. The aim of this study is to assess the post rectus sheath block pain relief in pediatric patients coming for umbilical surgery, and to evaluate the easiness of soft tissue puncture and ultrasonic appearance of two different needle types.

**Methods:** Twenty two (22) pediatric patients (age range: 1.5–8 years) scheduled for umbilical hernia repair were included in the study. Following the induction of general anesthesia, the ultrasonographic anatomy of the umbilical region was studied with a 5-16 MHz linear probe. An ultrasound-guided rectus sheath block in the lateral edge of both rectus abdominis muscles (RMs) was performed (total of 44 punctures). A 22 gauge short beveled sharp cutting needle 1.1x 30 mm needle A (BD Insyte – W, Vialon material. Spain) was used in one side, and a Stimuplex A insulated Needle 22G 50mm (needle B) was used on the other side. Surgical conditions, intraoperative hemodynamic parameters, and postoperative analgesia were evaluated.

**Results:** Ultrasonograghic visualization of the posterior sheath was possible in all patients. Needle A scored 72.7% of excellent needle tip and shaft view (16 out of 22) compared to 63.63% for needle B (14 out of 22). None of the needles scored poor view. The ultrasound guided rectus sheath blockade provided sufficient analgesia in all children with no need for additional analgesia except for one child who postoperatively requested morphine 0.1 mg/kg intravenously in recovery room. There were no complications.

**Conclusions:** Ultrasound guidance enables performances of an effective rectus sheath block for umbilical hernia in the lateral edge of the rectus muscle. Use of the sharp short beveled needle of 22 gauge intravenous (IV) cannula stylet provides easy, less traumatic skin and rectus muscle penetration and better needle visualization by the ultrasound.

**Keywords:** surgery: umbilical hernia; ultrasonography; umbilical peripheral nerve block, anesthesia; analgesia, postoperative; anesthetic techniques, regional, rectus sheath block.

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Introduction

Umbilical hernia repair is a common operation in pediatric surgery. It is carried out in children over 2 years old, usually under general anesthesia combined with a regional block (caudal block). It is done as a day case procedure; a peripheral nerve block is usually the choice. The rectus sheath block was described in adults, has been used for laparoscopic surgery in gynecology, and is one of the currently used techniques in pediatric umbilical surgery. However, it may be associated with complications such as retroperitoneal hematoma and possibility of peritoneal puncture. The paraumbilical block was described in 11 pediatric patients to avoid these complications and to improve the success rate of the block. Recently, direct ultrasonographic visualization of the brachial plexus, of the sciatic nerve in the popliteal fossa, the ilioinguinal/iliohypogastric nerves, and of rectus sheath has been done successfully in children.

The aim of this case series was to investigate the ultrasound visualization of the anatomy in the umbilical region in children and to describe an ultrasound-guided new needle type needle A (22G short beveled sharp cutting stylet needle 1.1 x 30 mm BD Insyte-W) that might improve the quality of the blocks and reduce the risk of complications compared with conventional needle B (Stimuplex A insulated facet tip Needle 22G 50 mm B Braun).

Methods

Approval of the IRB ethical committee (King Khalid University hospital, King Saud University, Saudi Arabia) was obtained (No14/3999/IRB), and informed consent from the parents was obtained in all cases. Twenty two children, age range 1.5–8 years, ASA physical status I or II, scheduled for umbilical hernia repair on an outpatient basis, were included in this case series. None had a history of convulsion, neuromuscular disease or hematological disorders and local anesthesia allergy. No premedication was given. Intraoperative monitoring included, ECG, pulse oximetry, non-invasive blood pressure, and end tidal carbon dioxide concentration.

After general anesthesia was induced and venous access established, fentanyl 2mc/kg was given and an appropriate size laryngeal mask airway was placed. Spontaneous ventilation with 1 MAC sevoflurane in a mixture of 50% air and oxygen was maintained in all cases throughout the procedure.

The ultrasonographic anatomy of the umbilical region was studied in each case, with 5-16MHz US linear probe (Sonosite M TURBO). The probe was positioned 1 cm above the umbilicus, and the adjustments in depth and gain were made in order to achieve the optimal sonographic view of both rectus abdominis muscle (RMs), their sheaths, and adjacent structures.

The sheath and lateral edge of the RM were localized, and the peritoneum and the aponeurosis of ipsilateral transverse abdominis (TM), internal and external oblique muscles (EOM&IOM) were identified (Figure 1). After aseptic preparation of the puncture site, the ultrasound probe was covered with sterile TEGADERM film (3M Health Care St. Paul, MN, USA) and sterile ultrasound gel was used (UltraPhonic Pharmaceutical Innovations, Inc, New Jersey, USA). The block was performed with 22G short beveled sharp cutting stylet needle 1.1 x 30 mm (BD Insyte – W, Vialon material, Spain) needle A (Figure 2, 7), assembled with extension set with T adaptor (VEINSYSTEM, Sigo, Ireland). The needle was introduced in-long axis parallel to the ultrasound probe (Figure 4) to reach the lateral border of the rectus muscle, and advanced slowly and carefully until the tip of the needle was seen just between the posterior aspect of the rectus abdominis and its sheath (Figure 1). A single injection of plain bupivacaine 0.25%, 0.25 ml/kg-1 was injected under the real-time ultrasound control. The procedure was repeated on the other side of the rectus sheath with the same drug volume and concentration, using a facet tip needle (Stimuplex A insulated Needle 22G 50 mm) needle B (Figure 3, 5, 6). All blocks were done by the same operator (AHS). A blinded observer with reasonable ultrasound guided regional block experience, and unaware of the study design was asked to assess the quality of the sonographic visualization of the needle tip and shaft and to rate the view as: +: poor, ++: good, +++: excellent.
Fig. 1
Short axis sonographic view of the periumbilical region shows: the rectus muscle surrounded by the rectus sheath (RS), Internal oblique muscle (I.O), External oblique muscle (E.O), Transversus abdominis muscle (T.A)

Fig. 2
Needle A, 22G short beveled sharp cutting stylet and needle tubing assembly

Fig. 3
Needle B: a facet tip insulated needle Stimuplex A
Fig. 4
Needle position; in plane technique lateral to the ultrasound probe

Fig. 5
Tip of Needle A: short beveled sharp tip, Needle B: facet tip

Fig. 6
Needle B tip and shaft visualization within the posterior rectus sheath fascial split by ultrasound during rectus sheath block and injection of local anaesthesia, the rectus sheath (RS), Internal oblique muscle (I.O), External oblique muscle (E.O), Transversus abodominis muscle (T.A), Local anaesthesia (LA)

Fig. 7
Needle A tip and shaft visualization within the posterior rectus sheath fascial split by ultrasound during rectus sheath block and injection of local anaesthesia, the rectus sheath (RS), Internal oblique muscle (I.O), External oblique muscle (E.O), Transversus abodominis muscle (T.A), Local anaesthesia (LA)
Surgery was then started and hemodynamic parameters were recorded throughout the surgery.

Fentanyl 1 mic/kg was administered in the event of an increase in heart rate or blood pressure of more than 10% from baseline or an increase in respiratory rate of more than 20% from baseline following the skin incision or at any time during the procedure and was defined as insufficient analgesia. At the end of the procedure, the laryngeal mask was removed and general anesthesia was discontinued. Children were taken to the post anesthesia care unit (PACU).

Postoperative analgesia was evaluated by a blind investigator using the modified CHEOPS pain scale 11 in the PACU every 10 min until discharge. Children who scored 5 at any of the evaluated times were given morphine 0.1 mg/kg IV.

In the surgical wards, trained nurses recorded the time when the child first required additional paracetamol 15 mg/kg suppository, supplement analgesia during the first day at home was with paracetamol 15 mg/kg PO every 6-8 h, and analgesia requirement were recorded during the day after telephone call.

**Results**

A total of 14 females and 8 males children were included in the study. Table 1 shows demographic data. Each patient received two punctures one on each side of the umbilicus, for a total of 44 punctures in 22 patients. No increases in the heart rate or blood pressure
were recorded intraoperatively (Figure 8, 9) also no increase on respiratory rate and no patient was given additional fentanyl. Different surgeons performed the cases and assessed the surgical conditions as good in all the patients. Needle A scored 72.7% of excellent needle tip and shaft view (16 out of 22) compared to 63.63% for needle B (14 out of 22). There was statistical difference between the two groups with more visibility of the needle in group A compared to group B needles (P<0.05) by using Fisher exact test as statistical analysis. None of the needles scored poor view (Table 2).

Table 1
Patient demographic data

<table>
<thead>
<tr>
<th>Total number</th>
<th>Mean age(years)</th>
<th>Mean weight(kg)</th>
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<tbody>
<tr>
<td>Female 16, Male 8</td>
<td>3.7 (1.5-8 years)</td>
<td>16 (10-27)</td>
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Table 2
Visualization score in needle A & needle B

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Needle A</th>
<th>Needle B</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>+++</td>
<td>++</td>
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<tr>
<td>2</td>
<td>+++</td>
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<td>3</td>
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<tr>
<td>22</td>
<td>+++</td>
<td>++</td>
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</tbody>
</table>

Peritoneum and the lateral edge of the rectus muscles was easily identified in all the cases and the punctures were performed without complication.

Only one child scored >5 in the modified CHEOPS Scale and was given morphine 0.1 mg/kg intravenous in the PACU. The nurses reported no supplement of analgesia.

All patients were discharged and no child received more than two doses of paracetamol 15 mg/kg -1 P.O at home.

Discussion

The rectus sheath block was first used in pediatric surgery by Ferguson et al. in 1996. The authors described that the tendinous intersections of the rectus sheath are only anterior and do not extend through the thickness of the muscle, so a potential space would exist between the posterior aspect of the muscle and its sheath. This potential space would allow dispersion of LA at several levels, enabling an effect on several intercostal nerves. The puncture was performed on each side of the abdomen, just above and lateral to the umbilicus, half-to-1 cm medial to the linea semilunaris. The block proved to be effective and safe both for umbilical and paraumbilical hernia repair.

In recent years, ultrasound is of increasing interest in regional anesthesia, as direct visualization of the anatomic structures allows optimal placement of the needle and thereby reduces the risk of inadvertent interneural, intravascular or adjacent structures injury (e.g. peritoneum). In our case series, we described an ultrasound guided technique of the 10th intercostal nerve block using a 22G short beveled sharp cutting needle (Needle A) in order to achieve smooth and easy puncture of the skin, subcutaneous tissue, rectus sheath and muscle penetration. When performing rectus sheath block in children with the facet tip needle (Needle B), the needle tip faces a highly compliant tissue compared to adults, and tends to push rather than penetrate the tissue, thus the operator’s hand need to apply more pressure on the needle with a hazard of inadvertent peritoneal injury. In contrast to peripheral nerve block, where facet tip needle is considered as a safety measure, rectus
sheath block does not approach specific nerve. The use facet tip needles in this block have no justification. Sonographic visualization of needle A was superior to needle B. However, other cannula styles of different brands need to be investigated. Economic wise, the cost of facet tip needle is five times that of stylet needle, which might influence needle type selection for the block. Before considering using stylet needle for rectus sheath block, further study with larger numbers of patients is required before implementing the use of short sharp beveled needle for rectus sheath block in children. In conclusion, Ultrasound guided rectus sheath block is effective and safe intra and postoperative analgesic approach in children and can be alternative to caudal block in day case surgery. The use of the short beveled sharp cutting needle overcomes technical difficulty while penetrating the soft tissue, have easy penetration and good needle tip and shaft visualization compare the facet tip needle.
References


BREAST CANCER RECURRENTENCE IN PATIENTS RECEIVING EPIDURAL AND PARA VERTEBRAL ANESTHESIA: A RETROSPECTIVE, CASE-CONTROL STUDY

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Abstract

Purpose: Studies have suggested an association between the use of regional paravertebral or epidural anesthesia and a reduction in tumor recurrence following breast cancer surgery. To examine this relationship we performed a retrospective case-control study of patients undergoing breast cancer surgery receiving regional, regional and general, or general anesthesia.

Methods: A retrospective chart review was performed of patients undergoing surgery for stage 0 to III breast cancer. Patients identified as receiving regional anesthesia were then matched for age, stage, estrogen receptor (ER) status, progesterone receptor status, and HER-2 expression with patients who received no regional anesthesia. Univariate (Pearson’s χ² test and odds ratio) and multivariate logistic analyses with backward stepwise regression were performed to determine factors associated with cancer recurrence.

Results: Between 1998 and 2007, 816 women underwent surgery for stage 0 to III breast cancer at our institution. Forty-five patients developed tumors. Univariate analysis showed the use of regional anesthesia trended towards reduced cancer recurrence, but it did not achieve statistical significance (p=0.06). Higher recurrence rates were associated with ER positive status (p=0.003) and higher tumor stage (p <0.0001). Age and HER-2 status were not associated with increased cancer recurrence (both p>0.11). Multivariate analysis confirmed ER status and stage as independently influential (p = 0.002 and p<0.0001 respectively).

Conclusion: Although we found a trend towards reduced breast cancer recurrence with the use of regional anesthesia, univariate analysis did not reach statistical significance.

Key words: Epidural anesthesia; Paravertebral Block; Regional Anesthesia; Recurrence.

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Introduction

Breast cancer is the most common cancer in women in the United States with an overall incidence of 118.7 per 100,000 females in the year 2010. Surgery remains the primary and most definitive treatment for breast cancer. Despite optimal surgical technique, tumor recurrence occurs in 10 to 20 percent of patients. The mechanism by which recurrence following surgery occurs is multifactorial and likely includes release of tumor cells into the bloodstream during surgery from tumor manipulation, increase of systemic and local growth factors during surgery, and perioperative immunomodulation. Recent studies suggest that paravertebral and epidural anesthesia may reduce breast cancer recurrence following surgery by decreasing surgical stress, minimizing the use of opioids, and avoiding certain inhalational agents. In order to explore the relationship between regional anesthesia and tumor recurrence we performed a retrospective case-control analysis comparing oncologic outcomes in patients receiving regional, regional and general, and general anesthesia for breast cancer surgery.

Methods

Between 1998 and 2007, 858 patients underwent surgical intervention for breast cancer at our institution. A retrospective chart review was conducted of these patients. Study exclusion criteria were male gender, stage IV disease at presentation, and use of local anesthesia alone. Eight hundred and sixteen (816/858) women underwent surgery for stage 0-III breast cancer. Of these, 213/816 (26.1%) patients received regional anesthesia with or without general anesthesia. Patients receiving any regional anesthesia were then matched at a ratio of 1:2 for age (less than 40, 41-50, 51-70, and 71 and older), cancer TNM stage, estrogen receptor (ER) status, progesterone receptor (PR) status, and HER-2 expression with those patients receiving no regional anesthesia. Twenty regional anesthesia patients could only be matched with one control. A total of 619 patients were, therefore, available for analysis. Univariate (Pearson’s χ² test and odds ratio) and multivariate logistic regression analyses with backward stepwise were performed using SAS (version 9.2, Cary, North Carolina) to determine factors associated with cancer recurrence. Age, cancer stage, ER, PR, HER-2, and anesthesia type were all evaluated. End points for the study were first local, regional, or distant metastatic recurrence.

Results

A total of 619 patients were included in the study. Two hundred and thirteen patients (213/619; 34.4%) received regional anesthesia and were matched with 406/619 (65.6%) controls who received only general anesthesia. Median age was 64.7 (range 25-95 years), and tumor size was 1.5 cm (range 0.1-10 cm). Five hundred (500/619; 80.8%) were ER+ tumors, and 50/619 (8.1%) were HER-2 positive tumors. The majority of patients were Caucasian (569/619). Thirty-seven were African American; the remainders were reported as Hispanic, Native American, or other. Mean follow-up was nine years (range 5-13 years). Two hundred and eighty-eight patients had breast conserving surgery. Three hundred and thirty-one had total mastectomy. Diagnoses included ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), invasive ductal carcinoma, tubular carcinoma, invasive lobular carcinoma, mucinous carcinoma, and other. The majority of cancers were located in the upper outer quadrant (208/619; 33.6%). All patients who underwent breast conservation surgery also received adjuvant radiation therapy. A total of six surgeons performed the operations.

Two hundred and thirteen (34.4%) patients received paravertebral or epidural anesthesia. Of those, 123 (57.7%) received solely regional anesthesia (Figure 1). Overall, 45/619 (7.3%) patients developed local, regional, or distant metastases at a mean follow-up of nine years (range 5-13 years). Recurrence occurred in seven patients who had regional anesthesia (5.7%), three patients who received regional and general anesthesia (3.3%), and 35 general anesthesia patients (8.6%). Univariate analysis (Pearson χ² and simple logistic regression) revealed statistically significant greater recurrence rates in patients who were ER positive and higher TNM stage. PR status, HER-2 status, and age were not found to be statistically significant.
Having a form of regional anesthesia, with or without general anesthesia trended toward lower recurrence rates, but did not reach statistical significance. When the anesthesia type was further divided into regional, regional plus general, and general, there was no significant difference in recurrence rate. See Table 1 for details. Multivariate analysis confirmed ER status and stage as independently influential (p = 0.002 and p<0.0001, respectively).

