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Abstract

Purpose The purpose of this report was to examine the closed-claims database to describe patient injuries from anesthesia gas delivery equipment.

Background Critical incidents from anesthesia gas delivery systems account for 20% of reported events. Gas delivery equipment includes any device used to convey gas to or from the endotracheal tube or mask. Common events include ventilator problems, circuit leaks, vaporizer problems, and gas supply problems. The last closed-claims database analysis of malpractice claims in 1997 found severe injuries (i.e., brain death or death) accounted for 76% of the gas delivery claims. The most common cause was misconnection or disconnection. Most events were deemed to be preventable with better monitoring. Since 1997 anesthesia machines have become more sophisticated with better disconnect monitors, and increased attention has been paid to performing the anesthesia machine pre-use checklist. The authors hypothesized the number of claims would have decreased over time given the improvements in anesthesia gas delivery equipment.

Methodology The investigators examined claims from the Closed Claims database from the 1970s to 2011. The database included a total of 9,806 claims. Inclusion criteria were all claims for surgical or obstetric anesthesia which used general anesthesia or regional plus general anesthesia (n = 6,022). For each gas delivery equipment claim, two of the authors independently classified the claim as due to equipment failure, provider error, or both equipment and provider error. They also assessed whether or not the event would have been preventable by an appropriate pre-anesthesia check-out. Claims were grouped into the periods of 1970-1989 versus 1990-2011 for analysis of changes in gas delivery equipment outcomes and payments.

Result There were 75 claims in 1970-1989 and 40 claims in 1990-2011 for anesthesia gas delivery equipment. Anesthesia gas delivery claims decreased significantly from the 1970s to the 2000s: 4% of claims during 1970s, 3% during 1980s, and 1% during 1990s and 2000s (P < 0.001). The last claim entered for a gas delivery claim was in 2006. Outcomes of gas delivery claims were less severe during 1990-2011 when compared to 1970s-1980s (Figure 1). Death or brain damage accounted for 80% of the claims in 1970-1989, whereas awareness (23%) was more common in 1990-2011. There was no significant difference in the percent of pneumothorax claims between 1970-1989 and 1990-2011 (16% vs. 25%); however, most of the earlier claims with pneumothorax resulted in death or brain damage. A lawsuit was filed in 87% of the claims in 1970-1989 and 91% of 1990-2011. Significantly more of the claims in 1970-1989 were for emergency surgery (n = 18, 34% vs. n = 5, 14%) and inpatient procedures (n = 41, 93% vs. n = 27, 73%). Most of the 1990-2011
claims resulted in payment (80%), which was similar to the earlier time period; however, payment amounts were smaller during 1990-2011 ($202,980) than during 1970-1989 ($818,805) (P = 0.002).

Of the claims in 1990-2011, provider error, either alone or in combination with equipment failure, accounted for 85% of claims (Table 1). A third (35%) of the claims were deemed preventable if only a thorough preanesthesia machine check had been performed. The most common outcome from a vaporizer problem was light anesthesia (n = 10, 71%) resulting in awareness (n = 9) or patient movement resulting in eye injury (n = 1). The reasons for light anesthesia included:

- failure to turn on the vaporizer (n = 3)
- failure to recognize an empty vaporizer (n = 2)
- vaporizer not mounted correctly (n = 2)
- vaporizer malfunction (n = 2)

Other vaporizer problems included unintentional volatile anesthetic overdose (n = 3), and in one case, carbon monoxide poisoning due to use of desflurane with desiccated Baralyme. Supplemental oxygen supply claims (n = 11) most commonly occurred outside the operating room and involved misuse of oxygen delivery tubing (n = 9) or supply tanks (n = 2). Events most commonly occurred in the post anesthesia care unit (n = 5), nonoperating room sites (n = 3), intensive care unit (n = 1), and during transport (n = 2). In 75% of these claims, actions of technicians or nurses contributed to the injury because they did not connect tubing properly or were unfamiliar with the oxygen supply equipment. All supplemental oxygen delivery tubing claims resulted in pneumothorax. In two of the oxygen supply tank claims, carbon dioxide was accidentally substituted for oxygen, both resulting in patient death. Breathing circuit claim events were commonly due to sticking inspiratory or expiratory unidirectional valves or plastic from the circuit blocking the flow. These events caused ventilation to become impossible (n = 4). Misconnection of circuits occurred in 2 cases. None of the breathing circuit claims were due to disconnections.

