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General

Practice Advisory for Preanesthesia Evaluation: An Updated Report by the American Society of Anesthesiologist Task Force on Preanesthesia Evaluation

Anesthesiology 2012;116:522-38
Committee on Standards and Practice Parameters

Abstract

Purpose  The purpose of this updated practice advisory was to assess available evidence, provide a reference context for how to conduct a preanesthesia evaluation, and suggest future research for preanesthesia evaluation. The advisory does not speak to generalized preoperative care; it is not for use in urgent or emergency situations nor does it provide a decision tree for making a specific anesthetic plan.

Background  The last ASA Practice Advisory on Preoperative Evaluation was published in 2002. An update was requested in order to review the additional approximately 10 years of published anesthesia research relevant to preoperative evaluation. The task force comprised ASA members and consultant physicians with “expertise or interest in preanesthesia evaluation” who evaluated and ranked this new data pool. Conclusions were formed from this consultation and via survey and consensus techniques. The criteria for preanesthesia intervention, testing and consultation is this advisory are predicated on the concept that the overall benefit of a test will outweigh any overall adverse effect.

Methodology  Practice advisories are reports that are not wholly supported in the literature; they are based on expert opinion, consensus, open forum comments and also whatever clinical data may be available. Advisories therefore rank below a standard or guideline in terms of their validity and generalizability. There is no formal statistical analysis of clinical data as there is in a metaanalysis.

In this practice advisory, the levels of evidence were categorized as:

- A (randomized controlled trials reporting statistically significant differences in patient outcomes)
- B (observational studies suggest differences in outcomes)
- C (literature is equivocal, ie., findings are inconsistent or contradictory)
- D (inadequate or insufficient literature from which to draw conclusions).

Advisory information was provided in the following areas: preanesthesia history and physical as well as the selection and timing of preoperative tests under routine or special circumstances. The appendices detail data that compared the differences in response between ASA members and consultants in the area of the appropriate timing of the preanesthetic evaluation and agreement on routine or special circumstance preoperative testing.

Result  The following tables summarize the most important parts of the advisory.

The literature strongly supports the position that identification of medical conditions preoperatively
significantly impacts perioperative morbidity and mortality (evidence category B, suggest difference in outcome). A majority of ASA members and consultants agreed that “at a minimum” the preop physical exam should include an airway examination (100% agreement), pulmonary exam with lung auscultation (85% to 88% agreement), and cardiovascular assessment (81% to 82% agreement). The advisory recommends that these 3 steps of the physical exam, along with documentation of vital signs, be performed and documented.

A wide range of category B research exists concerning the value of preanesthesia laboratory or diagnostic testing.

| Table 1: Review of Medical Records, Preanesthesia Interview, and Exam |
|-----------------|-----------------|-------------------------------------------------|
| **Severity of Medical Condition** | **Invasiveness of Surgery** | **Preanesthesia Evaluation should be done on the:** |
| Low             | Low or moderate  | Day of or day before surgery                    |
| High            | Low or high      | Day before surgery                              |
| Low             | High             | Day before surgery                              |

<table>
<thead>
<tr>
<th>Table 2: Preanesthesia Testing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient/Surgical Category</strong></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Asymptomatic patient</td>
</tr>
<tr>
<td>Patients with multiple cardiac risk factors or cardiorespiratory disease. <em>Age alone is NOT an indication.</em></td>
</tr>
<tr>
<td>Cardiovascular risk factors, type of surgery</td>
</tr>
<tr>
<td>Smoking, recent upper respiratory infection, chronic obstructive pulmonary disease (COPD), cardiac disease</td>
</tr>
<tr>
<td>Treated or symptomatic asthma, symptomatic COPD; scoliosis with restrictive lung function; time since last pulmonary evaluation; type and invasiveness of surgery</td>
</tr>
<tr>
<td>Liver disease, extremes of age, history of anemia, bleeding, or hematologic disorders</td>
</tr>
<tr>
<td>Bleeding disorders, renal dysfunction, liver dysfunction, type and invasiveness of procedure, possibly use of anticoagulant medicine or herbals</td>
</tr>
<tr>
<td>“Likely perioperative therapies,” endocrine disorders, risk of renal or liver dysfunction, use of certain medications</td>
</tr>
<tr>
<td>Urologic procedures or prosthetic implantation, symptoms of urinary tract infection</td>
</tr>
<tr>
<td>Females of childbearing age or for whom the result will alter management</td>
</tr>
</tbody>
</table>
testing for both asymptomatic and selected patients, however, a very large range of abnormal findings and outcomes were also found. Insufficient evidence was found to make specific recommendations. Those with merit are listed and the provider may determine that others are also necessary. Routine testing was not judged to be indicated.