Discussion

The role that anesthesia plays in the recurrence of disease following cancer surgery is complex and poorly defined. There are conflicting data at this point as to whether anesthetic technique can influence serological markers of cancer recurrence or the recurrence of clinically relevant metastatic disease4-11.

The results of this retrospective chart review indicate that while there is a trend towards lower chance of metastatic recurrence in breast cancer patients that receive regional anesthesia, it is not a statistically significant benefit. Only estrogen receptor status and cancer stage were independently influential factors on whether or not a recurrence was likely. However, a previously published report on this subject found that metastatic recurrence was significantly reduced in patients receiving regional anesthesia10. Our results are disappointing, as we had hoped to find a definitive benefit. Other previous in vitro data on this subject are mixed in that some cytokines associated with breast cancer are attenuated while others are not7-9.

The benefits of regional anesthesia for breast cancer surgery have been shown to include decreased nausea and vomiting, lower pain scores, and decrease length of stay12. The fact that our data had a trend towards lower recurrence in the regional anesthesia group is
encouraging, but not compelling. Although our data lack statistical significance, complications of regional anesthesia are rare, and because of the aforementioned benefits to using this technique, we advocate regional anesthesia for breast cancer surgery when possible. Whether or not a definitive benefit can be gained through the use of regional anesthesia is a question yet to be answered. The oncology literature has suggested that perhaps utilizing specific chemotherapeutic medications can mimic any benefit gained through anesthetic technique. Whether or not that would make anesthetic technique irrelevant in regards to breast cancer recurrence is unknown at this time. There is one prospective trial in the literature that addressed the use of epidural anesthesia and cancer recurrence in major abdominal surgery. Unfortunately this trial failed to demonstrate any difference in cancer free survival. A large randomized multicenter trial comparing regional and standard anesthetic techniques is currently being performed and the results of that study may help answer the question of whether or not anesthetic technique can influence recurrence in breast cancer.
References


EFFECT OF PRESSURE SUPPORT LEVEL, PATIENT’S EFFORT, AND LUNG MECHANICS ON PHASE SYNCHRONY DURING PRESSURE SUPPORT VENTILATION

GHAZI A. ALOTAIBI*

Abstract

**Background:** Pressure support ventilation (PSV) is used to encourage spontaneous breathing and facilitate weaning. During PSV, duration of the breath is not set, but controlled by the patient, and influenced by some ventilator settings. There is no guarantee that the PS breathe will match start and end of patient’s breathe. Indeed, patient-ventilator breath mismatching during PSV is the rule, not the exception.

**Objective:** This bench study was conducted to investigate effects of varying PSV, patient’s effort, and lung mechanics on trigger response time (TRT), and expiratory delay time (EDT).

**Methods:** We used an electromechanical lung simulator (ASL 5000) to create different clinical scenarios. The simulator was set at 15 b/min and inspiratory time of 1 sec. In experiment I, we used 5, 10, 15, and 20 cm H₂O of PS at each level of patient effort (Pmus) of 3, 6, and 10 cm H₂O. In the second experiment, we set airway resistance (R) at 5, 10, and 20 cm H₂O/L/s at each compliance (C) level of 30, 60, and 90 ml/cm H₂O. For each combination of setting, we analyzed 5 consecutive breaths and calculated TRT and EDT. Mean values of TRT and EDT for each scenario were reported and compared for trends and statistical significance.

**Results:** At each given Pmus, increasing PS produced shorter TRT. This effect seems to plateau at higher PS levels. Significant change (p<0.01) in EDT was noticed with increase in PS setting. Pmus alone did not affect trigger or cycle delay times. Increasing airway resistance caused an increase in TRT, expect when R5 was increased to R10 at compliance levels of 30 and 60 ml/cm H₂O. Similarly, increasing compliance significantly lengthened TRT. Higher R and C produced extended EDT, casing major expiratory asynchrony.

**Conclusion:** This study delineates direction of effect for certain individual variables on patient-ventilator synchrony. Results of this study should help clinicians understand the complexity of synchrony issue.

**Keywords:** Ventilator synchrony, lung model, trigger synchrony, expiratory synchrony, lung mechanics.

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Introduction

There has been a trend in mechanical ventilation practice to allow early spontaneous breathing to share work of breathing between the patient and ventilator. Studies have shown that maintaining spontaneous breathing during ventilatory support preserves diaphragmatic function, improves respiratory mechanics, and speeds up liberation from mechanical ventilation. Applying spontaneous breathing during mechanical ventilation requires a high degree of synchrony between the patient and ventilator. The ventilator is synchronous with the patient when it delivers inflation in a timely manner with the patient’s neural time, and provides flow and pressure sufficient to unload work of breathing. Literature indicates that level of synchrony in majority of ventilated patients may not be optimal. In a study of 60 ventilated patients on pressure support ventilation (PSV), significant asynchrony was reported in 27% of the patients. Mismatch between the patient’s ventilatory needs and the ventilator settings can lead to many deleterious effects, such as discomfort, increased patient’s work of breathing, longer duration of ventilation, and longer hospital and intensive care unit (ICU) length of stay.

Pressure support is a commonly used mode of gradual ventilatory support. PSV allows patient to control breathing profile. Breaths are triggered and terminated based on the patient’s efforts, lung mechanics, and certain ventilator settings. Patient-ventilator interaction during PSV has been investigated by numerous research studies. Starting and ending the mechanical breath in relation to the patient’s neural inspiratory time (Ti) has been a major concern during PSV. Phase synchrony refers to the extent at which ventilator breaths start and end with the patient’s neural inspiratory time. Optimal matching of mechanical inflation to the patient’s breath seems to be the exception not the rule. Ventilator triggering is controlled by setting pressure or flow threshold that the patient must achieve in order to trigger the ventilator. Trigger sensitivity, ventilator sensor performance, patient’s effort, flow rise, and presence of dynamic hyperinflation are among factors that could interfere with triggering function. Dyssynchrony during trigger phase has been reported in 26-82% of patients receiving assisted ventilatory support. Work excreted during asynchronous trigger phase could be as high as 50% of total work of breathing. Breath termination, or cycle, is modulated in most commercially available ventilators by setting a flow threshold so that the breath is terminated when a threshold value is reached. Improperly set cycle criteria results in a mechanical breath that is either preceded (early cycle) or comes after patient’s neural timing (delayed cycle). In both situations, workload on the patient increases, and discomfort ensues. Breath termination is affected by set expiratory threshold, flow profile, patient’s effort, and lung mechanics.

Based on available research work, timing mechanical breath to coincide with start and end of patient’s neural inspiratory time (Ti) is crucial for optimal patient-ventilator interaction. This interaction is affected by a delicate balance of several patient- and ventilator-related factors. Many investigators have studied effects of some ventilator settings and lung mechanics on patient-ventilator synchrony. However, effects of individual factor on phase synchrony during trigger and cycle have not been addressed clearly in these studies. Therefore, we conducted this bench research to study influences on varying PSV level, patient’s effort, airway resistance and lung compliance on trigger response and expiratory delay times.

Methods

Lung Simulator

To simulate different clinical scenarios, we used Active Servo Lung 5000 (ASL5000) (Ingmar Medical, Pittsburgh, USA). The ASL5000 is an electromechanical simulator, composed of a piston moving inside a cylinder. The simulator was connected to a software that allows variety of waveform depictions and calculated variables. Patients’ breathing profile can be configured and controlled by the application software, which uses Equation of Motion to achieve simulated settings. ASL5000 is classified as a high fidelity simulator with capability of initiating spontaneous breathing, varying breathing effort, and modulating resistance (R) and compliance (C).
Experimental Protocol

Puritan Bennet 840 ventilator (Galaway, Ireland) was connected the ASL5000 simulator via adult ventilator circuit with heated humidifier. Experimental setup is shown in Figure 1. The ventilator was set on 5 cm H₂O of pressure support (PS), 4 cm H₂O of positive end expiratory pressure (PEEP), 21% of oxygen, 2 L/min of flow trigger, and expiratory sensitivity (Esens) of 20%. Breathing rate on lung simulator was set at 15 b/min, inspiratory time (Ti) of 1 sec, rise time of 50%, breathing effort (reflected by muscle pressure, Pmus) of -3 cm H₂O with sine wave pattern, compliance (C) of 60 ml/cm H₂O, and resistance (R) of 5 cm H₂O/L/s. To study effects of changing PS level, patient’s efforts, and changes in lung mechanics on trigger and cycle functions, we conducted 2 experiments. See Table 1 for protocol settings.

Experiment I: Changing PS and Patient’s effort.

Using the baseline settings for the ventilator and lung simulator as above, we programmed a script file on the simulator to produce 3 levels of breathing efforts simulating low, medium, and high efforts. Pmus of -3, -6, and -10 cm H₂O were programmed in the script file to last for 300 breaths. For each Pmus setting, PS level was manually adjusted on the ventilator to achieve 5, 10, 15, and 20 cm H₂O every 20 breaths.

Experiment II: Changing Pulmonary Mechanics.

Using the baseline settings for the ventilator and lung simulator as above, we programmed another script file on ASL5000 simulator to produce 3 levels of lung compliance, simulating stiff, normal, and high compliance. Compliance settings of 30, 60, and 90 ml/cm H₂O were programed in the script file to last for 200 breaths. For each compliance level, Resistance of 5, 10, and 15 cm H₂O/L/s were programmed so that each resistance setting lasts for 20 breaths.
### Table 1
**Protocol for Pressure Support (PS), Muscle Pressure (Pmus), Resistance, and Compliance during Experiments I and II**

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<thead>
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<th>Experiment I</th>
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<tr>
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<td>15</td>
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<tr>
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<td>30</td>
<td>60</td>
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### Table 2
**Mean Measured Parameters during Experiment I**

<table>
<thead>
<tr>
<th>Pmus (cm H₂O)</th>
<th>3</th>
<th>6</th>
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<tbody>
<tr>
<td>PS (cm H₂O)</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>TRT (ms)</td>
<td>165</td>
<td>136</td>
<td>127</td>
</tr>
<tr>
<td>PFR (l/min)</td>
<td>56</td>
<td>90</td>
<td>124</td>
</tr>
<tr>
<td>PIP (cm H₂O)</td>
<td>9.8</td>
<td>14.9</td>
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<tr>
<td>VT (ml)</td>
<td>357</td>
<td>659</td>
<td>952</td>
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<tr>
<td>EDT (ms)</td>
<td>0</td>
<td>54</td>
<td>88</td>
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P<sub>mus</sub> = muscle pressure, PS = pressure support, TRT = trigger response time, PFR = peak flow rate, PIP = peak inspiratory pressure, VT = tidal volume, EDT = expiratory delay time.

### Table 3
**Mean Measured Parameters during Experiment II**

<table>
<thead>
<tr>
<th>Compliance (ml/cm H₂O)</th>
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<th>90</th>
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<td>Resistance (cm H₂O/L/s)</td>
<td>5</td>
<td>10</td>
<td>20</td>
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<tr>
<td>TRT (ms)</td>
<td>142</td>
<td>160</td>
<td>169</td>
</tr>
<tr>
<td>PFR (l/min)</td>
<td>59</td>
<td>38</td>
<td>24</td>
</tr>
<tr>
<td>PIP (cm H₂O)</td>
<td>9.7</td>
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<td>9.2</td>
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<tr>
<td>VT (ml)</td>
<td>349</td>
<td>279</td>
<td>204</td>
</tr>
<tr>
<td>EDT (ms)</td>
<td>-150</td>
<td>-41</td>
<td>55</td>
</tr>
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</table>

TRT = trigger response time, PFR = peak flow rate, PIP = peak inspiratory pressure, VT = tidal volume, EDT = expiratory delay time.
Data Collection and Measurement

Measurements were taken for each level of PS during the 3 settings of patient's effort (12 combinations), and for each level of Resistance during the 3 settings of compliance (9 combinations). Trigger response time, expiratory delay time, peak flow rate, peak inspiratory pressure, and exhaled tidal volume were recorded. For each combination of set parameters, measurement were recorded from 5 consecutive breaths after one-minute of stabilization period. As depicted in Figure 2, trigger response time (TRT) was measured as the time from the start of patient effort (drop in Pmus) to the point where airway pressure returns back to baseline (ie. PEEP). Expiratory delay time (EDT) was defined as the time from the end of patient's effort (Pmus returns back to zero) to the time when ventilator's flow reaches zero. Referring to Figure 2, EDT is positive when the ventilator ceases flow after end of patient's effort (late termination), or negative when the ventilator ends inflation while patient's effort still in action (early termination).

Data Analysis

Data was analyzed using SPSS version 16.0. The variables were described using means and standard deviations. All comparisons were tested for statistical significance using one-way ANOVA. Post hoc analysis was performed using Bonferroni’s correction method. Significance level was considered as \( p \) value < 0.01.

Results

Mean values of measured parameters are shown in Tables 2 and 3. Because of high precision of the lung simulator used in this study, standard deviation for each set of measurements was very small. Therefore, it was not shown in the tables.

Experiment 1

Effect of changes in PS and Pmus on TRT are shown in Table 2 and Figure 3. As PS increases, TRT decreases at all levels of Pmus. Within each Pmus level, all reductions in TRT were statistically significant (\( p < 0.01 \)), expect when PS10 was increased to PS20 at all Pmus levels. Table 2 shows effect of increased effort on TRT. Increasing Pmus did not significantly affect TRT at the same PS level, expect comparison between Pmus 3 and Pmus 10 at PS of 5, and comparison between Pmus 6 and Pmus 10 at PS of 5. As shown in Figure 3, it is notable that the effect of increased effort on TRT is mitigated by the increase in PS. Figure 4 depicts effect of PS and Pmus on EDT. At each given Pmus level, increases in PS increased EDT significantly (\( p < 0.01 \)). Increased Pmus alone did not change EDT at all PS
levels, except when Pmus was increased from 3 to 10 cm H$_2$O at PS of 15 and 20 cm H$_2$O. This finding suggests that the effect of increased patient’s effort on EDT becomes more apparent at higher PS settings.

**Experiment II**

Changes in pulmonary mechanics and their effects on TRT and EDT are shown in Table 2 and Figures 5-6. Figure 5 plotted effect of changes in compliance and resistance on TRT. At each given compliance level, there was a trend towards increase in TRT as resistance increases. That trend was statistically significant ($p<0.01$) in all comparisons except when R5 was increased to R10 at C30 and C60. Similarly, increases in lung compliance increased TRT at every given resistance. Effects of compliance on TRT were statistically significant ($p<0.01$) for all comparisons except when C30 was increased to C60 at R10, and C60 was increased to C90 at R5. In Figure 6, EDT is plotted as a positive bar when ventilator ends inspiration after the patient, and a negative bar when ventilator terminates inspiration prematurely. At any given compliance level, increases in resistance made the breath to terminate later, leading to delayed termination. All changes on EDT as a result of increased resistance were statistically significant ($p<0.01$), except when resistance was increased from 10 to 20 at higher lung compliance (C90). Similarly, increases in
lung compliance at any given resistance led to delayed breath termination. All comparisons were statistically significant ($p<0.01$).

**Discussion**

The main findings of the present bench study can be summarized as follow: (1) As level of set PS increases, time required to trigger the ventilator becomes shorter but expiratory delay time increases; (2) patient’s effort seems to have little effect on trigger and cycle delay times; (3) higher pulmonary resistance was found to be associated with longer trigger time and delayed breath termination; (4) as lungs become stiffer, trigger time becomes shorter and mechanical breaths tend to terminate earlier.

Pressure support is a very common mode of partial ventilation and waning. Pressure support level is adjusted to achieve optimal work of breathing and patient’s comfort. In our study, we report inverse relationship between PS level and TRT when other factors are unchanged. Speed of pressurization was set at a medium value (50%) throughout this study. Reduction in TRT as a consequence of increased PS level can be explained by the sharp rise of flow that accompanied higher PS. Increasing PS level involves higher $V_t$ and flow, pushing the negative airway pressure to return to baseline faster as compared to lower PS level. As a result, TRT becomes shorter. Reduction in TRT was attenuated when PS increases from 15 to 20 cm H$_2$O at all Pmus levels. We speculate that the rate at which negative airway pressure decays to baseline has reached its maximum at PS of 15 cm H$_2$O. Therefore, further increase in PS would not significantly affect TRT. Murata et al$^{17}$ studied the effect of different levels of inspiratory rise time and reported that faster rise time reduced duration of post-trigger phase (the time from maximum drop in airway pressure during trigger to the return to baseline). This finding support our explanation of TRT reduction as a result of increased PS. In real clinical situations, effect of increasing PS on TRT is extenuated by reduction in patient’s effort as a response to PSV unloading. In such case, less trigger effort will be exerted by patient, extending TRT or even causing missed trigger. The net effect may be unappreciable change in TRT, but depends on level of trigger work unloading by PS. This relationship between PS level and TRT has clinical implications. In clinical practice, it is common to wean PS level as patient recovers to allow more spontaneous breathing and muscle reconditioning. When PS reaches an under-assist level, effect on TRT becomes more exaggerated, prolonging trigger delay time and worsening patient-ventilator synchrony. Contrary to our finding, Thille et al$^{7}$ found that patient-ventilator synchrony was improved with lower PS. As explained by the authors, improvement in synchrony reported in their study was attributed to lower $V_t$, shorter inflation time, and reduction in intrinsic PEEP associated with lower PS. As a result, ineffective triggers were eliminated. In our study, intrinsic PEEP and ineffective triggers were not part of the protocol.

