## Patient Safety Tip of the Week

# March 3, 2015 Factors Related to Postoperative Respiratory Depression

Two of our most frequent topics have been opioid-induced postoperative respiratory depression and perioperative obstructive sleep apnea (OSA). See the extensive list of our prior columns at the end of today's column. This past month there have been a number of significant articles pertinent to both conditions.

We'll start with a review of closed claims with postoperative opioid-induced respiratory depression (Lee 2015). The authors searched the Anesthesia Closed Claims Project database between 1990 and 2009 for cases likely to include postoperative opioid-induced respiratory depression. They found 92 probable, possible or definite claims, 77% of which resulted in death or severe brain damage.

Most of the patients were middle aged, obese and had low ASA scores. 16% had OSA diagnosed preoperatively and another 9% were at high risk. Lower extremity orthopedic procedures were overrepresented (41%).

Nearly half received **opioids via more than one modality** and nearly half were on a **continuous opioid infusion** at the time of the event. Morphine and fentanyl were the two most commonly administered opioids. A third were also receiving **non-opioid sedating medications**. Significantly, a third had **more than one physician prescribing** opioids or other sedating agents. Just as significantly, only 16% were on doses of opioids that the reviewers thought were excessive.

Most events (88%) occurred within 24 hours of the surgical procedure, 13% occurring within 2 hours of transfer from the postoperative recovery room. In 12 of the cases nursing assessments had been done within 15 minutes prior to the event. Importantly, **60% of patients had been described as somnolent, with or without snoring, prior to the event**. And reviewers felt that nursing checks were inadequate in at least one respect in 31% of cases. **Respiratory monitors and pulse oximetry were in use in less than half**, and none of those were on telemetric pulse oximetry. Reviewers felt that **97% of the events were possibly or probably preventable by better monitoring**.

Their findings suggest a substantial gap in understanding the signs and symptoms of this opioid-related postoperative phenomenon. In particular, **somnolence and snoring were often underappreciated** as critical signs of impending respiratory depression. That was a

point we noted in our February 12, 2013 Patient Safety Tip of the Week "CDPH: Lessons Learned from PCA Incident".

It's hoped that reporting of incidents and near misses of such cases may improve our understanding of all the factors involved in enabling these unfortunate events. The most recent APSF Newsletter discusses the **Obstructive Sleep Apnea (OSA) Death and Near Miss Registry**, which now accepts case reports (Posner 2015). That article describes what is required in case reports and notes that case report forms and instructions can be downloaded from the registry website.

Following reports on serious complications following tonsillectomy in children (Goldman 2013, Cote 2014) that implicated postoperative respiratory depression and obstructive sleep apnea worsened by opioid therapy, there have been a number of editorials about "the elephant in the room". Brown and Brouillette (Brown 2014), commenting on the Goldman and Cote and other studies, discussed many of the physiological aspects of respiratory depression and OSA and opioid therapy in children. They note that not only do opioids blunt the ventilator response to hypercarbia and hypoxemia and blunt the arousal responses to OSA but they also note that hypoxemia reduces the dose of narcotics required to alleviate pain in children.

While the Goldman, Cote, and Brown papers dealt with pediatric patients, Benumof (Benumof 2015) noted the bigger problem (the "elephant in the room") involves all patients undergoing all surgeries. He notes the prototypical "dead in a bed" patient is an obese adult patient with severe OSA receiving opioids postoperatively without continuous electronic monitoring, oxygen supplementation or CPAP. He further calls attention to the creation of the Obstructive Sleep Apnea (OSA) Death and Near Miss Registry mentioned above. Brown and Brouillette, responding to Benumof's letter, again note that not all cases of OSA are diagnosed before surgery and again mention the McGill Oximetry Score as a potential tool that might be of use in screening (Benumof 2015). That system supplements a careful clinical assessment with home nocturnal pulse oximetry. They acknowledge, however, that the tool needs to be validated in a number of populations.

And, speaking of children, don't forget that the recent warnings about use of codeine in children first originated after deaths of pediatric patients receiving codeine after adenotonsillectomy for OSA (see our What's New in the Patient Safety World columns for September 2012 "FDA Warning on Codeine Use in Children Following Tonsillectomy" and March 2013 "Further Warning on Codeine in Children Following Tonsillectomy" and our May 2014 "Pediatric Codeine Prescriptions in the ER"). These highlighted the fact that those patients with CYP2D6 ultrarapid metabolism were especially prone to post-tonsillectomy respiratory depression and suggested that codeine not be used in children undergoing adenotonsillectomy for OSA.