Results obtained from the medical record within 6 months of surgery are acceptable if no substantive changes have occurred in the medical history. More recent results may be necessary if the patient’s medical condition has changed or when the test is necessary for a specific anesthetic technique.

Overall, an adequate preanesthesia evaluation should include:

1. review of “readily accessible” medical records
2. a patient interview
3. a directed preanesthesia examination
4. indicated preoperative tests
5. appropriate other consultations.

At a minimum, the physical exam should include an assessment of the airway, lungs, and heart.

**Conclusion**  No substantive changes in the current recommendations for preanesthesia evaluation were made in this updated advisory.

**Comment**

Absent the development of a task force made up of CRNAs, our profession will continue to be held to advisories, guidelines, and standards formulated by our physician colleagues. I found it interesting that there was not full consensus about the need to perform even a cursory exam of the heart, lungs and vascular system as part of the preanesthetic evaluation. Up to 15% of the physician anesthesiologists felt that pulmonary auscultation should not be required and up to 19% of physician anesthesiologists felt that a cardiac exam (presumptively auscultation and peripheral pulses) should not be required routinely in a preoperative physical exam. Wow. These are very basic elements of patient assessment and are required at the level of the admitting nurse at every institution in which I practice!

Although no changes were advised, a rereading of any practice advisory is a helpful reminder of current recommendations. It is relatively common to compare one’s own practice to published standards and defend that practice if you find you deviate from an advisory (I’ll bet everyone reading this did so.) This is a fundamental principle of quality assessment and improvement. Do you “under” order preoperative testing and if so has there been an adverse effect on your patient’s outcome? Do you “over” order preoperative testing? What are the consequences on outcome? On cost?

Being aware of where your practice stands – preferably an awareness based in data – is a meaningful part of professional practice. My general view is that a thorough history and physical exam provides the most useful information; some conclusions drawn from this process may be confirmed by testing. The key to practicing the *art* of anesthesia is knowing when to decelerate during the preoperative process. Avoiding a problem is so much easier than fixing one.

Penelope S. Benedik, PhD, CRNA, RRT
A COMPARISON OF EPIDURAL ANALGESIA AND TRADITIONAL PAIN MANAGEMENT EFFECTS ON SURVIVAL AND CANCER RECURRENCE AFTER COLECTOMY: A POPULATION-BASED STUDY

Anesthesiology 2012;116:797-806
Cummings KC, Xu F, Cummings LC, Cooper GS

Abstract

Purpose The purpose of this study was to compare survival and cancer recurrence rates in colectomy patients who did or did not receive perioperative epidural analgesia.

Background Colon cancer is the third leading cause of death in the United States. Recurrence of cancer after colectomy may be affected by immunosuppressive factors such as surgical stress, blood transfusion, anesthetic agents, and opioids. Several previous research studies have reported reduced cancer recurrence and improved survival rates with the use of epidural analgesia. However, results after cancer surgery are mixed. The main hypothesized benefit of epidural analgesia on reducing mortality and cancer recurrence is in the reduction of anesthetic agent exposure and opioid requirements.

Methodology This was a population-based cohort study using the Surveillance, Epidemiology, and End Results Medicare database to compare cancer recurrence and survival rates after colorectal surgery in patients who had received perioperative epidurals or those who did not. The study included patients aged 66 years or older diagnosed with nonmetastatic colorectal cancer between 1996 and 2005. Patients were excluded if they had stage IV cancer, developed a subsequent second malignancy, a prior diagnosis of cancer, renal disease, history of familial adenomatous polyposis or inflammatory bowel disease, or underwent a laparoscopic procedure. Survival was measured until death or 8 months, whichever came first. Cancer recurrence was measured up to 4 years after the cancer diagnosis or death in patients who survived at least 12 months after their surgery. Medicare databases were examined to determine whether or not the patient received an epidural, the type of surgical procedure, patient comorbidities, and perioperative complications. Perioperative complications examined did not include cardiopulmonary complications, i.e., myocardial infarction or pulmonary embolism.

The primary outcome was survival time in patients with and without the use of epidural anesthesia/analgesia techniques. The secondary outcome was colon cancer recurrence rates. Statistical analysis was appropriate. A P < 0.05 was considered significant.

Result The study included 42,151 patients. Of those, 23% had epidurals at the time of their colon cancer resection. The two groups had often minor, but statistically significant differences in several patient characteristics. Patients who received epidurals...
were slightly younger (77.8 vs. 78.1 years, P < 0.001), had lower comorbidity scores, where more likely male (44.5% vs. 42%, P <0.001), were more often married (53% vs. 49%), and more likely lived in the Midwest (36% vs. 18%). Patients who received epidurals were more likely to have rectosigmoid or rectal cancers (26% vs. 19%, P < 0.001). The need for a blood transfusion was similar between the two groups (9% vs. 9.4%, P = NS).