Manipulation of PS does not only affect trigger
phase, it extends to influence breath termination. Higher levels of PS produce larger VT and longer inflation times. If patient’s neural Ti does not change considerably, mechanical breath continues beyond patient’s neural timing. Because expiratory trigger point is set as a percent threshold (20% in our protocol), higher VT and flow will cause cycle point to be reached late, causing delayed breath termination. Delayed breath termination is uncomfortable to patient and could recruit active expiratory muscles, increasing work of breathing. In patients with airflow limitation diseases, such as asthma and COPD, late termination of the breath could be very harmful. Less time will be available for expiration, leading to dynamic hyperinflation and worse patient-ventilator synchrony. According to our study, lowering PS led to shorter EDT. This could be clinically important during weaning process of PSV mode. Clinical experience supported by literature findings indicate that higher PS is associated with poor patient-ventilator synchrony. When PS is reduced, cycle synchrony is expected to improve. It should be noted that as PS is further reduced, shorter mechanical breaths and early termination could occur. Our observations about PS and EDT support the mathematical analysis by Yamada and Du18, who suggested that expiratory synchrony improves when PS is reduced.

According to our study, lowering PS led to shorter EDT. This could be clinically important during weaning process of PSV mode. Clinical experience supported by literature findings indicate that higher PS is associated with poor patient-ventilator synchrony. When PS is reduced, cycle synchrony is expected to improve. It should be noted that as PS is further reduced, shorter mechanical breaths and early termination could occur. Our observations about PS and EDT support the mathematical analysis by Yamada and Du18, who suggested that expiratory synchrony improves when PS is reduced.

We simulated 3 different levels of muscle pressure (Pmus) to reflect low, medium, and high patients’ efforts. Our findings indicated that the degree of effort did not significantly affect TRT or EDT. However, there was a trend towards reduction in TRT and increase in EDT as Pmus increases. With higher patient’s efforts, trigger threshold is expected to be reached sooner, decreasing TRT. The fact that the observed reduction in TRT did not reach statistical significance can be attributed to the pattern chosen for Pmus. At all Pmus levels used in this study, we configured the drop in pressure to simulate sine wave pattern. We chose to use this pattern of Pmus to study the effect of merely drop in Pmus when other factors are unchanged. We realize that in a real patient with increased effort, Pmus may decrease sharply reaching maximum drop at early stage of the trigger phase. We also used a neural timing of 1 sec at all 3 levels of Pmus. Using the same pattern of Pmus and fixed Ti for all levels of efforts in our experiment could be the reason for the non-significant effect of changing effort on TRT. However, our protocol revealed an important finding about effect of purely increase in Pmus on trigger delay time. It will be interesting to study effect of more vigorous efforts with different waveform pattern and inspiratory times on TRT.

In their mathematical modeling, Yamada and Du suggested that expiratory cycle of a breath is affected by the ratio of applied PS and patient’s generated pressure (PS/Pmus). According to this model, when Pmus becomes the main generator of flow and VT, expiratory synchrony improves. In our study, we found that all 3 levels of Pmus did not significantly affect EDT, except at higher PS levels (15 and 20 cm H2O). In line with the mathematical proposition, we can speculate that Pmus did not affect EDT because flow and VT were predominantly controlled by PS.

Our study also provides insight into effect of changes in pulmonary mechanics on both trigger and cycle phases of the breath. Increases in pulmonary resistance or compliance shifted synchrony window to the left. In such case, the mechanical breath will lag after neural breath and end well after patient finishes his breath. Reduction in resistance and compliance will produce the opposite effect. Both scenarios disrupt patient-ventilator synchrony. For a given PS setting, as resistance increases, required VT and flow necessary to maintain the target PS level are reduced. Lower inspiratory flow, in particular at the onset of the breath, may explain longer TRT observed with high resistance. On the other hand, larger VT and faster flow observed when ventilating high compliant lungs contribute to long TRT. Effect of resistance and compliance on EDT can be explained by the concept of time constant (Tc). Time constant is the time needed to empty about two thirds of exhaled volume19. It is the product of resistance and compliance. At longer Tc (as the case of increased resistance and/or compliance), expiratory flow decays at a slower rate. Therefore, it takes longer time to reach expiratory trigger point. This is the underlying cause for longer EDT that is associated with higher resistance and compliance. Our findings corroborate results of Tassaux et al12 who reported improvement in ventilator synchrony in COPD patients when expiratory trigger was increased to 70%. Longer Tc in these patients was
EFFECT OF PSV AND LUNG MECHANICS ON VENTILATOR SYNCHRONY

curtailed by setting expiratory trigger so that EDT is shortened. In patients with acute lung injury (short Tc), synchrony and work of breathing improved when expiratory trigger was decreased from 45% to 1%, preventing early cycle of the breath. According to the mathematical model mentioned above, expiratory synchrony is not affected by Tc alone, rather it is the effect of time constant divided by neural inspiratory time (Tc/Ti). In the present study, we tested different levels of Tc (as reflected by resistance and compliance) at a fixed Ti of 1 sec. Further research is needed to investigate effect of different Tc/Ti ratios on cycle synchrony.

Patient-ventilator interaction has been the subject of study for many research works that aimed to understand factors influencing synchrony. Of particular interest, two technical developments have been introduced recently to improve phase synchrony. Neurally adjusted ventilatory support (NAVA) is a mode of ventilation that uses electrical activity signals of the diaphragm to trigger and cycle the breath. Research studies indicated that this mode of ventilation produced better synchrony and imposed less work of breathing when compared to PSV. Special algorithm to automatically select breath termination criteria was incorporated in Newport ventilator. A preliminary study compared automated vs. fixed expiratory criteria reported improvement in synchrony and patient’s comfort with the automated algorithm.

This study has some limitations. First, we used an electromechanical lung model to simulate breathing. In a laboratory environment, we were able to test specific parameters while controlling possible confounding factors. This may not reflect clinical reality where outcomes are influenced by many interrelated variables. Therefore, direct extrapolation of this study findings to clinical practice should be done cautiously. Secondly, we did not use active exhalation feature of the lung model, which could have produced different results. The use of active exhalation seems more realistic clinically, but our aim was to investigate effect of some single variables on breath start and end. Thirdly, although we used clinically plausible settings, interpretation of our data should be limited to the range of settings used in this study. Finally, statistical differences reported in this study cannot be directly translated into clinical relevance. Because of high precision produced by the lung simulator, small changes in parameters could reach statistical significant. We used a stricter p values (< 0.01) to signify statistical significance. In one study, 15% increase in work of breathing was reported when trigger delay time increased from 89 to 115 ms.

In conclusion, using a high fidelity lung simulator, we created several scenarios resembling clinical conditions and studied “pure” effects of changes in PS, breathing effort, resistance and compliance on trigger and cycle delay times. Higher PS was associated with shorter trigger time but lengthened time to cycle the breath. Patient’s effort alone did not affect time to trigger or cycle the breath. Increased airway resistance and/or lung compliance disrupt phase synchrony by delaying time to trigger and extending mechanical breath beyond neural time.

Financial Support
None.

Conflict of Interest
None.

Acknowledgment
I would like to thank Mr. Ahmed Mansi for his assistance in setting up the lung simulator.
References


THE INCIDENCE OF POSTOPERATIVE RESIDUAL CURARIZATION FOLLOWING THE USE OF INTERMEDIATE-ACTING MUSCLE RELAXANTS AND RELATED FACTORS

OZLEM KOCATURK*, NIL KAAN**, NURTEN KAYACAN***
AND FATMA ERTUGRUL****

Abstract

**Purpose:** To evaluate the incidence of residual curarization (RC) and related risk factors in the early and late postoperative periods in patients receiving general anesthesia with intermediate-acting muscle relaxants.

**Methods:** Two-hundred and eight American Society of Anesthesiologists class I and II patients, aged 18-70 years, who underwent general anesthesia with intermediate-acting muscle relaxants, were included. Heart rate, blood pressure, oxygen saturation, tympanic temperature were recorded for each patient who was transported to the recovery room, every 10 minutes by a trained nurse. To define the efficacy of residual muscle relaxants, neuromuscular monitoring was performed, and Train of Four (TOF) ratios <90% were regarded as RC whereas ratios ≥90% were considered as adequate neuromuscular recovery in early and late recovery periods. Age, duration of anesthesia, repeated doses, reversal and types of intermediate-acting neuromuscular blockers were evaluated as risk factors for RC. Logistic Regression Analysis was performed to define the risk factors for RC in early and late periods.

**Results:** The RC rate was 10.6% in the early recovery period, and short duration of anesthesia, repeated doses and lack of reversal use were the risk factors for RC. However, RC rate was 2.9% in the late recovery period, and the only risk factor was repeated doses.

**Conclusion:** Reversal use was shown to reduce residual effects of intermediate-acting muscle relaxants in early recovery period, whereas risk of RC in 30 min in PACU was shown to increase with repeated doses of muscle relaxants.

**Keywords:** Residual curarization, train-of-four, intermediate-acting muscle relaxants, post-anesthesia care unit.

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Introduction

Postoperative residual curarization (RC) in the recovery unit is a very important clinical problem and is described as the relationship of the train-of-four (TOF) fade ratio to signs and symptoms of muscle weakness1-3. Even when the effects of a muscle relaxant clinically disappear, some receptors in the nerve muscle junction are still blocked by the muscle relaxant agents4,5.

Residual curarization was a problem due to the use of long-acting muscle relaxants in the past; however, it is also seen frequently with the use of intermediate-acting muscle relaxants6-11. High RC rates were reported by the use of both intermediate and long-acting muscle relaxants12-16.

Generally, a single TOF measurement in the recovery room is used to determine the incidence of RC. In some studies, TOF was measured immediately after extubation, while in others10,16-20 the measurement was made upon arrival of the patient to the recovery room. However, there are few studies on the early and late residual effects of intermediate-acting muscle relaxants12.

The purpose of this study was to detect the incidence of RC and to investigate the related factors, by neuromuscular monitoring in early and late periods of recovery in patients in the recovery room after general anesthesia with either vecuronium, rocuronium or atracurium.

Materials and Methods

The study was a prospective, observational investigation performed in the Department of Anesthesiology and Reanimation. After local ethic committee approval, written informed consents were obtained from all patients. Patients between 18 and 70 years of age in American Society of Anesthesiologists (ASA) physical status I or II were randomly assigned to receive an intermediate-acting neuromuscular blocking (NMB) agent (vecuronium, atracurium or rocuronium) during general anesthesia.

The exclusion criteria were: 1) the presence of a renal, hepatic or a neuromuscular disease; 2) body mass index >30%; 3) use of drugs known to interfere with neuromuscular transmission; 4) pregnancy; 5) refusal to participate the study; 6) craniotomies, cardiothoracic and vascular surgeries, emergency operations, surgeries requiring longer than 6 hours of anesthesia and operations requiring blood and fluid replacement.

A dose of 0.05 mg/kg midazolam was given intramuscularly as a premedication 30 min before surgery. The selection of anesthetic induction (intravenous propofol 2-3 mg/kg, fentanyl 1-2μg/kg, lidocaine 1 mg/kg) and maintenance drugs (1-1.5% isoflurane and 1.5-2% sevoflurane), muscle relaxants (vecuronium, rocuronium, atracurium), intraoperative additional muscle relaxant use, the decision of extubation, reversal use and transfer to the recovery room was at the discretion of the anesthesiologist.

Induction and maintenance doses of muscle relaxants are: vecuronium 0.1 mg/kg and 2 mg, rocuronium 0.5 mg/kg and 10 mg, atracurium 0.5 mg/kg and 10 mg, respectively. In the event of inadequate spontaneous respiration after surgery or if the last dose of muscle relaxant was in the last 40 minutes of the surgery or if weak motor responses to verbal stimuli were present after extubation, neostigmine at a dose of 0.05 mg/kg and atropine were given to the patients. After extubation, the patients breathed 100% oxygen by mask, and kept in the operating room. Patients, who had verbal and motor responses to verbal stimuli (take their tongue out, open their eyes, hold their hands up above their heads), and had adequate spontaneous respiration were transferred to the recovery room as per the decision of the anesthesiologist.

Neuromuscular monitoring was performed at the arrival and 30 minutes later in the recovery room.

TOF fade ratios were measured by using acceleromyography (TOF-Watch®-SX; Organon Teknika, Dublin, Ireland). The arm where the measurements were taken was immobilized with a splint and was positioned to assure free movement of the thumb during nerve stimulation. An acceleration transducer was taped to the distal interphalangeal joint of the thumb. Supramaximal TOF stimulation was delivered to the ulnar nerve via surface electrodes. Two consecutive responses to TOF stimulation (separated by 15 s) were obtained, and the average of the two values was recorded. If the measurements differed by
more than 10%, additional TOF ratios were obtained (up to four TOF values), and the closest two ratios were averaged.

The first measurement, taken as the patient arrives to the recovery room and the measurement taken 30 minutes after arrival were defined as “early recovery period” and “late recovery period”, respectively. TOF ratios <90% were considered as “the presence of RC” while TOF ratios ≥90% were considered as “the absence of RC”.

In the recovery room, routine hemodynamic monitoring of heart rate (HR), peripheral oxygen saturation (SpO₂), noninvasive blood pressure, and tympanic temperature was maintained. Patients’ age, gender, body weight, type of surgery, drugs used for anesthesia induction and maintenance, type of muscle relaxants and time of administration of additional doses during the intraoperative period, reversal usage, duration of surgery and anesthesia were recorded from the anesthesia sheet. Patients were monitored for at least 30 minutes in the recovery room by trained nurses. Age, type of muscle relaxant used, number of additional doses of muscle relaxants during the operation, use of reversals after surgery, duration of anesthesia and tympanic temperature changes were analyzed as the risk factors that may affect RC in the logistic regression model. The variables were grouped according to age (18–39 years, 40–59 years and 60–70 years), the type of muscle relaxants (vecuronium, rocuronium, atracurium), number of additional doses of muscle relaxant used during the operation (only for induction, 1 time, 2 times, 3 times and 4 times), reversal use after operation (yes/no), duration of anesthesia (0-90 min, 91-180 min, 181-270 min and 271-360 min) and tympanic temperature (34.4-35.4°C, 35.5-36.4°C and 36.5-37.6°C).

Statistical analysis

Statistical Program for Social Sciences (SPSS, Inc., Chicago, IL, USA) version 10.0 was used for statistical analysis. Logistic regression analysis was performed to define the risk factors for RC in early (0 min) and late (30 min) recovery periods. The Chi-square test was used for comparison of the frequency. The Kolmogorov-Smirnov test was used to test the normal distribution of data. Descriptive statistics were presented as mean±standard deviation and median (25%-75% percentile). The Wilcoxon T-test was used for changing values of HR, mean arterial blood pressures (MAP) and SpO₂ in recovery room over the time (mean ± SD). A p <0.05 was considered to be statistically significant.

Results

Two hundred and eighteen patients were enrolled in the study. Ten patients were excluded because of lack of data. Statistical analysis was performed on 208 patients. Patient characteristics, the duration of anesthesia, the duration of surgery and types of surgery are presented in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Patients characteristics, clinical parameters and surgical procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Characteristics</strong></td>
</tr>
<tr>
<td>Gender (Female/Male) 110/98</td>
</tr>
<tr>
<td>Age (year) 43.2±14.2</td>
</tr>
<tr>
<td>Weight (kg) 73.1±12.9</td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>I 158</td>
</tr>
<tr>
<td>II 50</td>
</tr>
<tr>
<td>Duration of anesthesia (min) 123.6±58.9</td>
</tr>
<tr>
<td>Duration of operation (min) 92.9±52.7</td>
</tr>
<tr>
<td>Surgery</td>
</tr>
<tr>
<td>Head and neck surgery 94</td>
</tr>
<tr>
<td>Laparoscopic abdominal surgery 34</td>
</tr>
<tr>
<td>Non-laparoscopic abdominal surgery 53</td>
</tr>
<tr>
<td>Extremity surgery 6</td>
</tr>
<tr>
<td>Others (breast, plastic, perineal surgery) 21</td>
</tr>
</tbody>
</table>

Data are presented as mean±standard deviation or number, where appropriate.

ASA: American Society of Anesthesiologists.
The induction of anesthesia was similar in all patients. Anesthesia was maintained with isoflurane in 147 patients, and sevoflurane in 61 patients. Rocuronium, atracurium and vecuronium was given to 51, 63 and 94 patients, respectively.

Residual curarization (TOF<90%) occurred in 22 patients (10.6%) in the early period and continued in six patients (2.9%) in the late recovery period.

The distribution of patients with RC according to risk factors during the early recovery period is presented in Table 2. No significant difference was observed in the number of patients with and without RC in terms of risk factor subgroups.

Lack of reversal use (Odd’s ratio 0.311, 95% confidence interval (CI) 0.104-0.932), short duration of anesthesia (Odd’s ratio 0.363, 95% CI 0.146 to 0.898) and increased number of additional doses of muscle relaxants (Odd’s ratio 2.762, 95% CI 1.420 to 5.373) were shown to increase the incidence of RC in the early postoperative recovery period (Table 3).