Ventilator claims resulted in the death or brain damage in 5 patients. All cases were due to the anesthesia provider’s failure to turn on the ventilator. In four of the five cases, the provider had disabled or turned off the ventilator alarms or disconnected the

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**Figure 1. Outcomes of Claims**

![Graph showing outcomes of claims from 1970-1989 and 1990-2011]

- Death/Brain damage
- Awareness
- Pneumothorax

1970-1989
1990-2011

P < 0.05
monitors. There were 2 anesthesia machine claims. In one case, a pediatric patient became hypoxic and had a cardiac arrest due to a machine leak that prevented ventilation. In this case no Ambu bag was available; however, the patient was successfully resuscitated without apparent injury. The other claim involved a stuck oxygen valve which resulted in increased nitrous oxygen flow rates.

**Conclusion**  The number of anesthesia gas delivery equipment claims and their severity decreased in 1990-2011 compared to 1970-1989. However, failure to do a thorough anesthesia machine check and errors by anesthesia providers or nurses and technicians continued to contribute to severe injury. Reasons identified included inadequate use of alarms, improvised oxygen delivery systems, and failure to ventilate manually in the event of difficult or impossible ventilation.

**Comment**

The results of this study support the argument that advancements in anesthesia machines, training, and monitors have helped reduce morbidity and mortality. However, despite all these advances, provider error still plays a major role in complications. Many of the claims reported could have been prevented had the anesthesia provider completed a thorough anesthesia machine check-out or scanned the patient and monitors. One should never be pressured to start a case without ensuring the anesthesia machine and resuscitation equipment is available and functioning. To me, these results emphasize the importance of being vigilant and thorough in your preparation and delivery of general anesthesia. The results also highlight the importance of training support staff and nurses how to properly use oxygen delivery equipment (i.e., Jackson Reese bags, oxygen tanks). I believe constantly scanning the patient, monitors, alarms, and minimizing distractions are all critical to the safe administration of anesthesia.

**Dennis Spence PhD, CRNA**

The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.
Abstract

Purpose The purpose of this study was to determine the effects of isoflurane and desflurane on postoperative cognitive function in elderly patients at one week after surgery.

Background Postoperative cognitive dysfunction (POCD) is associated with cognitive impairment and increased morbidity and mortality after major surgery. Isoflurane has been reported to induce neurotoxicity which is associated with POCD, and impairment in learning and memory. The exact cause of the neurotoxicity is not well understood, but some research suggests isoflurane is associated with increased caspase activation, apoptosis [cell death], neuroinflammation, and impairment in learning and function. Desflurane, on the other hand, has not been reported to cause similar neurotoxicity. It was hypothesized that isoflurane metabolism may generate greater amounts of trifluoroacetic acid in the blood compared to desflurane, and this acid may induce cytotoxicity and possibly POCD.

Methodology This was a prospective, randomized, controlled pilot study conducted at the Capital Medical University in Beijing, P.R., China. A total of 45 ASA I or II patients, aged 64 to 73, undergoing elective lower extremity or lower abdominal surgery were randomized to one of three groups:

1. spinal anesthesia alone
2. spinal anesthesia plus desflurane
3. spinal anesthesia plus isoflurane.

Patients were excluded if they had a Mini Mental Status Examination score below 24 (out of 30 points), history of alcoholism or drug dependence, psychiatric or neurological disease, severe visual or auditory disorders, or terminal status.

All patients had a battery of 11 cognitive tests administered preoperatively and at 1 week postoperatively. These tests were highly sensitive to different types of cognitive impairment. After baseline data was collected, patients in all three groups had spinal anesthesia induced with 2 mL of 1% tetracaine. No sedatives or opioids were administered during the surgery. Patients in the isoflurane or desflurane groups had general anesthesia induced with propofol and a laryngeal mask airway was placed. Inhaled anesthetics were titrated to keep the Bispectral Index between 50 and 60.