The 5-year colon cancer survival rate was 5 percentage points higher in the epidural group compared to the traditional pain management group, 61% vs. 56%. The median survival rate was 7.24 years in the epidural group and 6.09 in the traditional pain management group. After controlling for multiple patient characteristics, epidural use was found to be associated with improved survival (adjusted hazard ratio = 0.91, P <0.001). Patient characteristics that were controlled for included age, gender, race, marital status, education level, median income, year of diagnosis, Charlson comorbidity score, tumor grade, need for blood transfusion, cancer site, and surgical complications. Several other factors were identified as significant predictors of earlier mortality:

- older age
- African American race
- higher comorbidity score
- unmarried
- higher stage cancer
- distal cancer site
- diagnosis before 2005

The need for a blood transfusion was strongly associated with reduced survival (adjusted hazard rate = 1.34, P <0.001).

At four years, the cancer recurrence rate was 14.3% in the epidural group and 13.8% in the traditional pain management group. After adjusting for patient characteristics, there was no significant difference in the odds of cancer recurrence between the two groups. However, need for a blood transfusion was a significant predictor of cancer recurrence (odds ratio = 1.14, P = 0.01).

Conclusion  Epidural use was associated with improved survival, but not reduced cancer recurrence rates, when compared to traditional pain management techniques. It is not known if the association between epidural use and improved survival was causative. Blood transfusions had a clearly negative effect both on cancer recurrence and survival.

Comment  This is one of the largest studies examining colon cancer survival and cancer recurrence rates with or without the use of an epidural. Overall, I found it to be a well-designed study, with some interesting findings. However, it is important to point out that it was a retrospective study, and thus causation cannot be determined. Because data was collected from databases, we do not know specifics about how the epidurals were used perioperatively, and if the patients experienced any cardiopulmonary complications. There may also be other unmeasured
factors that may have contributed to the findings. More importantly, there were a number of differences between the groups that make me view the results cautiously; although, the investigators did statistically control for many of these differences. Additionally, the effect epidural use had on improving survival was small (hazard ratio = 0.91). Since the investigators were unable to record nonsurgical complications (e.g., myocardial infarction), we do not know what effect nonsurgical complications might have had on their results.

Not surprisingly, the use of an epidural had no effect on the rate of colon cancer recurrence. However, need for a blood transfusion had a negative effect on survival and cancer recurrence. This is consistent with what other investigators have found with allogenic blood transfusions during cancer surgery. The need for a blood transfusion could be a reflection of more advanced disease, sicker patients, and worse perioperative outcomes.

Despite the limitations of these findings, I am still a big proponent of epidural analgesia after open abdominal surgery for colon cancer, especially when a long midline incision is going to be used. However, the risks and benefits of epidural use should be weighed for each patient, and the plan discussed with the surgeon. If you wanted to provide some evidence supporting a long term benefit of epidural use on survival, I might consider using this data, though I would do it cautiously.

Dennis Spence, PhD, CRNA

Hazard Ratio is used to describe whether or not a treatment, in this case epidural use, reduces or increases survival. In this study the hazard ratio was the odds of a patient surviving longer when an epidural was used, however it does not convey any information about how much longer the patient will survive. For example, if the hazard ratio was 2 this implies that twice as many patients had the event, in this case death. In contrast, if the hazard ratio were 0.5 then half as many patients in the epidural group died at any point in time when compared to the traditional pain management group. When examining the hazard ratio, it is important to also look at the median survival rate of the event of interest.

For more CE credit on the effects of blood transfusion, consider attending the online webinar, “New Transfusion Guidelines” available on CRNAwebinars.com. 1 CE credit.

For more information on blood transfusion in anesthesia see the August 2010 issue of Anesthesia Abstracts.

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.
Effects of Crystalloid Versus Colloid and the α-2 Agonist Brimonidine Versus Placebo on Intraocular Pressure During Prone Spine Surgery

Anesthesiology 2012;116:807-15

Abstract

Purpose The purpose of this study was to test the hypotheses that during prolonged prone spine surgery intraocular pressure (IOP) would (1) increase less with goal-directed colloid administration compared to crystalloid, and (2) increase less when the α-2 agonist brimonidine eye drop was administered compared to placebo eye drops.