The distribution of patients with RC according to risk factors in the late recovery period is shown in Table 4. A significant difference was observed between the patients with and without RC regarding the number of additional doses of muscle relaxants (p <0.05) (Table 4).

The increase in the number of additional doses of muscle relaxants was the only factor that increased the risk of RC (Odd’s ratio 4.241, 95% CI 1.378 to 13.054) in the late recovery period. The effects of other risk factors were not significant (Table 5).

### Table 2
Distribution of patients according to risk factors affecting residual curarization during early recovery period

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Yes (n=22)</th>
<th>No (n=186)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>18-39</td>
<td>10</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>10</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>60-70</td>
<td>2</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Type of muscle relaxants</td>
<td></td>
<td></td>
<td>0.20</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>13</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Atracurium</td>
<td>5</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Rocuronium</td>
<td>4</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Number of additional doses of muscle relaxant</td>
<td></td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>Induction</td>
<td>11</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>1 time</td>
<td>5</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>2 times</td>
<td>4</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>3 times</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4 times</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Reversal use after operation</td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>yes</td>
<td>6</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>16</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td></td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td>0-90</td>
<td>8</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>91-180</td>
<td>12</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>181-270</td>
<td>1</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>271-360</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Tympanic temperature (°C)</td>
<td></td>
<td></td>
<td>0.32</td>
</tr>
<tr>
<td>34.4-35.4</td>
<td>2</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>35.5-36.4</td>
<td>11</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>36.5-37.6</td>
<td>9</td>
<td>62</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3
Effects of risk factors to residual curarization for the early recovery period (0 min)

<table>
<thead>
<tr>
<th>Residual curarization (0 min)</th>
<th>Beta</th>
<th>Wald</th>
<th>p</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.259</td>
<td>0.499</td>
<td>0.480</td>
<td>0.772</td>
<td>0.376-1.583</td>
</tr>
<tr>
<td>Type of muscle relaxants</td>
<td>0.561</td>
<td>3.403</td>
<td>0.065</td>
<td>1.752</td>
<td>0.966-3.180</td>
</tr>
<tr>
<td>Number of additional doses of muscle relaxant</td>
<td>1.016</td>
<td>8.956</td>
<td>0.003</td>
<td>2.762</td>
<td>1.420-5.373</td>
</tr>
<tr>
<td>Reversal use after operation</td>
<td>-1.169</td>
<td>4.352</td>
<td>0.037</td>
<td>0.311</td>
<td>0.104-0.932</td>
</tr>
<tr>
<td>Duration of anesthesia</td>
<td>-1.015</td>
<td>4.807</td>
<td>0.028</td>
<td>0.363</td>
<td>0.146-0.898</td>
</tr>
<tr>
<td>Tympanic temperature</td>
<td>0.116</td>
<td>0.084</td>
<td>0.772</td>
<td>1.123</td>
<td>0.514-2.455</td>
</tr>
</tbody>
</table>

CI: Confidence interval
The average central body temperatures of the patients were $36.1\pm0.6$ °C (with a range of $34.4^\circ\text{C}-37.4^\circ\text{C}$) and $36.2\pm0.5$ °C (with a range of $34.6^\circ\text{C}-37.4^\circ\text{C}$) in early and late recovery period, respectively.

SpO$_2$ of 21 patients fell below 94% in the early recovery period. In these patients, oxygen was delivered at a rate of 4 L/min via facemasks and additional reversals were given in three of them. Respiratory distress was not observed in any patient in the late recovery period.

Discussion

In this study, we showed that 10.6% of the patients who underwent general anesthesia with intermediate-acting muscle relaxants (vecuronium, rocuronium, atracurium) had RC upon arrival to the recovery room. It was found that shorter duration of anesthesia, lack of reversals use and repeated doses of muscle relaxants increased the risk of RC during early recovery period. In 2.9% of patients, TOF ratio was below 90% and RC continued up to 30 minutes after arrival to the recovery room. The intraoperative use of repeated doses of intermediate acting muscle relaxants was found to be a factor increasing the risk of RC in the late recovery period.

Baillard et al. investigated the frequency and risk factors of RC upon arrival to the recovery room. Short duration of surgery, lack of reversal use, no intraoperative monitoring and excess doses of muscle relaxants were found to increase the risk of RC. In

| Table 4 |
| Distribution of patients according to risk factors affecting residual curarization during the late recovery period |

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Residual curarization</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=6)</td>
<td>No (n=202)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>18-39</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>40-59</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>60-70</td>
<td>1</td>
</tr>
<tr>
<td>Type of muscle relaxants</td>
<td>VECURONIUM</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>ATRACURIUM</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>ROCURONIUM</td>
<td>0</td>
</tr>
<tr>
<td>Number of additional doses of muscle relaxant</td>
<td>Induction</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1 time</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>2 times</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3 times</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4 times</td>
<td>1</td>
</tr>
<tr>
<td>Reversal use after operation</td>
<td>Yes</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>0-90</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>91-180</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>181-270</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>271-360</td>
<td>1</td>
</tr>
<tr>
<td>Tympanic temperature (°C)</td>
<td>34.4-35.4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>35.5-36.4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>36.5-37.6</td>
<td>1</td>
</tr>
</tbody>
</table>

| Table 5 |
| Effects of risk factors to residual curarization for the late recovery period (30 min) |

<table>
<thead>
<tr>
<th>Residual curarization (30 min)</th>
<th>Beta</th>
<th>Wald</th>
<th>p</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.173</td>
<td>0.062</td>
<td>0.804</td>
<td>0.841</td>
<td>0.215-3.289</td>
</tr>
<tr>
<td>Type of muscle relaxants</td>
<td>1.189</td>
<td>2.517</td>
<td>0.113</td>
<td>3.283</td>
<td>0.756-14.264</td>
</tr>
<tr>
<td>Number of additional doses of muscle relaxant</td>
<td>1.445</td>
<td>6.344</td>
<td>0.012</td>
<td>4.241</td>
<td>1.378-13.054</td>
</tr>
<tr>
<td>Reversal use after operation</td>
<td>-1.827</td>
<td>2.182</td>
<td>0.140</td>
<td>0.161</td>
<td>0.014-1.817</td>
</tr>
<tr>
<td>Duration of anesthesia</td>
<td>-0.847</td>
<td>1.199</td>
<td>0.274</td>
<td>0.429</td>
<td>0.094-1.953</td>
</tr>
<tr>
<td>Tympanic temperature</td>
<td>-0.960</td>
<td>1.318</td>
<td>0.251</td>
<td>0.383</td>
<td>0.074-1.971</td>
</tr>
</tbody>
</table>

CI: Confidence interval
this study, the reduction in the incidence of RC over time was related to the physicians’ clinical practice. Residual curarization usually regarded as a concern with the use of long-acting muscle relaxants, can be frequently encountered with the use of intermediate-acting muscle relaxants. Naguib et al. in a meta-analysis, reported that the incidence of postoperative RC was significantly decreased by using intermediate-acting muscle relaxants. The decrease in the incidence was attributed to better clinical evaluation, widespread performance of intraoperative neuromuscular monitoring and increased use of intermediate-acting muscle relaxants in recent years.

Residual curarization (TOF<90%) rates with rocuronium in healthy adult patients undergoing elective orthopedic surgery were reported as 29% and 2.9% upon arrival to the recovery room and after 30 minutes, respectively. Debane et al. reported that TOF in 45% of the patients (who were given vecuronium, rocuronium or atracurium) were below 90% in the early recovery period. In our study, the RC incidence after the use of intermediate-acting muscle relaxants was 10.6% and 2.9%, in the early and late recovery periods, respectively. The lower RC incidence in our study was attributed to the monitoring of patients in the operating room until the patients showed verbal or motor responses to verbal stimuli and had adequate tidal volumes. In addition, considering the duration of surgeries, the number of additional doses used for maintenance of muscle relaxation was very low. This may also explain the low incidence of postoperative RC.

In Baillard et al. study, 42% of the patients who received vecuronium with no reversals were found to have RC. The cumulative doses of vecuronium were 7.7±3.6 mg and 6.2±2.7 mg in patients with and without RC, respectively. RC was shown to increase significantly with the increase in the cumulative dose. Similarly, we found that the increase in the number of additional doses of muscle relaxants was an important factor affecting RC both in early and late recovery periods. In addition, “number of additional doses of muscle relaxants” was the only factor affecting RC in the late recovery period. We thought that the cumulative effect of additional doses might be the most probable cause of this finding. Although, some studies confirmed the role of reversals and intraoperative neuromuscular monitoring in reducing the risk of RC, others claimed that these two factors had no effect on RC. Furthermore, it was emphasized that even high doses of reversals could not eliminate RC. In our study, reversals were administered according to the clinical findings of patients after the surgery. Reversals were given to 44% of patients. No significant difference was found in the incidence of RC between patients using reversals or not in the late recovery period. However, in the regression analysis, the use of reversals was found to be a factor for reducing RC in the early recovery period. The effect of neostigmine starts in 2-5 min and lasts until 30 to 45 min. Therefore the use of reversal not being an effective factor for reducing RC in the late recovery period may be attributed to a reduction in its effect over time. It is almost impossible to eliminate RC completely with routine clinical evaluation, neuromuscular monitoring or use of a reversal agent. However, it has been reported that objective neuromuscular monitoring may be useful when the reversals are not used.

Some studies reported that RC incidence was not related to the type of the intermediate-acting neuromuscular relaxant. In Hayes et al. study, RC (TOF <80%) incidence in patients using vecuronium, atracurium and rocuronium were found to be 64%, 52% and 39%, respectively upon arrival to the recovery room. No statistical difference was observed in RC rates by using different intermediate-acting muscle relaxants. However, in Khan et al study, the patients using rocuronium had higher RC incidence (37%) than in patients using vecuronium (17%). In our study, no significant difference was observed in RC incidences between patients using atracurium, vecuronium or rocuronium in early and late recovery periods. However, the RC incidences we observed were much lower compared to other studies.

Duration of anesthesia is a factor increasing the risk of RC in surgeries with short duration, in which a single-dose of intermediate-acting muscle relaxant is used. On the other hand, duration of anesthesia does not affect the risk of RC in long duration surgeries. It is postulated that the risk of RC may increase in surgeries with long duration with increased frequency of muscle relaxant use. Similarly, risk of RC was
found to increase with shorter duration of anesthesia in early recovery period, whereas duration of anesthesia had no effects on RC in the late recovery period in our study.

Hypothermia is known to prolong the effect of muscle relaxants. The elimination of muscle relaxants from the liver is related to body temperature, and hypothermia has been found to decrease the clearance of muscle relaxants. Although exact hypothermia limit leading to prolongation of the effects of muscle relaxants is not known, there are some studies showing increased incidence of RC when the central temperature is below 34°C. In the current study the central body temperatures of patients were within normal ranges and as such the “body temperature” could not be a risk factor for RC.

In conclusion, dose adjustment of intraoperative muscle relaxants in accordance with the duration of surgery and the use of reversals may reduce the risk of RC.

Conflict of interest
None.

Acknowledgments
We would like to thank to Mevlut Ture, MD Assoc. Prof. of Medical Statistics in Adnan Menderes University Medical School for helpful advice and suggestions about statistical issues.
References


IS UNILATERAL SPINAL ANESTHESIA SUPERIOR TO BILATERAL SPINAL ANESTHESIA IN UNILATERAL INGUINAL REGIONAL SURGERY?

Faruk Cicekci*, Huseyn Yilmaz**, Mehmet Balasar***, Mustafa Sahin**** and Fatih Kara*****

Abstract

Background: Unilateral spinal anesthesia is performed to provide restriction of sensory and motor block.

Objective: The aim of this study was to compare unilateral and bilateral spinal anesthesia, with regard to limiting the nerve block exclusively to the area of surgery.

Methods: This was a prospective, randomised, double-blind study, conducted in 40 consecutive outpatients scheduled for unilateral inguinal regional surgery. Patients in both groups received 0.5 % hyperbaric bupivacaine 15 mg + morphine 0.1 mg. Patients in the unilateral group (Group U) were placed in the lateral decubitus position for 10 minutes (min) on their side to be operated, while patients in the bilateral group (Group B) were placed in the supine position. The pin-prick test was used to assess the times to reach L1, T12 and T10 sensory blocks and the times to reach motor block. In addition, the sensory and motor block recovery times were recorded using a modified Bromage scale. Furthermore, the duration of the operation and the times to first analgesic requirement were noted.

Results: There were significant differences between Group U and Group B in the times to reach L1, T12 and T10 dermatome levels of sensory block, and the times to reach motor block using the modified Bromage scale on three levels. However, there was no difference in the time to ambulation, the time to complete sensory regression and the time to first analgesic requirement.

Conclusion: The time to reach sensory and motor blocks for unilateral spinal anesthesia could provide an advantage over bilateral spinal anesthesia in inguinal region operations.

Key words: Unilateral spinal anesthesia, bilateral spinal anesthesia, inguinal surgery.

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Introduction

Unilateral anesthesia is a specific regional anesthesiology technique. It was first described by Tanasichuk et al. in 1961 as ‘spinal hemianalgesia’ in patients who were to undergo extremity surgery. The basic objective of unilateral spinal anesthesia is to limit the nerve block exclusively to the area of the surgery and for the duration of the operation. Therefore, it is also often recommended for use in short-term surgical interventions that involve only one side of the body. The advantage of unilateral spinal anesthesia over bilateral spinal anesthesia is the lower incidence of hypotension and maintenance of cardiovascular stability, in addition to providing a stronger block on the side of surgery and accelerating the recovery of the nerve block.

In the present study, we aimed to investigate the effects of unilateral spinal anesthesia and bilateral spinal anesthesia on sensory and motor blocks in male patients undergoing short-term unilateral inguinal regional surgery.

Method and Materials

We conducted this study as a prospective, randomised, clinical trial. After gaining approval from the Ethics Committee (Ref. no. 2009/207) of the Medical Faculty of the University of Necmettin Erbakan, Turkey, we included 40 ASA (American Society of Anesthesiologists) I-II males between the ages of 18-65, who were due to undergo elective inguinal regional surgery and spinal anesthesia. All patients were premedicated with 0.1 mg kg⁻¹ intramuscular midazolam prior to their operations. Patients were randomized by sealed envelope assignment to receive either group U or group B, and administered both groups with a standard 0.5 % hyperbaric bupivacaine 3 ml (15 mg) + morphine 0.2 ml (0.1 mg), using a Quincke 25G spinal needle. We administered the injection intrathecally, via a median approach through the L4-5 vertebral interspace, in approximately 20 seconds, using a 5 cc syringe, by guiding the tip of the spinal needle to the side to be operated on in Group U, and caudal in Group B. The patients in Group U were placed in the lateral decubitus position on the side to be operated on for 10 minutes, and then in the supine position, while patients in Group B were placed in a supine position immediately after the intrathecal injection. The pin-prick test was used to assess the sensory block level of the patients, starting from the administration of the intrathecal injection. The times to reach L1, T12 and T10 sensory blocks and the times to reach motor block, as well as the sensory and motor block recovery times were recorded. Blocks were assessed by the modified Bromage scale (Table 1). Furthermore, the duration of the operation and the times to first analgesic requirement were determined. Patients characteristics as well as noninvasive systolic and diastolic blood pressure, heart rate and peripheral oxygen saturation (SpO₂) measurements preoperatively, and then at min 5, 10, 30, 45 and 60 of the operation were recorded. Any side effects and complications (cardiovascular findings, urinary retention, nausea/vomiting and itching) that occurred up until end of PACU (post operative care unit) were noted. Management of postoperative complications included 4 mg IV ondansetron for nausea/vomiting, 5 mg IV ephedrine for hypotension (mean arterial pressure <70 mmHg) and 0.08 mg IV naloxone for itching, in addition to performing urinary catheterization for urinary retention. Oral ketoprofen (50 mg) were administered at 8-hour intervals to provide additional postoperative analgesia.

<table>
<thead>
<tr>
<th>Modified Bromage Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = No motor block.</td>
</tr>
<tr>
<td>1 = Can flex knee, move foot, but cannot raise leg.</td>
</tr>
<tr>
<td>2 = Can move foot only.</td>
</tr>
<tr>
<td>3 = Cannot move foot or knee.</td>
</tr>
</tbody>
</table>

Sample size calculation was done by power analysis. This analysis was based on two samples with statistical significance of 0.05 and 89% power. The sample size required was 20 in each group. Data was analyzed using SPSS for Windows 15.0 software. The Bonferroni-corrected Mann-Whitney U-test was used to compare the independent variables, and the Chi-square test was used to compare the within-group data. Categorical data was analyzed using the Chi-square test. Continuous variables were described as mean±standard deviation (SD). P<0.05 was considered statistically significant.
Results

There were no significant differences in age, weight, height, duration of surgery and type of surgery between both groups (Table 2).

The times to reach L1, T12 and T10 dermatome levels of sensory block [mean±SD (standard deviation)] were 2±1.17 min, 3.34±1.54 min and 4.76±2.11 min, respectively, for Group U, and 4.19±1.54 min, 5.98±2.04 min and 8.06±3.3 min, respectively, for Group B. The difference between the two groups was statistically significant (p<0.05). The time to reach motor block, 0-3 on the modified Bromage scale, was 3.75±1.54 min, for Group U and 6.57±2.34 min, for Group B. The difference between the two groups was statistically significant (p<0.05), as shown in Table 3.