The investigators calculated a change score for each of the 11 tests. POCD was defined when 4 or more of the change scores were negative and the absolute value of each of these change scores was larger than 1 standard deviation of the baseline score of the same cognitive test, indicating lower cognitive function. Similar criteria were used to establish POCD in
previous research studies. The investigators compared the incidence of POCD and the mean number of tests with cognitive function decline between the three groups. Statistical analysis was appropriate. This was a pilot study so no power analysis was performed.

Result There were no significant differences in demographics, BIS values in the isoflurane and desflurane group, surgical procedures, blood loss, or surgical duration between the three groups. About half the patients were men (53%) with an average age of 69 ± 2 years. There were no differences in the preoperative Mini Mental Status exam between groups.

There was no significant difference in the mean number of 11 tests administered that showed a cognitive function decline between groups (P=0.77, Figure 1). However, when POCD was defined as “impairment in 4 or more” tests, there were more subjects in the isoflurane group that showed postoperative impairment on 4 or more tests (27%) than either the desflurane group (0%) or spinal anesthesia alone group (0%; P = 0.028). A study including about 30 times as many subjects as this pilot study would be needed to unequivocally demonstrate an increased rate of cognitive decline in any one group.

Conclusion This pilot study suggested that isoflurane may be associated with a higher incidence of postoperative cognitive decline than desflurane. A larger study will be needed to establish a convincing difference in cognitive function between agents.

Comment Elderly patients are at increased risk for POCD. These preliminary results suggest that isoflurane anesthesia may increase the incidence of POCD in elderly patients. What I found most interesting was that, by one measure, patients in the isoflurane group had some evidence of POCD within a week after surgery, while patients who received desflurane or spinal anesthesia alone did not. By another measure, the total number of subjects in each group that had a decline on postoperative cognitive tests, there was no discernible difference between groups. It should be noted that diagnostic criteria for POCD are not yet agreed upon.
It must be pointed out that this was a pilot study, so the results should be considered preliminary until larger studies are done. Additionally, these results may not apply to younger patients. However, given the fact that elderly patients recover faster and get out of the hospital sooner with desflurane (and sevoflurane) when compared to isoflurane, anesthesia providers might want to consider avoiding the use of isoflurane in elderly patients based upon recovery time alone.

**Dennis Spence, PhD, CRNA**

The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.
**Abstract**

**Purpose**  The purpose of this study was to describe perioperative outcomes after major noncardiac surgery in patients with a history of congenital heart disease.

**Background**  Advances in the medical and surgical management of pediatric congenital heart disease are allowing more and more patients to survive into adulthood. Unfortunately, there is little published evidence describing the outcomes of adults with a history of congenital heart disease undergoing major noncardiac surgery. It was hypothesized that these patients are at increased risk for perioperative complications when undergoing major noncardiac surgery.

**Methodology**  The authors examined records for the years 2002-2009 from the National Inpatient Sample, Healthcare Cost Utilization Project database for major noncardiac surgery admissions for patients with a history of adult congenital heart disease (ACHD). They compared these outcomes with a matched cohort in a 4 to 1 ratio (4 controls to 1 ACHD case). The matched cohort had similar comorbidity scores, age, gender, ethnicity, year, elective or emergent procedure, and primary surgical procedure type. Obstetric patients were excluded. The primary outcome was all-cause mortality and the secondary outcome was a composite of major nonfatal morbidity from pneumonia, acute respiratory failure, acute renal failure, deep vein thrombosis, stroke, pulmonary embolism, myocardial infarction, and cardiac arrest. Logistic regression was used to determine if ACHD diagnosis was predictive of the primary and secondary outcomes while controlling for demographic and procedural differences between the groups.

**Result**  The proportion of patients with ACHD undergoing major noncardiac surgery increased significantly from 0.07% in 2002 to 0.18% in 2009. Investigators identified 10,004 admissions in patients with ACHD and compared them to 37,581 admissions for the matched cohort. A majority of surgeries in ACHD patients occurred at nonteaching, small to medium size hospitals.