Background Postoperative visual loss after prolonged prone spine surgery is a rare, but devastating complication. Previous research has demonstrated that IOP can reach as high as 40 mm Hg after 6 hours of prone positioning. Furthermore, it is postulated that increased IOP may be related to a positive intraoperative fluid administration, as well as an increased episcleral venous pressure, during prone spine surgery. Increased IOP reduces ocular perfusion pressure, and is thought to contribute to postoperative visual loss.

One of the best ways to optimize fluid administration is through the use of goal-directed fluid therapy. Some investigations have suggested that colloids, such as 5% albumin, may be better for goal-directed fluid resuscitation during prone spine surgery because less intravascular volume shifts from the vascular to the interstitial space. Thus, colloids may reduce the increase in IOP compared to crystalloid administration. Additionally, α-2 agonists such as brimonidine are also effective at decreasing IOP. Brimonidine works by reducing the aqueous production and increasing uveoscleral outflow in the eye.

Methodology The investigators used a factorial randomized trial design to test their two hypotheses. A total of 60 patients undergoing complex spine surgery in the prone position were randomized to one of four groups:

- Group 1  5% albumin and placebo eye drops
- Group 2  5% albumin and bromonidine eye drops
- Group 3  lactated ringer’s solution and placebo eye drops
- Group 4  lactated ringer’s and bromonidine eye drops.

The eye drops were administered one hour before surgery, then every 8 hours for 24 h. Investigators were blinded to the type of eye drop administered.

All patients received 5-7 mL/kg LR preoperatively followed by 6-7 mL/kg/hr LR during surgery. Additional fluid resuscitation was guided by the use of an esophageal Doppler, based on patient group assignment (e.g., 5% albumin or lactated ringer’s).

Anesthesia providers were not blinded to fluid group. Packed red blood cells were administered if the hematocrit dropped below 30%. All patients were...
positioned prone with the head elevated 5 degrees and maintained in skull pins to allow access to the eyes and avoid pressure on the globe. End tidal CO$_2$ was maintained near 35 mm Hg. If a patient’s IOP reached 50 mm Hg, attempts were made to reduce IOP by hyperventilating the patient to an ETCO$_2$ of 30 mm Hg and giving diuretics to increase urine output. Mean arterial pressure was maintained within 10% of baseline to maintain ocular perfusion pressure.

The primary outcome was the time weighted average IOP using all available IOP measurements during the procedure. IOP was measured preoperatively, then every 30 minutes during surgery, then hourly for 4 hours after surgery. Statistical analysis was appropriate.

Result A total of 60 patients completed the study (n = 31 received 5% albumin and n = 29 received LR, n = 32 received bromonidine and n = 28 received placebo drops). No significant differences were found between the groups with regards to demographics, number of spinal segments, surgical duration, or preoperative blood pressure.

The combination of 5% albumin and bromonidine together reduced IOP at the end of surgery by 0 to 10 mm Hg. There was no significant difference in Time Weighted Average IOP between the two fluid groups (Figure 1); however, the bromonidine eye drops lowered Time Weighted Average IOP by approximately 4 mm Hg (P = 0.023). In the bromonidine group, the first IOP in the prone position, the last IOP, and the Time Weighted Average IOP in the postanesthesia care unit (PACU) were significantly lower when compared to placebo eye drops (P < 0.05; Figure 2). In the 5% albumin group IOP was lower at each of these time points, however the only significant difference was found at the end of the surgery (mean difference 5 mm Hg; P = 0.03). The IOP increased at a significantly slower rate in the 5% albumin group compared to the LR group (2 mm Hg/h vs. 3.1 mm Hg/h, P = 0.03). In contrast, no difference was found in the IOP increase over time when comparing bromonidine or placebo eye drops.

A majority of patients experienced at least one episode of ocular perfusion pressure < 40 mm Hg. In the albumin group...
68% had at least one episode of ocular perfusion pressure < 40 mm Hg compared to 79% in the LR group (P = NS). In those who received bromonidine 72% vs. 75% had ocular perfusion pressures < 40 mm Hg (P = NS). Approximately 20% of all patients experienced at least one episode of IOP > 50 mm Hg. In the 5% albumin group 35% of patients had moderate or severe facial edema compared to 68% in the LR group (P = 0.0027). No patient experienced postoperative visual deficits.

**Conclusion**

Bromonidine administration resulted in slightly lower average IOP, whereas 5% albumin had little effect. However, 5% albumin and bromonidine together reduced IOP at the end of surgery by 0 to 10 mm Hg. Bromonidine blunts the increase in IOP associated with prone spine surgery, however maintaining adequate blood pressure might play a more important role in maintaining ocular perfusion pressure.