The time to ambulation (Bromage scale 0) was 223±83.4 min for Group U, and 271.2±78 min for Group B. The difference was not statistically significant. The time to complete sensory regression was 332.4±108 min for Group U, and 351.6±79.8 min for Group B and the difference was not statistically significant. The time to the first analgesic requirement was 462.6±213.6 min for Group U, and 355.2±142.8 min for Group B. There was no significant difference between the two groups (Table 4). There was no significant difference between the groups in terms of the preoperative and postoperative systolic arterial pressure, diastolic arterial pressure, heart rate and peripheral oxygen saturation values (Table 5).

The comparison of postoperative complications (nausea/vomiting, hypotension, bradycardia, itching and urinary retention) did not reveal a significant difference between the two groups (Table 6).

---

Table 2
Demographic data, duration of surgery, type of surgery, according to group. Mean±SD

<table>
<thead>
<tr>
<th></th>
<th>Group U (n=20)</th>
<th>Group B (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>46.2±11.7</td>
<td>41.4±11.2</td>
<td>0.408</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173.5±6.7</td>
<td>173±6.5</td>
<td>0.856</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.7±3.5</td>
<td>74.2±8.5</td>
<td>0.466</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>40.4±10.5</td>
<td>38.8±11.2</td>
<td>0.465</td>
</tr>
<tr>
<td>Type of surgery (inguinal hernia/varicocele)</td>
<td>12/11</td>
<td>11/10</td>
<td>0.256</td>
</tr>
</tbody>
</table>

Table 3
Sensory and motor blocks characteristics. Mean±SD

<table>
<thead>
<tr>
<th></th>
<th>Group U (n=20)</th>
<th>Group B (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>The time to reach L1 dermatome levels of sensory block (min)</td>
<td>2±1.17</td>
<td>4.19±1.54</td>
<td>0.029</td>
</tr>
<tr>
<td>The time to reach T12 dermatome levels of sensory block (min)</td>
<td>3.34±1.54</td>
<td>5.98±2.04</td>
<td>0.015</td>
</tr>
<tr>
<td>The time to reach T10 dermatome levels of sensory block (min)</td>
<td>4.76±2.11</td>
<td>8.06±3.3</td>
<td>0.018</td>
</tr>
<tr>
<td>The time to reach motor block Bromage Scale 3 (min)</td>
<td>3.75±1.54</td>
<td>6.57±2.34</td>
<td>0.042</td>
</tr>
</tbody>
</table>

Table 4
Recovery times of sensory and motor block. Mean±SD

<table>
<thead>
<tr>
<th></th>
<th>Group U (n=20)</th>
<th>Group B (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>The time to complete sensory regression (min)</td>
<td>223±83.4</td>
<td>271.2±78</td>
<td>0.827</td>
</tr>
<tr>
<td>The time to ambulation (min)</td>
<td>332.4±108</td>
<td>351.6±79.8</td>
<td>0.690</td>
</tr>
<tr>
<td>Time of the first analgesic requirement (min)</td>
<td>462.6±213.6</td>
<td>355.2±142.8</td>
<td>0.637</td>
</tr>
</tbody>
</table>
Table 5
*Systolic blood pressure, diastolic blood pressure, heart rate and peripheral oxygen saturation values. Mean±SD*

<table>
<thead>
<tr>
<th></th>
<th>Group U (n=20)</th>
<th>Group B (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic blood pressure (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>143±25.4</td>
<td>131±17.3</td>
<td>0.726</td>
</tr>
<tr>
<td>5</td>
<td>130±28.6</td>
<td>124±20.8</td>
<td>0.656</td>
</tr>
<tr>
<td>10</td>
<td>123±16</td>
<td>121±15.4</td>
<td>0.867</td>
</tr>
<tr>
<td>15</td>
<td>124±14</td>
<td>120±15.5</td>
<td>0.948</td>
</tr>
<tr>
<td>30</td>
<td>122±12.9</td>
<td>119±12.6</td>
<td>0.876</td>
</tr>
<tr>
<td>45</td>
<td>113±9.4</td>
<td>123±12.8</td>
<td>0.655</td>
</tr>
<tr>
<td>60</td>
<td>119±9.9</td>
<td>132±18.3</td>
<td>0.428</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>71.6±13.5</td>
<td>70±10.5</td>
<td>0.854</td>
</tr>
<tr>
<td>5</td>
<td>70±16.5</td>
<td>65±18</td>
<td>0.803</td>
</tr>
<tr>
<td>10</td>
<td>69±13.5</td>
<td>61±10.5</td>
<td>0.643</td>
</tr>
<tr>
<td>15</td>
<td>64±11.5</td>
<td>63±10.2</td>
<td>0.597</td>
</tr>
<tr>
<td>30</td>
<td>63±12.6</td>
<td>63±8.5</td>
<td>0.612</td>
</tr>
<tr>
<td>45</td>
<td>55±8.5</td>
<td>73±5.7</td>
<td>0.588</td>
</tr>
<tr>
<td>60</td>
<td>58±11.5</td>
<td>72±7.7</td>
<td>0.312</td>
</tr>
<tr>
<td><strong>Heart rate (beats.min⁻¹)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>86±18.4</td>
<td>86±14.7</td>
<td>0.768</td>
</tr>
<tr>
<td>5</td>
<td>80±19.5</td>
<td>86.3±19.2</td>
<td>0.433</td>
</tr>
<tr>
<td>10</td>
<td>77±17.2</td>
<td>78.1±12.2</td>
<td>0.790</td>
</tr>
<tr>
<td>15</td>
<td>75±15.2</td>
<td>73.8±11</td>
<td>0.883</td>
</tr>
<tr>
<td>30</td>
<td>76±13.2</td>
<td>81±9.7</td>
<td>0.752</td>
</tr>
<tr>
<td>45</td>
<td>73±7.5</td>
<td>71.7±7.7</td>
<td>0.655</td>
</tr>
<tr>
<td>60</td>
<td>74±7.2</td>
<td>74±1.7</td>
<td>0.823</td>
</tr>
<tr>
<td><strong>SpO2 (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>97±1.1</td>
<td>97.5±1</td>
<td>0.987</td>
</tr>
<tr>
<td>5</td>
<td>97±1.1</td>
<td>97±1</td>
<td>0.945</td>
</tr>
<tr>
<td>10</td>
<td>96±1</td>
<td>97±1</td>
<td>0.897</td>
</tr>
<tr>
<td>15</td>
<td>97±1.0</td>
<td>97±0.7</td>
<td>0.878</td>
</tr>
<tr>
<td>30</td>
<td>97±1.1</td>
<td>97±0.7</td>
<td>0.836</td>
</tr>
<tr>
<td>45</td>
<td>98±0.7</td>
<td>97±0.7</td>
<td>0.798</td>
</tr>
<tr>
<td>60</td>
<td>97±0.5</td>
<td>97.5±0.7</td>
<td>0.953</td>
</tr>
</tbody>
</table>

Table 6
*Postoperative complications. Mean±SD*

<table>
<thead>
<tr>
<th></th>
<th>Group U (n=20)</th>
<th>Group B (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Itching</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1</td>
<td>3</td>
<td>0.850</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>
**Discussion**

Small doses of local anesthetics that are used only for the blockage of the side to be operated on can provide an efficient block when administered at a slow pace, by guiding the needle tip to the relevant side and placing the patient in the lateral decubitus position for 10-15 min. Previous studies have suggested that the average waiting period for keeping the patient in the lateral decubitus position for unilateral spinal anesthesia, performed using hyperbaric bupivacaine, is 10-15 min. In our pilot study, we found that 10 min was sufficient for the lateral waiting period. Lateral position is advantageous in terms of fast surgical adaptation, rapid recovery, low number of side effects and complications and ease of administration. Esmaoglu et al. reported the time for the sensory block level to reach L1 as being 4.19±2.8 min in a unilateral group of patients who were administered bupivacaine. However, Pitkänen reported this time as being 5.3±1.1 min. In our study, the time to reach L1 sensory level was 1.72 min for L1, 2.87 min for T12 and 4.15 min for T10 in the unilateral group. In the current study, we postulate that the sensory level was reached in a shorter time because of the high dose of hyperbaric bupivacaine (15 mg/3 ml). Liu et al. found that the duration of the sensory block was 196±44 min for 7.5 mg hyperbaric bupivacaine and 177±53 min for hyperbaric bupivacaine with opioid, while Casati et al. found that the duration of the sensory block was 190±51 min for a unilateral spinal anesthesia application in a bupivacaine group, which was consistent with our findings of 240.6 min. We suggested that this could be due to the addition of morphine to hyperbaric bupivacaine.

In a study using 8 mg 0.5% hyperbaric bupivacaine, Moller et al. reported the time to motor block Bromage scale 3 as 5.6±1.0 min. In our study, the short time to reach motor block might have been due to the addition of higher amounts of hyperbaric bupivacaine and morphine.

The duration of the motor block on the same side is the key factor affecting the time to discharge. Whiteside et al. reported that patients were mobilised in approximately 331 min in a group of patients receiving 15 mg of bupivacaine, which was similar to our current recovery time of 346.8 min.

The addition of opioids to hyperbaric bupivacaine can accelerate the onset time and increases the quality of analgesia in both the intraoperative and postoperative periods. Milligan et al. found that the time to first analgesic requirement following surgery was significantly longer in a group of patients who received bupivacaine and morphine, compared to patients who received bupivacaine alone. In our study, analgesic requirement was needed in 20 of the 40 patients, and the time to first analgesic requirement was 363 min in the unilateral group and 350.4 min in the bilateral group.

Spinal anesthesia is associated with certain cardiovascular and respiratory side effects. However, in the current study, no deteriorations of hemodynamic stability in either the unilateral or the bilateral group were noted.

Furthermore, no major postoperative complications were observed. Whenever these complications occurred, they were not at such a level that they required an intervention in either group.

**Conclusion**

We conclude that the time to reach sensory and motor blocks in inguinal regional surgeries using unilateral spinal anesthesia could provide an advantage over bilateral spinal anesthesia, particularly enabling the surgeons to start these surgeries more rapidly.

**Conflict of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Acknowledgements**

**Author Contributions:**
Concept/Design: Faruk Cicekci, Huseyin Yilmaz
Drafting Article: Faruk Cicekci, Mehmet Balasar
Data Collection: Faruk Cicekci,
CICEKCI F. et al

Data analysis/Interpretation: Fatih Kara, Mustafa Sahin
Statistics: Fatih Kara

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10. Whiteside JB, Burke D, Wildsmith JAW: Comparison of ropivacaine 0.5% (in glucose 5%) with bupivacaine 0.5% (in glucose 8%) for spinal anaesthesia for elective surgery. Br J Anaesth; 2003, 90(3):304-308.
THE EFFECTS OF PROVISION OF ANESTHESIA ON ONE-YEAR MORTALITY IN PATIENTS WITH SEVERE COMPlications

JUN Ko USHIRODA*, SATOKI INouE**, YU TanAKA** AND MASAHIKO KawAGUCHI**

Abstract

Background: General anesthesia in patients with comorbid conditions may affect their intermediate or long-term outcomes. In this study, we evaluated the effects of provision of anesthesia on mortality in critical patients with comorbid conditions by retrospectively investigating one-year mortality in patients with ASA physical status more than III who underwent minor surgery for relative indications and nonfatal reasons.

Methods: Data were collected during the period between January 2006 and December 2011. Eligible patients were those with ASA physical status more than III who underwent minor surgery under general anesthesia for relative indications and nonfatal reasons. Preoperative clinical information was collected from the patient’s clinical charts. Comorbidity was quantified using the Charlson comorbidity index. All the patients were evaluated for in-hospital mortality and were followed-up for mortality at one-year.

Results: During the study period, 14,979 patients underwent general anesthesia. Thirty six patients satisfied the eligibility for enrollment. Charlson comorbidity index of the patients ranged from one to five. No patients died during their hospital-stay; however, 4 patients were lost to follow up. Therefore, one-year mortality rates for each Charlson index category were 0%.

Conclusion: The postoperative one-year mortality in patients with ASA physical status more than III undergoing minor surgery under general anesthesia for relative indications and nonfatal reasons was expected to be considerably small regardless of the Charlson index category.

Key words: Comorbidity, Charlson comorbidity index, Anesthesia, Mortality.

Introduction

Modern anesthesia management allows us to provide surgical interventions for considerably critical patients with comorbid conditions although it is still challenging. On the other hand, it has been discussed that deep anesthesia was associated with mortality among middle-aged and elderly surgical patients1-3. Therefore, it is very likely that provision of anesthesia itself for critical patients with comorbid conditions may affect their intermediate or long-term outcomes. However, little is known about the effects of provision of anesthesia on mortality in critical patients with comorbid conditions because it is practically impossible to provide only anesthesia without surgery just for

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the sake of answering this question.

To answer the above question as much as possible, we arbitrarily assumed that the situations of patients with ASA physical status more than III undergoing minor surgery for relative indications and nonfatal reasons resemble the situations of providing only anesthesia without surgery for critical patients with comorbid conditions. It is not unreasonable to suppose that drugs including anesthetics, analgesics and muscle relaxants, endotracheal intubation, positive pressure ventilation and fluid infusion associated with general anesthesia would have more effect on patients’ outcome than minor surgical procedure.

In this study, we evaluated the effects of provision of anesthesia on mortality in critical patients with comorbid conditions by retrospectively investigating one-year mortality in patients with ASA physical status more than III who underwent minor surgery for relative indications and nonfatal reasons.

**Materials and Methods**

Approval for review of patient’s clinical charts was obtained from the Nara Medical University Institutional Review Board (Approval No.533). Data were collected during the period between January 2006 and December 2011. Eligible patients were those with ASA physical status more than III who underwent minor surgery under general anesthesia for relative indications and nonfatal reasons. Therefore, patients who underwent cardiovascular surgery, neurosurgery, oncological surgery, trauma surgery, debridement, drainage or amputation, and any emergency surgery were excluded.

Preoperative clinical information was collected from the patient’s clinical charts. Comorbidity was quantified using the Charlson Comorbidity Index. Additional data including type of surgery, anesthesia and operation time, intraoperative fluid balance were also collected. All the patients were evaluated for in-hospital mortality and were followed-up for mortality at one-year using the clinical charts, telephone interviews, or postal questionnaires. If the patient had died in the follow-up period, the date of death was recorded.

The Charlson comorbidity index originally can predict one-year mortality for a patient who may have a range of comorbid conditions. Each condition is assigned a score of 1, 2, 3, or 6, proportional to the relative risk of death (at one-year) associated with that disease (Table 1). The sum of the integers makes up the Charlson score, and the Charlson score was prospectively consolidated into four previously defined groups known as the Charlson Index: 0 points (none), 1–2 points (low), 3–4 points (moderate), and 5–6 points (high) as originally described. It has been reported that the Charlson index at the hospital admission due to a specific medical condition has a good correlation with 1-year mortality rates. In addition, illness severity, which was rated as “not to mildly ill”, “moderately ill”, or “severely ill” as previously described, within the same Charlson index category also has a good correlation with 1-year mortality rates. We assumed that the “not to mildly ill” conditions were similar to the situations that patients with ASA physical status more than III undergo minor surgery for relative indications and nonfatal reasons. It is reasonable to suppose that specific illness conditions providing minor surgery for relative indications and nonfatal reasons are not so severe. The original mortality rates from the work of Charlson and colleagues are presented in the Table 2.

<table>
<thead>
<tr>
<th>Charlson comorbid conditions</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Dementia</td>
<td>1</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>1</td>
</tr>
<tr>
<td>Ulcer disease</td>
<td>1</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>2</td>
</tr>
<tr>
<td>Renal disease</td>
<td>2</td>
</tr>
<tr>
<td>Any tumor</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes with end-organ damage</td>
<td>2</td>
</tr>
<tr>
<td>Leukemia</td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
</tr>
<tr>
<td>Moderate/severe liver disease</td>
<td>3</td>
</tr>
<tr>
<td>Metastatic solid tumor</td>
<td>6</td>
</tr>
<tr>
<td>AIDS</td>
<td>6</td>
</tr>
</tbody>
</table>
Table 2
One-year mortality rates from the work of Charlson and colleagues

<table>
<thead>
<tr>
<th>Charlson comorbidity index category</th>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness Severity</td>
<td>0</td>
<td>1-2</td>
<td>3-4</td>
<td>&gt;5</td>
</tr>
<tr>
<td>Not to mildly ill</td>
<td>7%</td>
<td>16%</td>
<td>41%</td>
<td>64%</td>
</tr>
<tr>
<td>Moderately ill</td>
<td>6%</td>
<td>17%</td>
<td>39%</td>
<td>76%</td>
</tr>
<tr>
<td>Severely ill</td>
<td>12%</td>
<td>30%</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>7%</td>
<td>21%</td>
<td>43%</td>
<td>78%</td>
</tr>
</tbody>
</table>

The gray zone shows the one-year mortality rates of the “not to mildly ill” conditions in patients with each Charlson comorbidity index category. We referred these values as predicted mortality in our patients.