Patients admitted with ACHD for major noncardiac surgery had a 1.13 times greater odds of mortality (4.1%) compared to the matched cohort (3.6%, \(P = 0.03\)). Similarly, they had a higher rate of major nonfatal morbidity (21.4% vs. 16%; odds ratio (OR): 1.44, \(P < 0.001\)). ACHD patients had almost double the hospital length of stay (4.8 vs. 2.9 days, \(P < 0.001\)) and total hospital charges ($42,171 vs. $26,982, \(P < 0.001\) ) compared to the matched cohort. Deep vein thrombosis and stroke were 2 times more common in ACHD patients (\(P < 0.001\)).
Patients with complex ACHD lesions had the highest mortality rate at 7.3%. Complex adult congenital heart disease lesions included:

- tricuspid atresia or stenosis
- pulmonary atresia
- common ventricle
- hypoplastic left heart syndrome
- cor bioculare
- truncus arteriosus

The next highest mortality rates were in patients with ventricular septal defects (6.3%), followed by Ebstein anomaly (6.2%), Tetrology of Fallot (5.8%) and pulmonary stenosis (5.4%).

Predictors of mortality included age, female gender, nonwhite race, nonelective surgery, Medicaid insurance status, surgery type, large hospital size, teaching hospital, higher comorbidity, and a history of ACHD (OR = 1.29, P < 0.001). The surgical type with the highest mortality was thoracic noncardiac (OR = 8.80, P < 0.001), followed by neurosurgery (OR = 5.29, P < 0.001), and orthopedic surgery (OR = 3.68, P < 0.001).

**Conclusion**

ACHD patients were at increased risk for perioperative morbidity and mortality. Further work is needed to improve the care and reduce their perioperative risk.

**Comment**

I felt this was an important study to review because we will continue to see an increasing number of patients with repaired pediatric congenital heart defects survive to adulthood. Thus, anesthesia providers will encounter these patients as they present to the operating room for surgery. It is essential that providers understand that ACHD patients are at greater risk for perioperative complications.

Patients with ACHD can have long-term complications such as heart failure, severe pulmonary hypertension, arrhythmias and conduction defects, residual shunts, and valvular lesions. They may also be at increased risk of bleeding due to erythrocytosis, be at risk for a difficult airway, have seizure disorders, restrictive or obstructive lung disease, and renal and liver dysfunction. They may also require endocarditis prophylaxis. If the patient has a systemic-to-pulmonary shunt, then one must remember that arterial blood pressure and pulse oximetry cannot be measured on the ipsilateral side of the shunt. Additionally, central venous access should be performed cautiously.

The anesthetic plan should be based on an understanding of the patient’s unique cardiopulmonary circulation post-repair, potential airway anomalies, comorbidity, urgency, and type of surgical procedure. Anesthesia providers should ensure the patient is optimized and consider consulting with cardiologists and other experts with experience in caring for ACHD patients.

**Dennis Spence PhD, CRNA**


The views expressed in this article are those of the author and do not reflect official policy or position of the Department of the Navy, the Department of Defense, the Uniformed Services University of the Health Sciences, or the United States Government.
THE EFFICACY OF 2 DOSES OF EPIDURAL MORPHINE FOR POSTCESAREAN DELIVERY ANALGESIA: A RANDOMIZED NONINFERIORITY TRIAL

Anesth Analg 2013;117:677–85
Singh SL, Rehou S, Marmai KL, Jones PM

Abstract

Purpose  The purpose of this study was to determine if 1.5 mg epidural morphine provided equivalent (“noninferior” in research terms) analgesia and fewer side effects compared to 3 mg epidural morphine when administered as part of a multimodal analgesic regimen after cesarean delivery.

Background  Multimodal analgesic regimens which consist of epidural morphine, acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDS) are commonly administered after cesarean delivery. These regimens allow for administration of lower dosages of epidural morphine that decrease the incidence of side effects such as pruritus and postoperative nausea and vomiting (PONV). A recently published systematic review recommended 4 mg epidural morphine as the optimal dosage that provides good analgesia with an acceptable side effect profile. Unfortunately, this review included studies which included women having cesarean deliveries who had not labored and did not use a multimodal analgesic regimen. This study sought to evaluate opioid consumption in the first 24 hours after cesarean delivery in women administered either 1.5 or 3 mg of epidural morphine combined with acetaminophen and ketorolac.