**Comment**

Postoperative visual loss is a rare complication after prone spinal fusion surgery. It is a hot topic in anesthesia because it is such a devastating complication. Unfortunately we know very little about the pathophysiology. More importantly, we do not have a good handle on how to prevent it. The investigators of this study used a very sophisticated research methodology to investigate if two methods, goal-directed fluid therapy with colloids and administration of bromonidine eye drops would prevent increases in IOP. They found that bromonidine reduced average IOP during surgery better than placebo, but colloid did not. However, colloid administration resulted in a significantly lower IOP at the end of surgery and a slower rate of IOP increase when compared to crystalloid. Therefore, I think colloid may have some benefit in prone spine surgery in possibly reducing the incidence of postoperative visual loss. Further research is needed to confirm this.

The authors speculated that their aggressive management of hypotension and the use of goal-directed therapy most likely minimized the beneficial effects of the colloid on IOP. I believe their use of goal-directed therapy guided by esophageal Doppler helped them precisely determine when the patients needed fluid boluses. Goal-directed therapy using advanced monitoring techniques is the best way to
manage fluid resuscitation during surgeries with potential for significant blood loss or fluid shifts. Certainly, it is much better than using our outdated formulas to determine fluid requirements. Anesthesia providers should become proficient with goal-directed therapy and gain experience with the various monitoring devices and techniques.

Dennis Spence, PhD, CRNA

**Causes of postoperative visual loss** include either central retinal artery occlusion and ischemic optic neuropathy. Central retinal occlusion is caused by compression of the eye, whereas the causes of ischemic optic neuropathy are poorly understood.

A randomized controlled trial that uses a **factorial design** allows for the independent evaluation of two or more experimental interventions. That is why the investigators in this study were able to separate out the effects of bromonidine and colloid administration on IOP. Readers are referred to an easy to read review article on randomized controlled trial designs by Stolberg et al at http://www.ajronline.org/content/183/6/1539.full.pdf+html.

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 Application of Dexmedetomidine in Children Undergoing Vitreoretinal Surgery

Lili X., Jianjun S, Haiyan Z

Abstract

Purpose The purpose of this study was to determine how dexmedetomidine affected intraocular pressure, hemodynamic patterns, extubation responses and emergence characteristics (i.e. delirium) in the pediatric patient undergoing vitreoretinal surgery.

Background Administering an anesthetic for small children having ophthalmic surgical procedures can be challenging. Rendering the patient immobile and preventing anesthetic related increases in intraocular pressure are often necessary. Typically, the volatile agent sevoflurane is used because it is well tolerated when used for an inhalation induction, has a low toxicity profile, and provides stable vital signs as well as rapid emergence. However, emergence delirium may occur in up to 80% of pediatric patients. Some intravenous anesthetic agents have been used in an effort to reduce or eliminate emergence delirium but responses have been inconsistent. Dexmedetomidine, a selective alpha-2 adrenergic receptor agonist, has sedative, analgesic, anxiolytic, and sympatholytic properties. In addition, it does not cause respiratory depression. This research was conducted to determine if dexmedetomidine could be added to a standard sevoflurane anesthetic to minimize or eliminate behavior that typically caused an increases in intraocular pressure (IOP) during emergence.

Methodology This was a prospective, randomized, double blind clinical trial. A total of 60 children, aged 3-7 years, were enrolled. The children were placed in 1 of 2 groups as follows: Group D received dexmedetomidine 0.5 µg/kg diluted in normal saline to a volume of 10 mL over 10 minutes subsequent to a sevoflurane inhalation induction and placement of an IV. Group P received a placebo of normal saline 10 mL during the same time frame. All children received a standardized anesthetic which included 1-2% end-tidal sevoflurane and a remifentanil infusion. Baseline intraocular pressures were measured after inhalation of sevoflurane and again 10 minutes after the dexmedetomidine or placebo infusion. All children were extubated awake and the cough reflex was observed for the first 15 minutes following extubation with the incidence and severity assessed via a 4 point scale. Also documented was the incidence of airway irritability after extubation, the severity of emergence delirium, and pain scores via a modified CHIPPS scale.

Results There were no statistically significant differences in the demographic profiles between the two groups.
1) IOP was no different between groups at the two time points it was measured.
2) MAP and HR were lower during extubation in the D group (P<0.05)
3) Coughing episodes (10 vs. 21) were fewer in the D group (P<0.05)
4) Coughing was less severe (3 moderate & 7 minimal in group D; vs. 2 severe, 7 moderate & 12 minimal in group P) in the D group (P<0.05)
5) The incidence of emergence delirium / agitation (10% vs. 43%) was lower in the D group (P<0.05)
6) Time to emergence & time to extubation were no different between groups.

The remaining variables measured between the 2 groups, such as time to extubation; airway irritability (laryngospasm, bronchospasm); and pain scores, were not significantly different between groups.