Descriptive statistics were used to summarize the demographics and intraoperative data. Categorical variables were reported as percentages. The continuous variables were described using the mean and standard deviation. One-year mortality rates with 95% confidence intervals were calculated for each Charlson Index category. If necessary, to determine correlation of the Charlson Index category with one-year mortality, the Spearman’s rank correlation coefficient was calculated. In addition, the Kaplan–Meier estimation method was used to obtain the survival distribution estimates for each Charlson Index category. The statistical difference of survival distributions among the categories was examined using the log-rank test. Statistical significance was defined as \( P<0.05 \).

Results

During the study period, 14,979 patients underwent general anesthesia. Of those, 36 patients with ASA physical status more than III underwent minor surgery under general anesthesia for relative indications and nonfatal reasons (Table 3). Of the eligible 36 patients, no patients died during their hospital stay; however, 4 patients were lost to follow up after discharge.

Patients characteristics are presented in the Table 3. The majority of the performed operations was

Table 3
Descriptive statistics of patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>65.1±14</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>19(52.8%)</td>
</tr>
<tr>
<td>female</td>
<td>17(47.2%)</td>
</tr>
<tr>
<td>In hospital mortality (%)</td>
<td>0%</td>
</tr>
<tr>
<td>Charlson index category</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>21</td>
</tr>
<tr>
<td>3-4</td>
<td>9</td>
</tr>
<tr>
<td>≥5</td>
<td>6</td>
</tr>
<tr>
<td>Performed Operation</td>
<td></td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>6</td>
</tr>
<tr>
<td>Gynecology</td>
<td>4</td>
</tr>
<tr>
<td>Urology</td>
<td>4</td>
</tr>
<tr>
<td>Orthopedics</td>
<td>22</td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>175.3±96.8</td>
</tr>
<tr>
<td>Anaesthesia time (min)</td>
<td>220.5±118.7</td>
</tr>
<tr>
<td>Intraoperative fluid balance (mL)</td>
<td>1382.7±233.7</td>
</tr>
</tbody>
</table>

Table 4
Charlson comorbid conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>8 (22%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1 (2.7%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>7 (19.4%)</td>
</tr>
<tr>
<td>Dementia</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>6 (16.6%)</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>0</td>
</tr>
<tr>
<td>Ulcer disease</td>
<td>0</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>1 (2.7%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6 (16.6%)</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>8 (22.2%)</td>
</tr>
<tr>
<td>Any tumor</td>
<td>2 (5.5%)</td>
</tr>
<tr>
<td>Diabetes with end-organ damage</td>
<td>15 (41.6%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>0</td>
</tr>
<tr>
<td>Moderate/severe liver disease</td>
<td>0</td>
</tr>
<tr>
<td>Metastatic solid tumor</td>
<td>0</td>
</tr>
<tr>
<td>AIDS</td>
<td>0</td>
</tr>
</tbody>
</table>
orthopedics. There was no patient with Charlson Index of 0. There were 6 patients with Carlson Index point =5, who were categorized in Carlson index category ≥5; however, there was no patient with Carlson index point ≥6. Carlson comorbid conditions are presented in the Table 4. All 32 patients survived one-year postoperatively. The one-year mortality rates with 95% confidence intervals for each Carlson Index category were 0% (95% confidence interval = 0% to 0%). Because all patients in any Carlson Index categories survived one-year, correlation of the Carlson Index category with one-year mortality and the survival distribution could not be determined from our data. In this regard, looking at the one-year mortality rates of illness severity at “not to mildly ill” conditions from the original work of Carlson’s4, which we referred, the one-year mortality rate increased as Carlson Index severity increased (See the gray zone in Table 2).

Discussion

Our results revealed that the postoperative one-year mortality in patients with ASA physical status more than III undergoing minor surgery under general anesthesia for relative indications and nonfatal reasons was expected to be considerably small regardless of the Carlson Index category. As mentioned before, we assumed that the situations that patients with ASA physical status more than III undergo minor surgery for relative indications and nonfatal reasons resemble the situations that we provide only anesthesia without surgery for critical patients with comorbid conditions. Therefore, it might be postulated that the effects of provision of anesthesia on mortality in critical patients with comorbid conditions are not significant. However, a prerequisite may be necessary that the comorbid condition should be stable because the scheduled surgery should be canceled if the comorbid condition itself is life-threatening.

There is a lack of definition of “comorbidity”, but it seems that the following concept is widely accepted; a medical condition existing simultaneously but independently with another condition in a patient. In addition, a newer concept has been also proposed that a medical condition in a patient that causes, is caused by, or is otherwise related to another condition in the same patient8. According to these concepts of “comorbidity”, development of another medical condition is required whenever the term “comorbidity” is intended to use. Otherwise, the term “comorbidity” could not be used if development of another medical condition were not observed in patients with specific medical conditions. Nevertheless, another medical condition indicates significant events including acute injuries and illness. It has been recognized that the Carlson Index is strongly associated with mortality rates in emergency patients as well as in medical inpatients4-7,9,10. We could not simply apply the absolute mortality rates observed in the specific medical conditions to the others even with the identical Carlson index; however, it is safe to say that the patients with higher Carlson Index category will have higher mortality rates after sustaining any significant events including acute injuries and illness. On the contrary, the Carlson index in our patients who underwent minor surgery under general anesthesia showed no association with one-year mortality. As mentioned before, we need to consider comorbid medical conditions when significant medical events occur. Therefore, it may be concluded that no significant medical events consequently occurred in our patients. In other words, it can be said that minor surgery under general anesthesia is not a condition that can deteriorate comorbid diseases. The effects of provision of anesthesia itself on comorbid conditions should be less significant than the combined effects of anesthetic and minor surgical procedures. Thus, it is reasonable to suppose that provision of anesthesia itself does not fulfill the medical events that can threaten comorbid conditions.

In clinical settings, there seems to be no objection that the effects of surgical reason with absolute indication or major surgical procedures on mortality exceeds provision of anesthesia in most cases. Therefore, the effects of provision of anesthesia itself on comorbid conditions can be negligible in such cases. However, anesthesiologists frequently encounter situations where they need to consider the effects of provision of anesthesia on mortality in critical patients with comorbid conditions. As mentioned above, it is when critical patients with comorbid conditions undergo a minor surgery for relative indication and nonfatal reasons. With our results, we could come to the postulation that there is no need to refuse to
provide anesthesia management, for the concern about significant effects of anesthesia on patient’s outcome. However, as mentioned before, this proposal may be rejected when the comorbid condition is unstable and life-threatening in itself.

There are several limitations in this study. First, we did not see the effects of provision of anesthesia itself on mortality in critical patients with comorbid conditions in the true meaning. It is difficult to make a real answer; however, there is a laboratory report giving a clue to this question. Culley and colleagues investigated whether general anesthesia with isoflurane-nitrous oxide shortens life expectancy in aged rats. They reported that general anesthesia does not reduce life expectancy in aged rats. We need to consider a discrepancy of human and animal studies and the hypothesis regarding old age as a comorbid condition; however, it is not unreasonable to think that this study supports our opinion. Second, we recruited for our study surgical patients who had actually undergone scheduled operations. However, critical patients with comorbid conditions, should have existed, would most likely have their scheduled surgeries canceled after considering their comorbid conditions, relative indications, and nonfatal reasons. The mortality rates might have been affected if these patients had undergone scheduled operations. One of the reasons for this concern might be on account of the retrospective nature of this study design. However, such a selection bias is thought to be difficult to avoid in clinical settings even in a prospective study because there must be cases where patient selection is completed before anesthesia consultation. Therefore, a necessary prerequisite might be that the comorbid condition should be stable when deriving any conclusion based on the obtained results in this study. Third, 4 patients were lost to follow up (10%). It has been suggested that plausible assumptions regarding outcomes of patients lost to follow-up could change the interpretation of results even with the median percentage of participants lost to follow-up is 6%. Therefore, we might need to be careful to interpret our study results while taking it into consideration that 10% patients were lost to follow up. Lastly, we extracted only 36 eligible patients from our study population. In addition, no patient died within one year after anesthesia possibly due to the small population. The conclusion drawn from this study might exceed the capability of the present data. Accordingly, much larger data base would be required to confirm our results.

In conclusion, the postoperative one-year mortality in patients with ASA physical status more than III undergoing minor surgery under general anesthesia for relative indications and nonfatal reasons is considerably small regardless of the Charlson Index category. With this finding, we might postulate that the effects of provision of anesthesia on mortality in critical patients with comorbid conditions are not significant. However, to derive this conclusion, we need at least a prerequisite that the comorbid condition should be stable.

Study funding
Departmental financial source only supported this study.

Conflicts of Interest
None.

Acknowledgement
None.
References


TEACHING ULTRASOUND PROCEDURAL SKILLS-LOW COST PHANTOMS AND ANIMAL MODELS

JACEK A. WOJTCZAK* AND SONIA PYNE**

Abstract

Acquiring the necessary cognitive and psychomotor skills to perform ultrasound guided procedures may require initial training. Growing evidence shows that simulation can help in the acquisition of procedural skills. Commercially available phantoms are expensive, have non-tissue like haptics, are preformed with fixed targets and do not allow for additional targets to be imbedded.

In this study we have described several new phantoms and animal models that are inexpensive, easy to assemble and allow a rapid change of targets. Such phantoms can provide an ideal initial learning opportunity in a zero-risk environment.

Key words: ultrasound phantoms, ultrasound-guided procedural skills.

Introduction

Ultrasound (US) guided nerve blocks, cricothyroid punctures and vascular cannulations require, for safety reasons, initial training in animal models or phantoms. In-vitro models can facilitate learning of scanning techniques and hand-eye coordination skills. The elastomeric phantoms that are usually used for training lack tissue feedback, are expensive, rapidly deteriorate and become unusable due to needle tracks. In this study we describe new, improved animal models and phantoms that can be used in teaching ultrasound guided procedural skills.

Methods

We have prepared and evaluated low-cost phantoms (gelatin/agar or tofu bars with immersed tubular structures or plastic spine models), animal models (intact porcine heads, infrahyoid airway) and hybrid models (animal tissues immersed in gelatin or tofu, human hand placed on the foam to model lung with rib cage).

US scanning was performed using BK Medical Flex Focus 400 and Sonosite S-Series systems.

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Results

Retrobulbar blocks are usually placed blindly in awake patients without US guidance. Severe complications of this blind technique have been reported. Real-time US guidance provides visualization of the eye and the optic nerve before and during insertion of the needle which can improve the quality and safety of the block. Intact porcine head models (Fig. 1) obtained in the slaughterhouse allow for supervised training to avoid ocular perforation and injection of local anesthetic into the optic nerve or sheath.

Cricothyroid membrane punctures were performed in the porcine infrathyroid airway embedded in gelatin (Fig. 2 and 3) which allowed visualization of the posterior wall of the airway.

Vascular cannulations were performed in tofu models. Thin polyethylene tubings filled with saline were inserted into tofu bars (Fig. 4). Thin walls allowed easy penetration of the needle and confirmation of the successful cannulation.

Ultrasound-guided placement of the spinal needle was performed in plastic lumbar and sacral spine models immersed in gelatin or water bath (Fig. 5).
Fig. 3

Upper panels - transverse ultrasound scans of the porcine thyroid cartilage immersed in gelatin (left); porcine cricothyroid membrane puncture (right) with needle reverberation artifact. Lower panels – transverse (left) and longitudinal (right) scans of the trachea immersed in gelatin. Needle visible in the trachea.

Fig. 4

Vascular puncture performed in tofu models. Polyethylene tubings filled with saline were inserted into tofu bars to mimic blood vessels.
Ultrasound-guided thoracentesis was performed in the model consisting of the experimenter’s hand placed on top of the water-filled container with a wet foam. Metacarpal bones of the human hand simulated a rib cage and a wet foam simulated a diseased lung immersed in the pleural fluid (Fig. 6).

**Discussion**

Ultrasound guidance improves safety, success rate and efficacy of various procedures provided that the tip of the needle is visualized at all times. This skill can be taught in animal models and phantoms. Optimizing the image of the needle with ultrasound beam alignment and reaching a target inside the phantom or the animal model may require a considerable number of attempts. The cumulative sum (cusum) charts revealed that novice operators acquire such abilities at variable rate. Appropriately designed models may allow for controlled, supervised learning, including a formative feedback between trials and construction of individual learning curves. An important benefit of using animal models is that it also allows teaching of the ultrasound anatomy. Imbedding the animal tissue in gelatin or gelatin/agar mixture for improved durability of the phantom enhances the quality of the ultrasound image while preserving tissue feedback.
The role of ultrasound in central neuraxial blockade has been underappreciated due to the perceived difficulty in imaging through the narrow acoustic window produced by the vertebra. However, the interlaminar window permits passage of sound waves. The intervertebral level can be identified and the depth to the epidural and intrathecal spaces can be estimated.

Practicing on cadavers allows participants to study the sonographic anatomy and practice sonographically guided blocks with realistic tactile feedback, but they are often limited by the quality of sonograms and have to be conducted in credentialed facilities.

In-vitro models as described in this study allow visualization of the osseous and soft tissue anatomy and can facilitate the teaching of scanning techniques and hand-eye coordination skills that are required for real-time sonographically guided blocks.

Procedural skills in the field of anesthesiology are assessed poorly compared with other domains of learning as they are often given less importance than the assessment of knowledge and judgement-based skills. This is partly because there has been no universally accepted and comprehensive way to assess procedural skills. It is our goal to further develop and optimize our in-vitro models to enable an objective assessment of procedural skills by our anesthesia trainees.

**Conflict Of Interest**

None.
References


CASE REPORTS

AWAKE TRACHEAL INTUBATION WITH COMBINED USE OF KING VISION™ VIDEOLARYNGOSCOPE AND A FIBEROPTIC BRONCHOSCOPE IN A PATIENT WITH GIANT LYMPHOCELE

MOHAMED R. EL-TAHAN*, D. JOHN DOYLE**, ALAA M. KHIDR*, MOHAMED A. REGAL***, AYMAN B. EL MORSY*** AND MOHAMED EL MAHDY*

Introduction

Airway devices such as the GlideScope® videolaryngoscope or the Airtraq® optical laryngoscope can facilitate fibreoptic-guided intubation1-4. In this report we show how a fiberoptic bronchoscope (FOB) guided through a channeled King Vision™ videolaryngoscope can aid awake tracheal intubation, as we illustrate in a patient with a giant lymphocele complicated by airway edema.

Case Presentation

A 33 year-old, 160 cm, 106 kg gentleman with 7 years of progressively enlarged chest and neck swelling presented with orthopnea and dyspnea and was scheduled for lymphocele excision. The patient’s hemogram, electrolytes, creatinine, and liver tests were normal. Pulmonary function tests showed a mild restrictive pattern (FEV₁ 68%, FVC 78%, and FEV₁/FVC 87% of predicted). A left anterior multi-cystic, non-tender chest wall swelling measuring 50 × 35 cm with dilated superficial veins was noted. This extended to surround the anterior neck as a collar and extended beyond the thyroid cartilage (Figures 1a and b). Neck movements were impossible, mouth opening was 3.5 cm, and the Mallampati score was II. Chest radiography showed a huge pedunculated left-sided chest wall mass extending to the neck, and compression of the middle third of the trachea. The trachea was deviated to the right (Figure 2). The lymphocele extended beyond the thyroid cartilage, precluding tracheostomy or suprasternal needle tracheotomy. CT demonstrated a large multiple loculated cystic mass arising from the chest wall superficial to the pectoralis muscles compressing the middle third of the trachea, obstructing approximately 40% of the tracheal lumen and extending beyond the thyroid cartilage. The major neck vessels and superior vena cava were patent (Figures 3a and 3b).

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Fig. 1
Photographs showing the extension of the huge left anterior chest wall and neck lymphocele.
(a) Anterior view (b) Right lateral view.

Fig. 2
Postero-anterior views of the chest x-ray showing a huge left anterior chest wall and neck lymphocele with no intra-thoracic extension.

Fig. 3
CT scan showing extension of the multi-cystic septated anterior neck and chest swelling.
(a) Coronal view (b) Sagittal view.
A plan for intubation was adopted, with the primary plan constituting of awake intubation using a FOB in conjunction with a King Vision™ videolaryngoscope, and with a back-up plan involving the use of an airway introducer, a tube exchanger and an intubating laryngeal mask airway, depending on the difficulties encountered.

A cardiothoracic surgeon was on standby to aspirate the neck cysts, or to initiate rigid bronchoscopy and jet ventilation. Cardiopulmonary bypass was available in the event of a failed airway or cardiovascular collapse. The upper airway was anesthetized with 2 mL of 10% lidocaine delivered by nebulization. The patient then gargled 1.5 mL of 10% lidocaine, followed by 2% lidocaine gel applied to the back of the tongue. Oxygen was delivered via nasal cannula, with sedation provided with an infusion in conjunction with 1 mg of midazolam.

Laryngoscopy was performed in a semi-sitting position using a King Vision™ video laryngoscope, where moderate hypopharyngeal edema and a grade III view of the glottis were observed. A 5.2-mm FOB loaded with a 7.5-mm endotracheal tube (ETT) was advanced via the King Vision™ video laryngoscope channeled blade. The ETT was then advanced into the trachea, while the glottis was visualized via the King Vision™ video laryngoscope.