Methodology  This was a double-blind, noninferiority study of 90 ASA I-III parturients undergoing cesarean delivery after a failed trial of labor with an existing epidural. Parturients were excluded if they had received a combined-spinal epidural, were allergic to study medications, had a history of long-term opioid use or substance abuse, or had chronic pain. Parturients were randomized to receive either 1.5 mg or 3 mg epidural morphine. All patients received ketorolac 30 mg IV every 6 hours for the first 24 hours and acetaminophen 975 mg on arrival to the post-anesthesia care unit, then every 6 hours for the first 24 hours. Rescue analgesia included oral oxycodone 5-10 mg every 4 hours as needed. Nausea and vomiting was treated with ondansetron 4 mg and metoclopramide 10 mg IV every 8 hours as needed. Diphenhydramine 25 to 50 mg IV was administered for moderate pruritus every 4 hours, and naloxone 0.1 mg SQ for severe pruritus every 1 hour as needed.

An anesthesia provider not involved in data collection bolused the epidural catheter with 2% lidocaine with fentanyl 50 µg to achieve a T-4 sensory level. IV ondansetron 4 mg was administered intraoperatively for nausea and vomiting prophylaxis. At skin closure, depending on randomization, 1.5 or 3 mg of epidural morphine diluted to 5 mL was administered. Staff and providers caring for the patient were blinded to group assignment.
The primary outcome was the difference in opioid consumption (morphine equivalents) in the first 24 hours. For the 1.5 mg dose to be considered equivalent (noninferior) to the 3 mg dose, the difference in median morphine equivalents at 24 hours would have to be < 3.33 mg. Secondary outcomes were opioid consumption between 24 and 48 hours, pain scores, time to first analgesic request, overall pain relief, maternal satisfaction, quality of recovery, and adverse effects. Statistical and power analysis were appropriate. An intention to treat analysis was used.

**Result** There were 44 subjects in the 1.5 mg group and 43 in the 3 mg group. No significant differences were found in baseline characteristics between the groups. Investigators found that 24-hour opioid consumption in the 1.5 mg epidural morphine group was equivalent to the 3 mg epidural morphine group (Figure 1). No differences were found in total opioid consumption between 24-48 hours or in the time to request for pain medications (Table 1). Overall pain scores were less than 3.5 on a 0-10 numeric rating scale in both groups (Table 1). Patients were highly satisfied in both groups and quality of recovery scores were significantly higher at 24 hours (P = 0.03) but similar at 48 hours (P = NS; Table 1).

The incidence of adverse effects was higher in the 3 mg group than the 1.5 mg group during the first 12 hours postoperatively (Figure 2). The risk of moderate or severe pruritus was lower at 6 hours (relative risk = 0.44, P = 0.013) and 12 hours (relative risk = 0.41, P = 0.006) in the 1.5 mg group. No differences were found at any of the other time points. The risk of moderate or severe PONV was lower at 6 hours in the 1.5 mg group (relative risk = 0.22, P = 0.03), but similar at the other time points. No significant differences were found in sedation scores between the groups at any time point.
Table 1. Outcomes

<table>
<thead>
<tr>
<th>Opioid Consumption in mg</th>
<th>1.5 mg group</th>
<th>3 mg group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median total 0-24h</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Mean 0-24-h (SD)</td>
<td>2.4 (3.3)</td>
<td>2.5 (6.6)</td>
<td>-</td>
</tr>
<tr>
<td>Median total 0-48h</td>
<td>7.5</td>
<td>2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Median time 1st request</td>
<td>21.6</td>
<td>22.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Mean Pain Scores**

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<tr>
<th></th>
<th>1.5 mg group</th>
<th>3 mg group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 hours</td>
<td>3.1</td>
<td>3.4</td>
<td>NS</td>
</tr>
<tr>
<td>48 hours</td>
<td>3</td>
<td>3.1</td>
<td>NS</td>
</tr>
<tr>
<td>Overall Satisfaction 24 h</td>
<td>96%</td>
<td>90%</td>
<td>NS</td>
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</tbody>
</table>