**Conclusion**

This study demonstrated that pediatric patients having vitreoretinal surgery who received dexmedetomidine 0.5 µg/kg over 10 minutes in a one time dose exhibited less coughing compared to placebo during extubation, had a lower MAP and HR during extubation, and lower incidences of emergence delirium. Dexmedetomidine did not influence IOP or intra operative vital signs compared to placebo.

**Comment**

It is widely accepted that IOP is largely dependent upon the balance between the formation and drainage of aqueous humor and somewhat affected by changes in choroidal blood volume, vitreous volume, and extra ocular muscle tone. Choroidal blood flow and hence IOP decrease when the mean arterial pressure falls below 90 mmHg. While previous studies found that the administration of dexmedetomidine resulted in lower IOP, it may have been the result of a lower MAP induced by the drug versus the direct effects of dexmedetomidine on alpha-2 receptors. Nonetheless, there are certain situations that warrant a reduction in IOP, such as certain eye procedures. Dexmedetomidine appears to have a role in preventing increases in IOP from occurring. Additionally, the drug itself appears to be quite favorable in terms of its sedative properties, especially in regards to the prevention of emergence delirium often seen in the pediatric patient. While emergence delirium itself may not create a physiologic crisis (unless it progresses to or precipitates an airway emergency), it is quite unsettling to the patient, the caregivers, and certainly the parents of the child. And one could reasonably ask, might preventing agitation during emergence also prevent increases in IOP?

Many of the properties of sevoflurane provide favorable outcomes in the pediatric patient; it would be a shame to reduce its use due to the moderately high incidence of emergence delirium. Administering other medications to minimize emergence delirium has proven problematic, for example narcotics or benzodiazepines, which can cause respiratory depression and prolonged emergence. The sedative, analgesic, anxiolytic, and sympatholytic properties of dexmedetomidine appear helpful for promoting a smooth emergence when combined with sevoflurane in the pediatric patient.

Mary Golinski, PhD, CRNA
Dexamethasone for prophylaxis of postoperative nausea and vomiting associated with neuraxial morphine administration: A systematic review and meta-analysis

Anesth Analg 2012;114:813-22
Allen TK, Jones CJ, Habib AS

Abstract

Purpose The purpose of this systematic review was to determine if dexamethasone prophylaxis was efficacious in reducing the incidence of postoperative nausea and vomiting (PONV) after the administration of neuraxial morphine.

Background Previous research has demonstrated that dexamethasone is effective in decreasing PONV. However, its role in reducing PONV after neuraxial morphine is less clear.

Methodology The investigators performed a systematic review of the literature to identify articles published from 1966-2011 on dexamethasone and neuraxial morphine-induced postoperative nausea and vomiting. Only randomized controlled trials comparing single dose dexamethasone with placebo where included when a single dose of neuraxial preservative-free morphine was administered.

Result Eight studies were included in this systematic review; 4 cesarean deliveries and 4 total abdominal hysterectomies. In these studies, 473 patients received dexamethasone and 295 patients received placebo. All subjects were female. Doses of dexamethasone ranged from 2.5 to 10 mg. Seven of the eight studies where published in Taiwan, while the remaining study was published in the United Kingdom. All seven of these studies were published by the same research group. Spinal anesthesia was the primary technique in one study, combined spinal anesthesia in one study, and in six studies epidural anesthesia was the primary anesthetic technique.

Dexamethasone, in doses ranging from 5 to 10 mg, significantly reduced the incidence of postoperative nausea (19% vs. 36%, Figure 1). Above 5 mg, there was no added benefit for prevention of nausea. Dexamethasone 2.5 mg was ineffective in decreasing the incidence of postoperative nausea. After total abdominal hysterectomy, dexamethasone reduced the incidence of postoperative nausea by over 15 percentage points, 15% vs. 32% in the control group, and by 18 percentage points after cesarean delivery (23% vs. 41%). Dexamethasone reduced postoperative nausea when compared to placebo after epidural morphine (14% vs. 31%). However, no difference was found in postoperative nausea following intrathecal administration of morphine (52% vs. 58%); although, only 2 studies examined the use of intrathecal morphine.
Dexamethasone was effective in reducing the incidence of postoperative vomiting by 15 percentage points (15% vs. 30%). Only doses of 5 mg, 8 mg and 10 mg were effective in reducing vomiting. There was no evidence of a dose response relationship as the dose increased. Postoperative vomiting was reduced by 16 percentage points after total abdominal hysterectomy (9% vs. 25%) and cesarean delivery (20% vs. 36%). When examining the route of morphine administration, dexamethasone was effective in reducing vomiting after epidural morphine (9% vs. 24%); but, again, not following intrathecal morphine (50% vs. 55%).