After intubation, anesthesia was induced using propofol and remifentanil and maintained with desflurane and remifentanil, with no muscle relaxant administered.

The surgeon excised the cysts through neck collar and left sub-mammary incisions. Intraoperative vital signs remained stable throughout the 4 hour surgery. After the surgery, the patient was extubated, and was observed in the surgical intensive care unit for 24 hours.

Discussion

Experience indicates that awake fiberoptic intubation is successful in 88–100% of difficult airway patients. The flexible FOB is the preferred instrument in such patients, but the presence of restricted neck movement, pharyngeal edema or bleeding can preclude its use.

The use of video laryngoscopes as a FOB conduit can be helpful where the use of FOB alone is unsuitable. A channeled laryngoscope like as the Airtraq® optical laryngoscope facilitates fibroptic-guided intubation using either a small FOB inserted through the ETT mounted in the guiding channel and then directed into the glottis or by using a large FOB inserted through the guiding channel and directed into the glottis, followed with railroading the ETT over its shaft. Additionally, video laryngoscope-assisted awake fiberoptic intubation has been shown to be a potentially useful technique in difficult airway management.

An expected problem in patients with a huge cervical partially-obstructing mass is hypopharyngeal edema. Awake tracheostomy was precluded in this case with the extension of the lymphocele beyond the thyroid cartilage.

In contrast to the fibreoptic bronchoscope, the King Vision™ video laryngoscope has many advantages: it is relatively inexpensive and easy to handle. It offers a 160 degree field of view, potentially eliminating the need for extensive manipulation of the bronchoscope, and is better suited for the tracheal intubation of patients with pharyngeal swelling as it displaces the pharyngeal tissue and may provide conduit for the FOB.

In conclusion, the combined use of King Vision™ video laryngoscope and a fiberoptic bronchoscope can be an effective method of awake tracheal intubation, as demonstrated in our patient with giant lymphocele.

Consent Statement

The patient’s written consent for publication of this report was obtained.

Conflict of Interest

All authors declare that they receive no support from any commercial organization or company, and have no conflicts of interest.

Financial support and sponsorship

None.
References


ANESTHESIA FOR ARTHROSCOPIC SHOULDER SURGERY
IN THE BEACH CHAIR POSITION: MONITORING OF CEREBRAL
OXYGENATION USING COMBINED BISPECTRAL INDEX
AND NEAR-INFRARED SPECTROSCOPY

HIROAKI KAWANO* AND TOMOMI MATSUMOTO**

Abstract

Recent research has shown that cerebrovascular complications following shoulder surgery performed in the beach chair position under general anesthesia arise secondary to cerebral ischemia. Appropriate management of cerebral oxygenation is thus one of the primary goals of anesthetic management during such procedures. The present report describes the case of a 65-year-old male patient, in which both bispectral index (BIS) and near-infrared spectroscopy (NIRS) were used to monitor cerebral oxygenation. During the positioning, we observed an increased suppression ratio (SR) while BIS and regional cerebral oxygen saturation (rSO₂) were at adequate level. In view of the difference in blood pressure between the heart and the base of the brain, blood pressure was maintained to ensure adequate cerebral perfusion. Although intraoperative rSO₂ was at or around the cut-off point (a 12% relative decrease from baseline), no marked decrease in BIS or further increase in the SR was observed. Monitoring of cerebral perfusion using combined BIS and NIRS optimized anesthetic management during the performance of arthroscopic shoulder surgery in the beach chair position.

Key words: General anesthesia, Beach chair position, Cerebral oxygenation, Bispectral index, Near-infrared spectroscopy.

Introduction

Several reports have described serious complications secondary to general anesthesia for shoulder surgery performed in the beach chair position1,2. Recent research has identified a causal relationship between the beach chair position and cerebral hypoperfusion3,4, and it is widely accepted that the beach chair position may be associated with a decrease in cerebral perfusion5,6.

The present report describes optimal management of cerebral oxygenation during arthroscopic shoulder surgery performed in the beach chair position. This involved the monitoring of cerebral oxygenation using a combination of bispectral index (BIS) and near-infrared spectroscopy (NIRS).

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Case report

The 65-year-old male patient (166 cm, 67 kg) was admitted to our hospital for arthroscopic shoulder surgery. He had undergone arthroscopic rotator cuff repair in the lateral decubitus position 7 months before, but his symptoms had not improved. During the initial procedure, intraoperative monitoring included electrocardiography, noninvasive blood pressure monitoring, capnography and pulse oximetry, and the anesthetic management was successful with no complications. His medical history included insulin-dependent diabetes mellitus, hypertension and congestive heart failure.

No preanesthetic medication was administered prior to the arthroscopic procedure. On arrival in the operating room, his blood pressure was 161/72 mmHg, his heart rate was 68 beats/min, and his arterial oxygen saturation was 98% on room air. The patient was monitored with electrocardiography, capnography, and pulse oximetry. In addition to these routine monitoring procedures, an arterial catheter was inserted into the left radial artery to allow invasive blood pressure monitoring, and BIS monitoring was applied. At the same time, regional cerebral oxygen saturation (rSO₂) was measured using NIRS (INVOS 5100C; Covidien, Boulder, CO, USA). Throughout the procedure, the rSO₂ was recorded from the left (LrSO₂) and the right (RrSO₂) hemispheres using two probes, which were positioned on the left and right sides of the forehead respectively. Prior to induction, the LrSO₂ and RrSO₂ were 59% and 51%, respectively (baseline values). General anesthesia was induced with intravenous remifentanil (0.5 µg/kg/min), propofol (70 mg), and rocuronium (40 mg), and endotracheal intubation was performed. The patient was then placed in the beach chair position. The external auditory meatus, which represents the base of the brain, was positioned 40 cm above the atrial level. Thus, it was calculated that the blood pressure at the base of the brain would be approximately 30 mmHg lower than at the arm. To maintain the mean arterial pressure (MAP) above 80 mmHg, a continuous infusion of intravenous dopamine (2-5 µg/kg/min) was administered. In addition, all episodes of hypotension (defined as MAP < 80 mmHg) were treated with intravenous ephedrine (4 mg) or phenylephrine (0.1 mg). Anesthesia was maintained with oxygen (2 l/min), air (2 l/min), sevoflurane (1.0%), and remifentanil (0.2-0.3 µg/kg/min). Neuromuscular blockade was maintained with intermittent rocuronium. As postoperative analgesia, approximately 60 min before the end of the procedure, intravenous fentanyl (200 µg) was administered, and intravenous patient-controlled analgesia infusion (fentanyl 20 µg/ml; basal infusion 1 ml/h, bolus 1 ml, lockout time 10 min) was started.

In response to anesthetic induction, MAP decreased from 108 to 59 mmHg, which resulted in an increase of the suppression ratio (SR) to 19. At this point, the BIS and rSO₂ were stable. With intravenous administration of ephedrine (4mg), the MAP increased and the SR returned to 8. After the patient was placed in the beach chair position, the SR rapidly increased to 21. BIS and rSO₂ were in the 40-50 and 45-50 ranges, respectively, and signal quality index was more than 75%. The patient’s MAP was 70 mmHg. This was treated with intravenous administration of ephedrine (8 mg), and the SR improved (Fig. 1). Thereafter, there was no further increase in the SR. The intraoperative systolic blood pressure was 90-160 mmHg, the MAP was 70-110 mmHg, the heart rate was 50-70 beats/min, and the end-tidal CO₂ was 35-40 mmHg. The total dose of ephedrine was 40 mg and that of phenylephrine was 0.5 mg. The BIS was stable at between 40 and 60, and there were no episodes of any marked decrease in BIS. The LrSO₂ was stable at around 52% (range 50-54%), and the RrSO₂ was also stable at around 52% (range 50-53%). Surgery was completed without complications, and the patient emerged from anesthesia uneventfully. Once the patient had regained consciousness and was able to follow simple commands, the neuromuscular blockade was reversed and his trachea was extubated. The duration of the surgical procedure and anesthesia were 8 h:11 min and 9 h:40 min, respectively. Intraoperative total blood loss was 250 ml, urine output was 1450 ml and total infusion volume was 1750 ml. The patient remained stable during the 1-month inpatient postoperative period, and no postoperative complications were evident.
Discussion

The beach chair position (30-90° above the horizontal plane) is widely used for orthopedic shoulder arthroscopy procedures as it offers advantages such as excellent intraarticular visualization and reduced brachial plexus strain. Although Tange et al.7 reported that the use of the beach chair position under general anesthesia did not alter cerebral oxygenation, several studies have reported a causal relationship between the beach chair position and cerebral hypoperfusion3,4. According to a report by Murphy et al.3, shoulder surgery in the beach chair position was associated with a significant reduction in cerebral oxygenation compared with the use of the lateral decubitus position. Therefore, maintenance of adequate cerebral perfusion should be ensured during shoulder surgery performed in the beach chair position, even in healthy patients who are not at increased risk of ischemic stroke. Strict cerebral oximetry monitoring was necessary in the present case, as the patient was at high risk of cerebrovascular events.

The BIS is widely used as an indicator of the level of consciousness during general anesthesia. In addition, several reports have suggested that the BIS allows detection of cerebral ischemia8,9, since cerebral hypoperfusion decreases the BIS. Hayashida et al.9 described five children in whom 14 episodes of a simultaneous decreases in rSO2 and BIS occurred during episodes of acute hypotension within the course of cardiac surgery. In these patients, abrupt decreases in BIS in their patients associated with an acute slowing of the electroencephalogram (EEG), which is an early indication of cerebral hypoperfusion. In the present case, no marked reduction in BIS, a sign which may suggest cerebral hypoperfusion, was observed during the procedure.

In the present case, the SR increased to 21 following change of position from supine to beach chair position, while BIS and rSO2 were in a normal range. This is similar to previously reported cases where an increased SR was observed despite BIS values at an adequate anesthetic level and the possible role of hypoxemia was suggested10,11. SR derived from BIS monitoring estimates the percentage of burst suppression EEG pattern or isoelectric activity. It occurs during deep anesthesia, but several reports suggest that SR could be related to hemodynamics12 or metabolism such as hypothermia13 or hypoxia10. A causal relationship between SR and cerebral hypoxemia has been suggested in animal studies14. Furthermore, it has been shown that the presence of SR in critically ill patients was associated with increased mortality15. Therefore, although it is obvious that BIS monitor is not designed to detect cerebral ischemia, it might be useful for detecting cerebral hypoperfusion. Because MAP decreased from 108 to 59 mmHg in response to anesthetic induction,
and because hypoxia, hypocapnia, and anemia, all of which might cause cerebral hypoperfusion, were not present, the first episode of SR increase was thought to be due to hypotension. However, the second episode of SR increase in the present case may have been related to cerebral hypoperfusion associated with the beach chair position. It is well recognized that the beach chair position may be associated with a decrease in cerebral perfusion as mentioned above. In our patient, an elevation of the SR was a useful sign for the detection of the beach chair position-related cerebral hypoperfusion.

NIRS is a noninvasive technique for the continuous monitoring of rSO$_2$ and it has been used to detect cerebral ischemia and hypoxia in patients undergoing procedures such as cardiovascular surgery and carotid endarterectomy (CEA). Although various studies have investigated the optimal cut-off point for a decrease in rSO$_2$ in order to identify the occurrence of neurological complications in patients undergoing CEA$^{16,17}$, the rSO$_2$ threshold indicating cerebral ischemia ranges from a 12-20% relative decrease. It may therefore be difficult to judge whether pharmacological or physiological intervention is required when the rSO$_2$ is at or around the cut-off point like the present case. Furthermore, it has been shown that EEG and somatosensory evoked potentials (SEP) correlate directly with changes in cerebral blood flow, whereas no such data related to rSO$_2$ are currently available. Therefore relying on rSO$_2$ alone to monitor the adequacy of cerebral perfusion might be dangerous and inadequate in terms of avoiding neurological complications. Consequently, both BIS and rSO$_2$ were measured with NIRS. Hayashida et al.$^{18}$ reported that the combination of BIS and NIRS can be a convenient method of ischemic/anesthetic monitoring, i.e., that by monitoring both BIS and NIRS, it is possible to judge whether cerebral hypoperfusion, as indicated by a decrease in rSO$_2$, is at the saturation level at which cerebral dysfunction will occur.

In conclusion, appropriate management of cerebral oxygenation is essential during any surgical procedure performed in the beach chair position. We recommend the use of cerebral oximetry monitoring devices. In the present case, monitoring of cerebral oxygenation using a combination of BIS and NIRS optimized anesthetic management during the performance of shoulder surgery in the beach chair position.

**Conflict of interest**

None.

**Funding**

None.

**Acknowledgments**

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References

IMPOSSIBLE MASK VENTILATION AFTER AN UNUSUALLY LOW DOSE FENTANYL-INDUCED MUSCLE RIGIDITY IN A PATIENT WITH ESSENTIAL TREMOR: A CASE REPORT AND REVIEW OF THE LITERATURE

Vassilios Dimitriou*, Ioannis Zogogiannis**, Despoina Liotiri***, Freddie Wambi****, Nasser Tawfeeq****, Adnan Koumi**** and Georges Geldhof*****

Abstract

Although opioid-induced muscle rigidity occurs more commonly with large doses and rapid administration of the drugs, there is a number of cases reported, where muscle rigidity was experienced with lower doses of opioids. We present and discuss a case of muscle rigidity induced by an unusually low dose of fentanyl as primary agent during induction of anesthesia. A 79 year old male patient, scheduled for hernia repair, and with a preoperative physical examination of slight hand tremor, received a bolus of 100mcg (1.2mcg/kg) fentanyl as primary agent for induction. About 40sec later he stopped responding, lost consciousness and developed neck and masseter muscle spasm with jaw closure and thoracoabdominal rigidity. Blood pressure was increased significantly. Ventilation was impossible. Rapid oxygen desaturation led us to proceed with IV propofol 150mg and suxamethonium 100mg. Opioid-induced muscle rigidity may cause life-threatening respiratory compromise and should be readily recognized and treated by anesthesiologists.

Key words: Anesthesia, opioids, muscle rigidity, essential tremor.

Introduction

Opioid administration produces intense analgesia and decreased sympathetic response to attenuate stress response to painful surgical stimulation. Because of these advantageous clinical properties, opioids have increasingly seen wide-spread use in anesthesia. Unfortunately, the profound analgesia of high-dose opioid administration may be accompanied by prolonged respiratory depression and intense muscle rigidity. Opioid-induced muscle rigidity was first described by Hamilton and Cullen in 19531. At the same time with the introduction of fentanyl in anesthetic practice (1981), fentanyl-induced muscle rigidity started to be reported both in adults and children2,3,4. Thereafter, muscle rigidity after opioid administration became a well documented effect, most commonly with lipophilic synthetic opioids such as fentanyl, alfentanil, remifentanil and sufentanil, although its pathophysiology is not as well clarified5-7. It is not a common adverse effect and its true incidence is unknown.

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The development of muscle rigidity accompanies induction of anesthesia with opioids and in most cases has been reported in preterm and term infants or after administration of high doses of opioids. However, a recent case report concerning fentanyl-induced muscle rigidity during sedation for bronchoscopy, increased the concern about the safety of opioid administration in minor interventions requiring sedation that is very common in the everyday anesthetic practice. There are other cases where muscle rigidity has been induced after low doses of opioids but in accordance with other factors. The usual clinical presentation varies from mild symptoms of muscle spasm, up to severe and potentially life-threatening symptoms like inability of ventilation and clonus. We report a case of muscle rigidity induced by an unusually low dose of fentanyl as primary agent during induction of anesthesia.

**Case History**

A 79 year old male patient (height 177cm, weight 82kg) with history of arterial hypertension and coronary artery disease under treatment, was scheduled for hernia repair. Preoperative physical examination performed revealed slight hand tremor and otherwise was normal. His laboratory results were normal. The patient did not receive premedication. In the operating room standard monitoring was applied and the patient was preoxygenated and received a bolus of 100μg fentanyl as primary agent for induction, in order to attenuate the response to laryngoscopy. About 40sec later he stopped responding, lost consciousness and developed neck and masseter muscle spasm with jaw closure, thoracoabdominal rigidity, upper limb flexion and lower limb extension without any sign of lateralization. Blood pressure increased significantly (from 125/80mmHg to 195/110mmHg). Ventilation was impossible even with four-handed bag-mask ventilation. The inability to open the mouth due to masseter muscle spasm made it impossible to insert an oropharyngeal or laryngeal mask airway. A nasopharyngeal airway was inserted and mask ventilation was initiated with no improvement. Rapid oxygen desaturation (SpO2 <85%) led us to proceed with IV propofol (150mg) and suxamethonium (100mg). Subsequently, the muscle spasm subsided and ventilation and oxygenation were resumed successfully with an increase of SpO2 to 100%. Laryngoscopy and tracheal intubation were successful. The operation was completed uneventfully and the patient awakened one hour later. When questioned postoperatively the patient had no recall of the event. After neurology consultation the patient was submitted to a CT and MRI scan which were normal. The postoperative complete neurology examination concluded that the patient suffered from essential tremor.