**Satisfaction with Pain Control**

<table>
<thead>
<tr>
<th></th>
<th>1.5 mg group</th>
<th>3 mg group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfaction 48 h</td>
<td>93%</td>
<td>95%</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Quality of Recovery Scores**

<table>
<thead>
<tr>
<th></th>
<th>1.5 mg group</th>
<th>3 mg group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 h</td>
<td>15</td>
<td>14.5</td>
<td>0.03</td>
</tr>
<tr>
<td>48 h</td>
<td>17</td>
<td>17</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Note.* The quality of recovery scores were assessed using a 9-item, 3-point scale (0 = not at all, 1 = some of the time, 2 = most of the time with a maximum score of 18). IQR = interquartile range.

Figure 2. Incidence of Moderate or Severe Adverse Effects

*Note.* The incidence of moderate or severe pruritus was 27% lower at 6 hours and 30% lower at 12 hours in the 1.5 mg group. The incidence of moderate to severe PONV was 16% lower at 6 hours postoperatively in the 1.5 mg group.
Conclusion  Epidural administration of 1.5 mg morphine when used in a multimodal analgesic regimen was found to be equivalent to 3 mg of epidural morphine. The 1.5 mg dose is recommended, given the equivalent analgesia and lower incidence of moderate to severe pruritus and PONV in the first 12 hours after surgery.

Comment  I found this to be an extremely well-designed, clinically-relevant study which demonstrated use of lower doses of epidural morphine when combined with around-the-clock acetaminophen and ketorolac significantly reduced pruritus and PONV without sacrificing analgesia. Instead of trying to show the 1.5 mg was better than 3 mg of epidural morphine, the investigators designed this study to demonstrate whether or not a 50% reduction in the dose of epidural morphine would provide equivalent reductions in opioid consumption during the first 24 hours. These findings are important because they support the trend in obstetric anesthesia to provide the lowest possible, yet effective, dosage of epidural morphine after cesarean delivery. I recommend anesthesia providers consider these results the next time they do a cesarean delivery under epidural anesthesia. I also recommend, when possible, to administer around-the-clock acetaminophen (IV or PO) and ketorolac.

Dennis Spence PhD, CRNA
Obstetric Anesthesia

A Retrospective Assessment of the Incidence of Respiratory Depression After Neuraxial Morphine Administration for Postcesarean Delivery Analgesia

Anesth Analg 2013;117:1368–70

Abstract

Purpose The purpose of this study was to define the incidence of respiratory depression in post-Cesarean section women who received either epidural or subarachnoid morphine.

Background Morphine is not uncommonly administered via epidural or subarachnoid routes for post-Cesarean section pain control. Neuraxial morphine is known to be the cause of both early and late respiratory depression, but in postpartum women the incidence of neuraxial morphine associated respiratory depression is unknown. It has been reported to be between 0% and 0.9%. Perhaps partially due to uncertainty about the magnitude of the risk of respiratory depression in this patient population, some anesthesia providers do not use neuraxial morphine in post-Cesarean section women, especially if they are obese or may have obstructive sleep apnea.

Methodology This was a retrospective study using existing in-hospital databases as the data source. From December 2006 through 2011 all women who underwent Cesarean section with neuraxial anesthesia received neuraxial morphine unless they had a morphine allergy. Postop, BP, HR, RR, oxygen saturation, and sedation scores were monitored at defined intervals. Standing orders prescribed naloxone for a RR less than 8 bpm or Richmond Agitation Sedation Scale ≤ -3. NSAIDs and acetaminophen / oxycodone 1 or 2 tablets were administered for breakthrough pain. Respiratory depression was defined by the need to administer naloxone or call the “rapid response team” to treat respiratory depression.

Result The study included 5,036 post-Cesarean section women who received neuraxial morphine; epidural morphine in 1,080 women and subarachnoid morphine in 3,554 women. [Editor’s Note: the authors did not explain the discrepancy of 402 women not included in either the epidural or subarachnoid groups.] Most women (63%) had a BMI ≥ 30 kg/m² and over 17% of women had a BMI ≥ 40 kg/m². Mean BMI was 34 kg/m². Over 90% of women received a 3 mg epidural morphine dose or a 0.15 mg subarachnoid morphine dose. The range of epidural doses was from 1 mg to 5 mg; and subarachnoid doses were 0.05 mg to 0.25 mg. There were no cases of respiratory depression requiring intervention as prescribed by standing orders. This made the upper 95% confidence interval for the incidence of respiratory depression 0.07% or 1 in 1,429 post-Cesarean women who had received neuraxial morphine.
Conclusion  In this study of over 5,000 women who received neuraxial morphine for post-Cesarean section pain management there were no cases of early or delayed respiratory depression. This made the 95% confidence interval for the rate of respiratory depression no greater than 0.07%.