Undoubtedly, the use of codeine after adenotonsillectomy for OSA has diminished significantly after these reports and warnings. However, that does not mean that there has been a switch to safer alternatives. Two recent reports illustrate safety issues that have

occurred with use of morphine and tramadol, respectively, in children after adenotonsillectomy for OSA. Kelly and colleagues conducted a prospective randomized clinical trial in children who had sleep disordered breathing who were scheduled for tonsillectomy with or without adenoid removal (Kelly 2015). Children were randomized to receive acetaminophen with either oral morphine or oral ibuprofen. On the first postoperative night oxygen desaturations were improved in 68% of the ibuprofen group vs. only 14% in the morphine group. In fact, the number of desaturation events increased substantially in the morphine group. There were no differences seen in analgesic effectiveness, tonsillar bleeding, or adverse drug reactions. The study was actually terminated early after the interim analysis demonstrated the increased risks with morphine. The authors conclude that ibuprofen in combination with acetaminophen provides safe and effective analgesia in children undergoing tonsillectomy and that post-tonsillectomy morphine use may be unsafe and its use should be limited.

The second paper (Orliaguet 2015) described a 5-year old boy who underwent adenotonsillectomy who received one oral 20 mg dose of **tramadol** and was brought back to the ED the day after surgery with unresponsiveness, pin-point pupils, poor respiration, and oxygen desaturation. He responded dramatically to noninvasive ventilation and intravenous naloxone and fully recovered. CYP2D6 genotyping confirmed the pattern associated with ultrarapid metabolism. Like those in the first paper, the authors suggest use of NSAID's as an alternative to opioids in children with OSA undergoing tonsillectomy.

Unlike the case in adults, where tools like STOP-BANG are often used to predict OSA, there is no consensus on tools to predict OSA in children. In their study focusing on death and neurological injuries following tonsillectomy Cote et al. concluded that at least 16 children could have been rescued had respiratory monitoring been continued throughout first- and second-stage recovery, as well as on the ward during the first postoperative night (Cote 2014). Those authors stressed the need for a validated pediatric-specific risk assessment scoring system to assist with identifying children at risk for OSA. That might help determine which children are not appropriate to be cared for on an outpatient basis. In our May 13, 2014 Patient Safety Tip of the Week "Perioperative Sleep Apnea: Human and Financial Impact" we noted screening tools for OSA have been of relatively little value in children (Wild 2014). The authors found that, though identifying 85% of children with moderate to severe OSA, the American Society of Anesthesiologists screening tool for moderate to severe OSA (MSOSA) had a 78% false positive rate. The McGill Oximetry Score mentioned above (Brown 2014, Benumof 2015) is promising. It has a 97% positive predictive value vs. polysomnography in children and may help identify severity although an inconclusive study does not rule out milder OSA (Brown 2014). But it's yet to be tested in a randomized, controlled trial. The recently reported CHAT (Childhood Adenotonsillectomy) study (Mitchell 2015) identified a number of clinical parameters that correlate with severity of OSA. However, information on demographics, physical findings, and questionnaire responses did not robustly discriminate different levels of OSAS severity.

While we strongly recommend screening for OSA and respiratory risk prior to surgery, it is probably not possible to identify all patients at risk for respiratory depression when exposed to opioids. Therefore, monitoring becomes critical. Our Patient Safety Tips of the Week for February 19, 2013 "Practical Postoperative Pain Management" and May 6, 2014 "Monitoring for Opioid-induced Sedation and Respiratory Depression" discuss many of the important clinical signs and symptoms and use of tools such as the Pasero Opioid-induced Sedation Scale (POSS) and the Richmond Agitation and Sedation Scale (RASS). As above, we need to better educate everyone on recognition of somnolence and snoring as danger signs. But the Lee study (Lee 2015) and numerous anecdotal reports clearly show that episodic vital sign monitoring is grossly inadequate in identifying postoperative respiratory depression. **Continuous monitoring** is needed. In our March 26, 2013 Patient Safety Tip of the Week "Failure to Recognize Sleep Apnea Before Surgery" we noted that means continuous monitoring of respiratory rate and pattern, oxygenation status, and capnography. Capnography has now become the standard of care for monitoring patients with OSA who are on opioids. As in our February 12, 2013 Patient Safety Tip of the Week "CDPH: Lessons Learned from PCA Incident" sidestream capnography used in unintubated patients may not be particularly good at detecting hypercarbia but is useful in monitoring respiratory rate and detecting apnea. And don't forget that sedative/hypnotic drugs may also be dangerous in patients with OSA, particularly when used in conjunction with opioids.

Monitoring is probably the most important aspect of care of the patient with suspected OSA and there remain problems with the threshold-based alarm systems most often used today. Lynn and Curry (Lynn 2011) described 3 patterns of unexpected in-hospital deaths (see our February 22, 2011 Patient Safety Tip of the Week "Rethinking Alarms"). The third pattern they describe is one that is typically seen in sleep apnea. In this pattern one sees repetitive reductions in airflow and oxygen saturation during sleep followed by arousals. The arousals rescue the patient but **eventually the capacity or reserve of the patient to recover with arousals becomes impaired** (often in response to narcotics or sedatives) and the patient may experience **sudden death during sleep**. The authors discuss the inability of currently used oximeters to recognize this pattern. They even imply that this pattern may give rise to oximeters alarming and being interpreted as "false" alarms attributed to motion artifact, etc. because when staff respond to the alarm the patient is now awake, breathing normally and has a normal oxygen saturation.