**Discussion**

We reported a case of an unusually low dose fentanyl-induced muscle rigidity. Since the patient did not receive any premedication and fentanyl was the sole agent during induction, there is no doubt for the cause of muscle rigidity. To our knowledge this is the first case of muscle rigidity with such a low dose of fentanyl (1.2mcg/kg) and so early (40sec) at induction. Low dose opioid-induced rigidity have been reported in preterm and term infants, or patients with risk factors like neurological diseases, metabolic disorders and medications modifying dopamine levels. Our patient was only receiving antihypertensive therapy including an ACE inhibitor and a beta adrenoreceptor antagonist. The essential tremor which was diagnosed postoperatively could have been a contributing role.

When used intraoperatively, the administration of a nondepolarizing neuromuscular blocking agent concurrently with fentanyl prevents rigidity. Although chest wall rigidity occurs more commonly with large doses and rapid administration, there is a number of cases reported, where muscle rigidity was experienced with lower doses of opioids. Additionally, this occurred in our case as well as in a patient undergoing bronchoscopy. Skeletal muscle rigidity has been recognized, most commonly with lipophilic synthetic opioids such as fentanyl, alfentanil, remifentanil, and sufentanil. This rigidity can primarily affect the chest and abdominal musculature, resulting in the “wooden chest syndrome.” Chest wall rigidity
UNUSUALLY LOW DOSE FENTANYL-INDUCED MUSCLE RIGIDITY

decreases chest wall compliance and may result in ineffective spontaneous ventilation and may also make assisted ventilation more difficult\textsuperscript{6,18}. 

The ventilatory difficulty may be contributed to vocal cords closure, to the jaw closure and the thoraco-abdominal rigidity\textsuperscript{20,21}. Although a nasopharyngeal airway can be inserted, airway obstruction caused primarily by glottis closure, may make it difficult to ventilate the patient manually. The incidence of glottis closure in patients with opioid induced muscle rigidity ranges from 50-100% depending on the opioid used, the dose and the rate at which it is administered\textsuperscript{21}. Although Muller and Vogt\textsuperscript{mann22} reported the adverse effects to be self-limited and brief, all other case reports required treatment with naloxone administration, neuromuscular blockade, and/or mechanical ventilation. Pretreatment with an alpha-2 adrenergic agonist (clonidine and dexmedetomidine) has been shown to decrease the incidence of opioid-induced rigidity, whereas serotonergic agents have been found effective in animal studies\textsuperscript{23,24}. 

In our case the patient lost consciousness simultaneously with opioid-induced rigidity. This is in accordance with Streisand et al\textsuperscript{25} in a study in human volunteers. They reported that all subjects lost consciousness simultaneously with opioid-induced rigidity. Fentanyl was administered at a rate of 150 mcg/min and rigidity occurred at a dose of 15 mcg/kg\textsuperscript{25}. The onset of rigidity and unconsciousness occurred an average of 3 min after peak fentanyl plasma concentrations and was associated with plasma fentanyl concentrations consistent with drug action\textsuperscript{25}. In contrast Grell et al\textsuperscript{26} reported that, 11 of 12 patients developed rigidity that neither produced unconsciousness nor impaired spontaneous ventilation. Waller et al\textsuperscript{27} reported that patients could open their eyes to command and initiate a breath, despite the presence of chest wall rigidity during induction in anesthesia with fentanyl. However, in the studies of both Grell et al and Waller et al, fentanyl was administered at slower rates (30 and 50 mcg/min respectively) and chest wall rigidity occurred at doses of 7.3 and 8 mcg/kg respectively. It appears that a mild form of rigidity, associated with decreased chest wall compliance, can be detected with maintenance of consciousness and spontaneous ventilation. In our case fentanyl 100 mcg was given on a bolus which is common practice during induction in anesthesia. Rigidity occurred very early after 40sec, and at an unusually low dose of 1.2mcg/kg. Additionally, our patient became hypertensive with muscle rigidity. This is in accordance with other studies, since muscle rigidity does not affect only the respiratory system, but additionally induces significant hemodynamic changes, accompanied by CO2 retention\textsuperscript{3,13}. 

The exact mechanism of increased muscle tone after the rapid infusion of an opioid is not known. Experimental animal study\textsuperscript{28} indicated that stimulation of central mu1 opioid receptors increases efferent motor traffic, resulting in muscle contraction and rigidity. Additional data\textsuperscript{29} demonstrate that whereas systemic opiate-induced muscle rigidity is primarily due to the activation of central mu receptors, supraspinal delta-1 and kappa-1 receptors may attenuate this effect. 

Experimental studies in rats\textsuperscript{28,30} based on combined physiologic, pharmacologic, histochemical, and immunocytochemical evaluations have demonstrated, that fentanyl may elicit muscular rigidity by activating spinal motoneurons by acting on the locus ceruleus in the pons. The locus ceruleus is the principal source of central nervous system norepinephrine. It appears that the participation of the cerulospinal noradrenergic pathway in fentanyl-induced muscular rigidity is critical\textsuperscript{28}. In addition to the cerulospinal noradrenergic mechanism, the cerulospinal glutamatergic pathway and both NMDA and non-NMDA receptors in the spinal cord may mediate fentanyl-induced muscular rigidity in the rat\textsuperscript{30}. Fentanyl-induced muscular rigidity may involve disinhibition of spinal motoneurons via an action of norepinephrine and glutamate on separate neuronal populations in the spinal cord\textsuperscript{30}. 

Our patient was diagnosed postoperatively with essential tremor which is one common neurological disease. From the pathophysiology of the disease there are altered concentrations of some biochemical markers in these patients\textsuperscript{31}. They have reduced cerebrospinal fluid concentrations of gama-aminobutyric acid (GABA), glycine, and serine, with a slight increase in glutamate. Also there are abnormalities on thalamic GABA\textsubscript{a} receptors. In specific regions increased concentrations of norepinephrine are also found in
patients with essential tremor: 5-folds in locus ceruleus and 2-folds in cerebellar cortex. So it is possible that these abnormalities made the patient more vulnerable to fentanyl-induced rigidity even with an unusually low dose of opioid.

In summary, we presented and discussed the successful management of a case of muscle rigidity induced by an unusually low dose of fentanyl as primary agent during induction of anesthesia. Opioid-induced muscle rigidity causing respiratory compromise should be readily recognized and treated by anesthesiologists.

Sources of financial support

None.

References

HYPOTENSION ON INDUCTION: ANAPHYLAXIS OR CARDIAC FAILURE?

HIMANI V. BHATT* AND ELIZABETH A. M. FROST**

Abstract

Identification of the cause of hypotension after induction of anesthesia is critical as treatment differs. We describe a case of anaphylaxis in a patient with severe cardiac disease, diagnosed by echocardiography and successfully treated with immediate cardiovascular resuscitation, epinephrine, vasopressors and antihistamines.

Keywords: Cardiogenic shock, anaphylaxis, echocardiography.

Introduction

Hypotension is not uncommon after induction of anesthesia. However, when hypotension is severe, especially in patients with co-morbidities such as coronary artery or valvular disease, identification of the cause may be difficult.

We describe a case of cardiovascular collapse after induction in a patient scheduled for triple valve replacement.

Case

A 69 year-old female with severe valvular disease was admitted for valve replacement. She had moderate right ventricular dysfunction, severe tricuspid regurgitation and marked pulmonary hypertension. An arterial cannula and right pulmonary artery catheter were placed. Anesthetic induction included 4mg midazolam, 250 mg fentanyl, 50mg rocuronium and antibiosis. Fifteen minutes post induction, blood pressure declined to 50-60/30-40. We presumed a diagnosis of pulmonary hypertension crisis with right ventricular failure secondary to underlying valvular pathology and right ventricular dysfunction. However, pulmonary artery pressures remained unchanged, central venous pressure dropped to 3 mmHg and peak airway pressures increased to 38-40mmHg. Transesophageal echocardiography revealed a hyperdynamic heart. Suspecting anaphylaxis, treatment was instituted with epinephrine, vasopressin, norepinephrine, H-1 and H-2 blockers and steroids. Hemodynamic stability was reestablished. Serum tryptase levels exceeded 400 ug/L. We concluded that cardiac collapse was secondary to anaphylactic shock, exacerbated by cardiac pathology.

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Discussion

Anaphylactic reactions are rare intraoperatively and even when treated appropriately have a mortality rate ranging from 3.5-4.7%. Anaphylaxis is an immediate hypersensitivity reaction mediated by the interaction of an antigen with IgE causing activation and degranulation of mast cells and basophils. Vasoactive mediators such as histamine, prostaglandins, kinins, leukotrienes and tryptase are released causing severe hypotension, bronchospasm, laryngeal edema, and cardiovascular collapse.

Many perioperative agents have been implicated. Sixty to 70% of reactions are secondary to neuromuscular blocking agents (NMDAs), commonly succinylcholine and rocuronium. Latex is also often implicated. Other incriminating agents include antibiotics, hypnotics (thiopental, propofol and midazolam), opioids, local anesthetics, iodinated contrast materials, non-steroidal ant-inflammatory drugs and colloids.

Tests to identify allergens include serum tryptase levels, plasma histamine, and specific IgE concentrations. Tryptase and histamine levels should be drawn within one hour of the reaction but can take up to a week for results. Tryptase levels > 25ug/L are strongly suspicious of an anaphylactic etiology and have a positive predictive value of over ninety percent. Radioallergosorbent tests (RASTs) detect IgE antibodies to specific anesthetic drugs such as muscle relaxants and intravenous anesthetic agents.

Cardiogenic shock occurs in up to 7% of patients with myocardial infarction. It accounts for over 40-60% of in-hospital mortality within the first 30 days. Cardiovascular collapse is due to loss of contractile myocardium causing left ventricular (LV) dysfunction, further aggravated by a systemic inflammatory response with refractory vasodilation and myocardial depression. ST segment elevation myocardial infarction (STEMI) accounts for most cardiogenic shock; other causes include acute mitral regurgitation, ventricular septal defect, cardiac rupture/tamponade, dysrhythmias, and type I aortic dissection.

Differentiation of hypotension secondary to anaphylactic versus cardiogenic shock can be difficult intraoperatively. Severe hypotension, increased airway pressures, pulmonary congestion and cardiovascular collapse are common to both. However, bronchoconstriction, facial edema, and cutaneous manifestations including generalized erythema, urticaria and angioedema are characteristic of anaphylaxis. Hemodynamic consequences and changes in LV loading conditions are secondary to loss of vasomotor tone as opposed to deterioration of myocardial function. Other differences in hemodynamic parameters are shown in Table 1.

<table>
<thead>
<tr>
<th>Features of anaphylactic vs. cardiogenic shock</th>
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<td><strong>ANAPHYLACTIC</strong></td>
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<td><strong>SIMILARITIES</strong></td>
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<tr>
<td>Tachycardia</td>
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<td>Airway pressures - ↑↑ (Anaphylactic&gt;cardiogenic)</td>
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<tr>
<td><strong>DIFFERENCES</strong></td>
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<td>Wheezing/bronchoconstriction</td>
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<td>Facial edema/angioedema</td>
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<td>Systemic vascular resistance - ↓↓</td>
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<td>Pulmonary vascular resistance - ↓↓</td>
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<tr>
<td>Pulmonary capillary wedge pressure - ↓</td>
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<tr>
<td>Left ventricular end-diastolic/end-systolic pressure/area - ↓</td>
</tr>
<tr>
<td>Cardiac output/Cardiac index - ↑</td>
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<td>Ejection fraction - ↑</td>
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</table>

Transesophageal echocardiography (TEE) distinguishes between anaphylaxis and cardiogenic shock. Intraoperative assessment of regional wall motion abnormalities and LV end-diastolic and end-systolic diameters (LVEDid and LVESid) can differentiate conditions of decreased LV preload and
afterload versus myocardial dysfunction. Also seen are decreased stroke volume (SV) and ejection fraction (EF), increased LV end-diastolic and end-systolic area (LVEDA and LVESA), increased pulmonary artery pressures, diastolic dysfunction and valvular abnormalities such as mitral regurgitation secondary to ischemia. TEE features of anaphylaxis are increased SV and EF secondary to hyperdynamic LV function.3,17-19

Both conditions require immediate cardiopulmonary resuscitation. Treatment of anaphylactic shock requires interruption of antigen contact by discontinuing causative agents and intravascular volume expansion. Epinephrine is the drug of choice. Inhaled β2 agonists reverse bronchoconstriction. H1- and H2- blockers and corticosteroids attenuate histamine-related adverse effects and prevent delayed anaphylactic symptoms.1,3,4,17,20

Cardiogenic shock requires improvement of LV function and circulatory support to maintain organ perfusion until coronary blood flow is reestablished via angioplasty, thrombolytic therapy or surgery. Inotropic drugs (epinephrine, dobutamine, dopamine and phosphodiesterase inhibitors) improve myocardial performance. Vasodilators (nitroglycerin and nitroprusside) alter loading conditions and enhance the effects of inotropes. Diuretics improve pulmonary edema and oxygenation/ventilation.11,13,15

Non-pharmacologic treatment options include intra-aortic balloon pump (IABP) and left ventricular assist device (LVAD) but require residual LV mass. Newer devices (i.e. Impella®) augment cardiac output, improve circulatory support and attenuate the systemic inflammatory response. Although these devices provide superior hemodynamic support, complications such as limb ischemia and bleeding increase.13,14,21-23

Conclusion

Severe hypotension during anesthesia may be due to several causes. Accurate diagnosis is imperative as the treatment required for cardiogenic shock differs significantly from that necessary to reverse anaphylaxis.

Conflict of interest

None.
References

ANESTHETIC MANAGEMENT OF A PATIENT AFTER FUNCTIONAL HEMISPHERECTOMY USING BILATERAL BISPECTRAL INDEX MONITORING

SHINICHI KIRA* AND KENTARO OKUDA**

Keywords: bilateral bispectral index monitoring; epilepsy surgery; medically intractable epilepsy; cerebral blood flow.

Dear Editor,

We report the use of bilateral bispectral index (BIS) monitoring during the maintenance of general anesthesia in a patient who had previously undergone functional hemispherectomy, and propose bilateral BIS monitoring to ensure the safe conduct of general anesthesia in patients who have had epilepsy surgery.

A 16-year-old woman with hypomelanosis of Ito (HI) was scheduled for surgical correction of a left wrist contracture and left cavus foot deformity under general anesthesia. She had left hemiplegia and right hemianopia, but otherwise normal cerebral function. At the age of 8 months she had undergone right functional hemispherectomy for medically intractable epilepsy caused by right hemimegalencephaly (HME), a recognized feature of HI. Nonetheless, she continued to take carbamazepine as anticonvulsant therapy. Laboratory tests revealed slight elevations in the serum concentrations of total cholesterol, creatine kinase, alanine transaminase, and \( \gamma \)-glutamyltransferase.

Asymmetric BIS values were anticipated in view of the known right hemispheric lesion and asymmetric cerebrovascular anatomy (Figure 1). Thus, bilateral BIS monitoring was established using two BIS sensors and two BIS-VISTA™ A-3000 monitors running algorithm version 4.0 (Covidien, Mansfield, MA) to titrate anesthetic depth and monitor intra-operative seizure activity. Bilateral BIS sensors were placed as described by Fudickar and colleagues1. A signal quality index of >50% was considered reliable. A regime of total intravenous anesthesia using propofol, rocuronium and remifentanil was chosen for anesthetic management. Ventilation was controlled to maintain normocapnia. Although a number of transient asymmetries between the right- and left-sided BIS values were observed, there were no significant differences (mean ± standard deviation: 43.8 ± 5.3 \textit{versus} 44.9 ± 9.2; \( P = 0.15 \)) during steady-state anesthesia. Surgery and anesthesia were concluded uneventfully, and the patient recovered without incident.

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Epilepsy surgery, such as functional hemispherectomy, is indicated in children with medically intractable epilepsy caused by HME. Cerebrovascular asymmetry may be evident after epilepsy surgery and changes in cerebral blood flow (CBF) are known to affect BIS values; however, we observed no significant differences between the right- and left-sided BIS values during steady-state anesthesia in this case. Nevertheless, we have already experienced significant differences in BIS values when recorded on both sides during general anesthesia in a patient with Sturge-Weber syndrome who had previously undergone hemispherotomy. Chiron and colleagues reported changes in CBF after hemispherectomy in a child with HME: single photon emission computed tomography (SPECT) showed that after surgery CBF had reduced from baseline levels in the abnormal cerebral hemisphere, but had increased in the normal hemisphere. The results of a SPECT study by Soufflet and colleagues suggest that changes in CBF before and after epilepsy surgery cannot easily be predicted. In their case series, mean CBF in the cerebral hemisphere affected by HME was decreased after surgery in 64% but normal in 36% of cases, whereas the mean CBF in the unaffected hemisphere was normal in 82% and increased in 18% of cases. Consequently, it is advisable to titrate anesthetic depth using bilateral BIS monitoring to ensure the safe conduct of anesthesia in patients who have had epilepsy surgery.

**Conflict of interest**

None.

**References**


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3. Abstract
4. Introduction
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6. Results
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8. Acknowledgements
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Do not repeat in details data or other information given in the Introduction or the Results sections. For experimental studies, it is useful to begin the discussion by summarizing briefly the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies. State the limitations of the study, and explore the implications of the findings for future research and for clinical practice. Link the conclusions with the goals of the study, but avoid unjustified statements and conclusions not adequately supported by the data.

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- 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.