Dexamethasone, in doses ranging from 5 to 10 mg, significantly decreased the need for antiemetic rescue therapy (16% vs. 35%). Dexamethasone reduced the need for antiemetic rescue therapy after total abdominal hysterectomy (13% vs. 31%), and after cesarean delivery (18% vs. 38%). Dexamethasone was also effective in reducing the need for rescue antiemetic therapy after epidural morphine (12.8% vs. 32.8%), but, again, it was not effective after intrathecal morphine (35% vs. 42%).

Dexamethasone statistically significantly reduced postoperative pain scores when compared to placebo; however the differences were not clinically significant (mean difference 0.30 mm on a 0-100 mm visual analogue scale). The incidence of pruritus was not reduced with dexamethasone (52% vs. 56%).

**Conclusion**  Dexamethasone was effective in reducing the incidence of PONV and need for rescue therapy after neuraxial administration of morphine in women undergoing total abdominal hysterectomy and cesarean delivery. Pain scores and the incidence of pruritus were unaffected.
Comment

Dexamethasone is one of several drugs that has been demonstrated to be efficacious in reducing PONV after administration of intravenous opioids. Results of this meta-analysis provide further support demonstrating dexamethasone efficacy after administration of neuraxial morphine in women undergoing total abdominal hysterectomy and cesarean delivery. This finding is important because the majority of patients who receive neuraxial morphine are women having these procedures.

What is surprising is that dexamethasone was not effective in reducing PONV after intrathecal morphine. The small sample size in the subgroup examining intrathecal morphine may have obscured the effect of dexamethasone. The timing of dexamethasone administration could have been part of the problem as well, because dexamethasone was administered before epidural morphine but after intrathecal morphine. Dexamethasone has a long onset of action, almost 2 hours, and thus may not be as effective when administered after intrathecal morphine, because PONV has a faster onset after intrathecal opioid administration. While these results are inconclusive, I think given the other findings of this study I would still administer dexamethasone prophylactically before intrathecal morphine administration.

One of the issues the authors of this systematic review found was that all but one study was published by the same research group. When I see this it always makes me view the results with a little skepticism. However,

given previous evidence based practice guidelines recommending the inclusion of dexamethasone for prevention of PONV, I think this is a minor issue.

Dennis Spence PhD, CRNA

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Nitrous oxide and long-term morbidity and mortality in the ENIGMA trial

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Abstract

Purpose The purpose of this study was to examine the incidence of death, myocardial infarction (MI), and stroke following anesthetics greater than two hours long with vs. without nitrous oxide. MI was defined by cardiac enzyme changes and either ECG changes, a procedure to improve coronary circulation, or pathologic findings of an MI. Stroke was defined as a new deficit lasting at least 24 hours.

Background Long term cardiovascular morbidity and mortality may be increased in patients with significant exposure to nitrous oxide. While a cause and effect link has not been established, a credible scientific rational can be described. Nitrous oxide inhalation results in the inactivation of methionine synthase and a dose-dependent increase in homocysteine that persists for some time after an anesthetic level exposure to nitrous oxide has ended. Bench science studies suggest that homocysteine may be thrombogenic. Elevated homocysteine levels may also result in immunosuppression and atelectasis. Excessive levels of plasma homocysteine impair vascular dilation and may “destabilize” coronary artery plaques. Previous studies have suggested that nitrous oxide may be associated with postoperative myocardial ischemia and other cardiovascular events.

The original analysis of the ENIGMA trial revealed that postoperative 30 day mortality and myocardial infarction were each higher in the group that received 70% nitrous oxide, but not statistically significantly. Plasma homocysteine was elevated in all patients who received nitrous oxide.

Methodology This was a secondary analysis of a prospective, multi-center, multi-national, randomized controlled trial. The secondary analysis was performed in an attempt to better assess the effects of nitrous oxide use on the incidence of postoperative death, MI, and stroke. In the original study, 2,050 patients having noncardiac procedures lasting longer than two hours were randomized to receive a general anesthetic with either 70% nitrous oxide and 30% oxygen or 80% oxygen and 20% nitrogen. Inclusion and exclusion criteria did not consider cardiovascular risk factors. Other aspects of the anesthetic were not controlled, but up to the discretion of the anesthesia provider.

In this secondary analysis, statistical methods were used in an attempt to prevent patient variables and differences in anesthetic technique from obscuring the differences in cardiovascular morbidity and mortality between groups. Patient variables included age, weight, ASA physical status, anemia, emergency...
surgery, and type of surgery. Differences in anesthetic technique included specific drugs used (other than nitrous oxide), MAC level of inhalation agent used intraoperatively, and duration of anesthesia.