Comment  Having rounded on lots of post-Cesarean section women who received epidural morphine, this study fits with my clinical impression; respiratory depression was rare. Itching and PONV were common. Fortunately we have made some progress over the years toward decreasing the incidence and bad outcomes from all three of these complications. Neuraxial morphine is, in my view, an important option for post-Cesarean pain relief.

One might ask, “How can an incidence of respiratory depression be calculated when none of the women had respiratory depression?” Rather than identifying an incidence of respiratory depression, the authors used a statistical technique to calculate the “worst case scenario” from the data they had. Basically, this study says, “From the number of patients we had, none of whom had respiratory depression, we are 95% sure the worst the real incidence of respiratory depression could be is 0.07%.”

Respiratory depression in post-Cesarean section women who received no more than 3 mg epidural morphine or 0.15 mg spinal morphine appears to be quite rare. Nevertheless, when respiratory depression occurs due to neuraxial morphine, it can result in severe harm if unnoticed. Fortunately, respiratory depression from neuraxial morphine virtually always has a slow onset and is easily treatable. A proper postoperative monitoring procedure should ensure the safety of these patients even in the rare cases where respiratory depression occurs.

Michael A. Fiedler, PhD, CRNA

Please see “THE EFFICACY OF 2 DOSES OF EPIDURAL MORPHINE FOR POSTCESAREAN DELIVERY ANALGESIA: A RANDOMIZED NONINFERIORITY TRIAL,” elsewhere in this issue for a discussion comparing 1.5 mg and 3 mg epidural morphine for post-Cesarean section pain management.
Association between neuraxial analgesia, cancer progression, and mortality after radical prostatectomy: A large, retrospective matched cohort study


Abstract
Purpose The purpose of this study was to determine whether the combination of general anesthesia and either spinal or epidural anesthesia was associated with a reduction in prostate cancer recurrence, metastasis, or mortality compared to general anesthesia alone.

Background Prostate cancer is among the most common cancers in men and has a recurrence rate of about 25%. T lymphocytes and natural killer cells [Editor’s note: both white blood cells] are involved in killing cancer cells in the circulation and thus, “host defense.” Surgical manipulation of a tumor may release tumor cells into the systemic circulation so lymphocyte host defense may be especially important during and following cancer surgery. The stress response during surgery, potent inhalation agents, and systemic opioid administration have each been identified as reducing the host defense. Subarachnoid opioids do not inhibit lymphocyte function. Neuraxial anesthesia reduces surgical stress, the need for potent inhalation agents, and the need for systemic opioids and so, may spare the host defense against cancer cells. This may result in lower rates of cancer recurrence. Human studies on this last point are mixed.

Methodology This was a retrospective study using the Mayo Clinic Prostatectomy Database as a data source. Records were drawn from 1991 through 2005. Combined regional - general anesthesia patients were “matched” with patients who received only general anesthesia. Patients were matched on the following criteria:
- age (± 5 years)
- year of surgery (± 5 years)
- cancer staging
- pathological Gleason score
- positive lymph nodes (yes or no)
- preoperative Prostate Specific Antigen (±1 ng/mL)

General anesthesia was not standardized but typically included propofol or pentothal; fentanyl, midazolam, succinylcholine, or vecuronium; and isoflurane, desflurane, or sevoflurane. General anesthesia patients may or may not have included nitrous oxide.
Neuraxial anesthesia most often consisted of a subarachnoid injection of 0.5% bupivacaine plus up to 0.6 mg morphine or 60 µg hydromorphone. When epidural anesthesia was used, either bupivacaine or lidocaine was used along with a 100µg fentanyl bolus and an epidural infusion of 70 µg to 120 µg fentanyl per hour for up to three days postoperatively.
The total dose of intraoperative and postoperative (48 hours) IV and PO opioids were recorded as IV morphine equivalents.