The issue of supplemental oxygenation is still much debated. We've mentioned on numerous occasions that supplemental use of oxygen may mask impending respiratory depression, particularly in those patients not being monitored with capnography, and may provide a false sense of security.

The issue of **perioperative use of CPAP** is also still in debate. If a patient has known OSA and has been on CPAP at home, they should get CPAP post-operatively (preferably with their own CPAP equipment brought in from home). But the evidence base for use of CPAP, NIPPV, BiPAP, or APAP in those not previously on CPAP at home is not robust. Our Patient Safety Tips of the Week for September 24, 2013 "Perioperative Use of CPAP in OSA" and May 13, 2014 "Perioperative Sleep Apnea: Human and Financial Impact"

suggest that CPAP can be effective in the perioperative period, though compliance with CPAP is suboptimal. Meta-analyses of perioperative use of CPAP in OSA have recently been presented in abstracts at national meetings by the Toronto group that has done so much OSA research. The first suggests that there is a trend toward significance in reducing postoperative adverse events in the CPAP-treated group compared to the non-CPAP group but still acknowledges that further research is needed on the value of perioperative CPAP (Nagappa 2014a). The second (Nagappa 2014b) suggests that perioperative CPAP significantly reduces perioperative AHI (apnea-hypopnea index). Length of stay was not significantly shortened in OSA patients on CPAP undergoing surgery, but this may be due to the small number of patients in the analysis.

Postoperative opioid-induced respiratory depression remains a significant problem and one that is very much preventable. Better recognition of at-risk patients and careful monitoring strategies are needed to prevent this adverse event.

**Other Patient Safety Tips of the Week pertaining to opioid-induced respiratory**

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| July 13, 2010 | "Postoperative Opioid-Induced Respiratory Depression" |
| May 12, 2009 | "Errors With PCA Pumps" |
| September 21, 2010 | "Dilaudid Dangers" |
| November 2010 | "More on Preoperative Screening for Obstructive Sleep Apnea" |
| January 4, 2011 | "Safer Use of PCA" |
| February 22, 2011 | "Rethinking Alarms" |
| May 17, 2011 | "Opioid-Induced Respiratory Depression – Again!" |
| September 6, 2011 | "More Tips on PCA Safety" |
| December 6, 2011 | "Why You Need to Beware of Oxygen Therapy" |
| February 21, 2012 | "Improving PCA Safety with Capnography" |
| September 2012 | "Joint Commission Sentinel Event Alert on Opioids" |
| September 2012 | "FDA Warning on Codeine Use in Children Following Tonsillectomy" |
| July 3, 2012 | "Recycling an Old Column: Dilaudid Dangers" |
| February 12, 2013 | "CDPH: Lessons Learned from PCA Incident" |
| February 19, 2013 | "Practical Postoperative Pain Management" |
| May 6, 2014 | "Monitoring for Opioid-induced Sedation and Respiratory Depression" |
| Tools: | PCA Pump Audit Tool and the PCA Pump Criteria |

**Our prior columns on obstructive sleep apnea in the perioperative period**:

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| June 10, 2008 | "Monitoring the Postoperative COPD Patient" |
| August 18, 2009 | "Obstructive Sleep Apnea in the Perioperative Period" |
| August 17, 2010 | "Preoperative Consultation – Time to Change" |
| July 2010 | "Obstructive Sleep Apnea in the General Inpatient Population" |

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| July 13, 2010 | "Postoperative Opioid-Induced Respiratory Depression" |
| November 2010 | "More on Preoperative Screening for Obstructive Sleep Apnea" |
| February 22, 2011 | "Rethinking Alarms" |
| November 22, 2011 | "Perioperative Management of Sleep Apnea Disappointing" |
| March 2012 | "Postoperative Complications with Obstructive Sleep Apnea" |
| May 22, 2012 | "Update on Preoperative Screening for Sleep Apnea" |
| February 12, 2013 | "CDPH: Lessons Learned from PCA Incident" |
| February 19, 2013 | "Practical Postoperative Pain Management" |
| March 26, 2013 | "Failure to Recognize Sleep Apnea Before Surgery" |
| June 2013 | "Anesthesia Choice for TJR in Sleep Apnea Patients" |
| September 24, 2013 | "Perioperative Use of CPAP in OSA" |
| May 13, 2014 | "Perioperative Sleep Apnea: Human and Financial Impact" |

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