While statistical methods were generally appropriate, the use of a paired t-test, while not uncommonly used in similar situations, may well have made it artificially easier to achieve statistically significant results.

**Result** This secondary analysis included 1,290 patients from the ENIGMA trial, approximately half of whom received nitrous oxide in their general anesthetic and half who did not. Only 11% of these 1,290 patients reported a history of coronary artery disease and even fewer, 4%, a history of stroke. Overall, 91 patients (4.5%) had a postoperative MI and 44 patients (2.2%) had stroke.

The overall risk of postoperative death was not increased in the nitrous oxide group (P= 0.82). Factors that were associated with higher rates of postoperative death included increasing age, male gender, abdominal surgical procedures, propofol maintenance, MAC equivalent less than 0.75, and longer duration of anesthesia. Likewise, the odds of a postoperative stroke was not increased in the nitrous group (odds ratio 1.01, P=0.97).

The odds of a postoperative MI in patients in the nitrous group, after adjusting for the effects of potentially confounding variables, was 1.59 (P=0.04). In patients with an MI, plasma homocysteine levels were significantly increased compared to preoperative levels and MI patients were more likely to have homocysteine levels above than the normal range.

**Conclusion** In cases longer than 2 hours, 70% nitrous oxide was associated with a 59% increase in the long term risk of an MI. Rates of postoperative stroke or death were not increased.

**Comment** Perhaps you can chalk it up to when I was trained, but I have long argued for the continued use of nitrous oxide in anesthesia. Over the years detractors have tried to tell us that nitrous oxide should be significantly curtailed or eliminated from anesthesia practice. “Nitrous oxide causes PONV,” they said. Studies were produced that supported and refuted this assertion. Eventually a well done metaanalysis showed that, indeed, nitrous did increase the risk of PONV, but only slightly. So, nitrous became a factor to include when considering the risk of PONV, but not a pariah. Next it was discovered that nitrous oxide inhalation temporarily and dose dependently inactivated methionine synthase, resulting in inhibition of DNA synthesis for up to six days postoperatively in critically ill patients. But this finding never seemed to result in any harm that was clinically detectable. Nitrous oxide was even blamed by the popular press in Europe for patient deaths involving misconnection of oxygen supply pipelines. But this had more to do with the lack of inspired oxygen monitoring than the presence of nitrous oxide. … That was then, this is now.
For years now, those who were watching nitrous oxide closely (and I confess, until now I wasn’t one of them) were seeing signs that it might be associated with adverse outcomes that resulted in real, noticeable, clinically significant, patient harm. The original ENIGMA trial and analysis suggested that the rate of death and myocardial infarction within 30 days postoperatively might have been higher in patients who received 70% nitrous oxide for at least 2 hours during their anesthetic but the results were not statistically significant. The problem with this is that when one collects data for a study, it is possible to have little clusters of things like an MI in one group that really have nothing to do with the study. We use statistics to be sure that the difference in the number of myocardial infarctions is really there, really real. And because the original analysis didn’t take other factors that could affect the incidence of MI into consideration, we call them confounding variables, even if the difference in myocardial infarction was real it might have been due to a confounding variable and not the nitrous oxide. So, in this secondary analysis, they adjusted the analysis to eliminate confounding variables and collected some additional data about patient health postoperatively. What they found was a 59% increase in the risk of a postoperative MI in patients who received 70% nitrous vs. 80% oxygen. While this finding still doesn’t indicate that nitrous caused the increase in myocardial infarctions, the association is strong enough that we must pay attention to it. In fact, if nitrous oxide does cause harm, it may be even more severe than suggested by the original ENIGMA study. Few of the patients in that study had cardiovascular risk factors. We have to wonder if nitrous is even more harmful in patients with preexisting cardiovascular risk. And, the study was conducted primarily in first world medical centers. The lack of a difference in postoperative death rates may simply have been due to high quality follow up health care.

The original ENIGMA trial was not without its limitations. Controls for confounding variables were not as strong as one would like. And the groups were not even directly comparable since the nitrous group received only 30% oxygen while the group without nitrous received 80% oxygen. But data collection for the ENIGMA-II study is just finishing and this follow up study should produce much stronger results. ENIGMA-II may well determine the future of nitrous oxide in anesthesia. In the meantime, we might do well to start modifying our approach from deciding when not to use nitrous oxide as part of our anesthetic to when we can justify including it.

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For a more complete discussion of this topic, consider attending the online webinar, “Nitrous Oxide: the ENIGMA Trials” available on CRNAwebinars.com. 1 CE credit.