Result During the study period, retropubic radical prostatectomy was performed in 1,642 patients under combined regional / general anesthesia. Of these, 83% received a spinal with morphine. These patients were compared to another 1,642 patients who received only general anesthesia by the matching criteria listed previously (total 3,284 study patient records). Follow-up was for an average of 8.6 years in regional / general patients and 9 years in general only patients. While patients in each group were identical on matching criteria, general anesthesia only patients were more likely to have:
- higher ASA physical status score (ASA III-IV 20% vs. 14%)
- more comorbidities
- positive margins during surgery (27% vs. 19%, P=0.001)
- radiation therapy (3% vs. 2%, P=0.002)

Combined regional / general patients were more likely to have had androgen deprivation therapy (10% vs. 4%, P=0.001).

Systemic opioids administered intraoperatively or during the first 48 hours postoperatively included:
- morphine
- fentanyl
- sufentanil
- meperidine
- hydrocodone
- hydromorphone
- oxycodone
- oxymorphone

Metastasis was more common in general anesthesia only patients with a hazard ratio of 2.73 compared to regional / general patients. Mortality from prostate cancer occurred 2.43 times more often in the general anesthesia only group (hazard ratio 2.43). Overall mortality was 1.35 times more likely in the general anesthesia only group (hazard ratio 1.35). Overall, when regional anesthesia was combined with general anesthesia for open radical retropubic prostatectomy, the rate of metastasis was slower and death was less likely during the follow-up period (8-9 years on average).

Conclusion Combined regional / general anesthesia for radical retropubic prostatectomy was associated with a lower rate of metastasis and a higher rate of survival compared to general anesthesia only patients.

Comment I believe regional anesthesia is underutilized so this study is immediately attractive to me. And in my judgement, this study does have merit. There is some evidence here that adding regional anesthesia to general anesthesia for open prostatectomies is associated with better long-term prostate cancer outcomes. Having said that, a critical review of the rationale provided for the improved outcomes has at least one noticeable hole in it. While it is true that the surgical stress response, potent inhalation agents, and systemic opioid administration reduce the host defense against cancer cells, it is unlikely that they each do so to the same degree. We can agree that adding regional anesthesia probably reduced the stress response and reduced the need for inhalation agents.
and systemic opioids. But a factor that was not controlled for was the use of nitrous oxide which we know has a strong inhibitory effect on white blood cell function, especially when exposure is for the length of time it takes to perform an open prostatectomy. IF general only patients had a high level of nitrous use (probably the case during the 1990s and early 2000s) and IF combined regional / general cases had a significantly lower level of nitrous use, this difference could explain the difference in cancer outcomes shown in this study. You can look at this in one of two ways. The glass half-empty viewpoint is that regional played no part; it was the nitrous oxide use. The glass half-full viewpoint is that using regional anesthesia reduced the need for nitrous, thus improving outcomes.

My bottom line is this. There is a possibility that the outcomes in this study were mostly due to an unknown difference in nitrous oxide use not reported by the study. But, regional anesthesia does reduce surgical stress and it does reduce the need for IV opioids which were documented in the study. Reducing the use of IV opioids does favor improved host defense against cancer cells. Also, the difference in metastasis rates was quite high; general anesthesia only patients were 2.7 times more likely to have metastasis. Given this, and given all the other benefits of regional anesthesia, e.g. reduced blood loss and infection rates, I favor accepting the broad conclusion of this study which is that adding regional anesthesia to general for open prostatectomies is good for patients.

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For information about the effects of nitrous oxide on leukocyte function see “LEUKOCYTE DNA DAMAGE AND WOUND INFECTION AFTER NITROUS OXIDE ADMINISTRATION” in the April, 2013 issue of Anesthesia Abstracts.

Hazard Ratio can be interpreted simply as how much more often the “hazard” occurred in one group compared to another. Thus, a hazard ratio of 2.73 for metastasis in the general anesthesia only group means that this group had metastasis 2.73 times more often than did the regional / general group.