



Learning From Others:

Anesthesia
Quality Institute
ANESTHESIA INCIDENT
REPORTING SYSTEM (AIRS)

A Case Report From the Anesthesia Incident Reporting System

Detailed review of unusual cases is a cornerstone of anesthesiology education. Each month, the AQI-AIRS Steering Committee will abstract a case and provide a detailed discussion based on a submission to the national Anesthesia Incident Reporting System. Feedback regarding this item can be sent by email to r.dutton@asahq.org. Report incidents to www.aqiairs.org.

Case 2012-10: Intrathecal Apnea

A 36-year-old ASA II man presented for resection of a liver mass. Preoperatively, the patient was given intrathecal morphine 0.25 mg. During the procedure, he received intravenous hydromorphone totaling 0.9 mg. The patient met criteria for extubation, but after removal of the endotracheal tube and transport to the PACU he was noted to have shallow breathing and arterial oxygen desaturation. Several minutes later he became apneic. The patient was ventilated with bag and mask for several minutes. Administration of naloxone 0.4 mg I.V. restored the patient to a regular respiratory rate, which was sustained throughout the PACU stay. The patient remained extremely sedated; additional doses of naloxone did not lead to increased arousal. The patient was monitored in the PACU for the next 24 hours, with gradual return of normal neurologic function. Further analgesia was not required until 12 hours postoperatively.

Discussion

Postoperative respiratory failure (PRF) is a quality indicator that is tracked nationwide. Among all hospital discharges after elective surgery, a discharge is considered to have PRF if it carries a secondary diagnosis code for acute respiratory failure, not present on admission. According to the Agency for Healthcare Research and Quality, the overall rate of postoperative respiratory failure in 2008 was 9.5 per 1,000 discharges, down from the 2004 rate of 10.4 per 1,000 discharges.¹

Data from the National Surgical Quality Improvement Program (NSQIP) have been used to assess PRF, defined as failure to wean from mechanical ventilation within 48 hours of surgery or an unplanned postoperative reintubation.² Using this definition, 3.1 percent of NSQIP patients in 2007 developed PRF. However, it is likely that cases of opioid-related respiratory depression such as this one are minimally represented in that data set and are greatly under-reported, as most do not result in

re-intubation. Thus, the true incidence of these cases remains unknown.

As of this writing, 18 of the 604 submissions to the AIRS database describe postoperative respiratory depression. Causes include excessive opioid administration, inadequate recovery from neuromuscular blockade, laryngospasm, prolonged sedative effects of methadone (which can outlast the analgesic effects) and medical issues such as pulmonary edema. The route, frequency and quantity of opiates administered in the perioperative period all influence the risk of postoperative respiratory depression. Postoperative respiratory depression is especially problematic in patients administered opioids by both the systemic and neuraxial route, and in those with increased sensitivity to opioids, such as patients with obstructive sleep apnea and intermittent hypoxemia. Furthermore, even with relatively modest opioid doses it is not unusual for a patient to become "re-sedated" once the excitement of emergence and extubation has passed and they are tucked comfortably into a quiet and darkened PACU bay.

Intrathecal opioids have gained a place in the anesthetic armamentarium for effective long-duration analgesia, particularly for obstetric and major abdominal and thoracic surgery. In some studies, intrathecal morphine has been found to offer more intense analgesia than intravenous PCA morphine,³ and it provides more continuous and less labor-intensive analgesia once the initial dose is given. The dose of intrathecal narcotics required to produce analgesia is much lower than the intravenous dose, which creates potential for postoperative respiratory depression if a dosing error occurs.

When administered intrathecally, opioids can travel cephalad within the CSF, spread inward to the spinal cord and spread outward into the epidural space. The degree to which each of these effects occurs differs for lipophilic opioids (e.g., fentanyl) and hydrophilic opioids (e.g., morphine.) Lipophilic opioids deliver fast-onset but short-duration analgesia with little cephalad spread, producing a band of spinal levels near

the level of injection. Hydrophilic opioids will remain largely confined to the CSF and bind to opioid receptors in the spinal cord, resulting in a slow onset and wide band of affected spinal levels for a long period of time. For long-acting agents, spinal fluid circulation may eventually carry the drug all the way to the brain stem. For this reason, respiratory depression is uncommon with intrathecal fentanyl (primarily redistributed to the epidural space) or sufentanil (primarily redistributed to plasma), but a significant risk with intrathecal morphine.

Intrathecal opioid is much more potent than intravenous opioid; however, potency ratios vary greatly between drugs. For example, morphine has a 1:200 IT:IV potency ratio, but fentanyl's is only 1:4 due to differences in the binding and distribution of the drugs to opioid receptors in different tissue beds. The duration of intrathecal morphine is so long that although initial onset can occur as quickly as one hour, the peak analgesic effect does not occur until approximately six hours after administration.³ The peak respiratory depressant effect also occurs around this time. If a patient is in the O.R. for five hours, the peak respiratory depression may occur an hour after the patient arrives in the PACU. For this reason, any supplemental intravenous opioids used for the case should be short-acting and carefully titrated.

Naloxone is the primary medication used to rescue patients suffering from opioid-induced respiratory depression. It has a short duration of 30 to 45 minutes, meaning that multiple doses or a continuous infusion may be required to sustain reversal of long-acting narcotics. As this case demonstrates, a single dose (1 to 4 mcg/kg) can resolve respiratory depression for a time, but the neuraxial opioid will always last longer than the naloxone. For this reason, any patient treated with neuraxial opioid who experiences respiratory depression or apnea should be placed on a continuous naloxone drip (1-5 mcg/kg/hr, titrated to effect) and should remain in a closely monitored setting.

The ASA Task Force on Neuraxial Opioids has published a practice guideline on the management of respiratory depression associated with neuraxial opioids⁴:

- For a single injection of neuraxial lipophilic opioid (fentanyl), monitoring should be done for a minimum of two hours: continuously for 20 minutes, then periodically after that.
- For a single injection of neuraxial hydrophilic opioid (morphine), monitoring should be done for a minimum of 24 hours: continuously for 20 minutes, then every one hour to 12 hours, and every two hours until 24 hours.
- For a single injection of extended-release hydrophilic opioid (e.g., liposomal morphine), monitoring should be done for a minimum of 48 hours: continuously for 20 minutes, then every one hour to 12 hours, every two hours until 24 hours, and every four hours until 48 hours.

Recommendations:

Prevention of postoperative respiratory depression after intrathecal opioid treatment can be achieved through an understanding of the relative potency, kinetics and context-sensitive half-life of the agents involved. A hospital-wide policy for postoperative monitoring of patients who have received intrathecal opioids should be established. Nursing units that routinely receive patients with neuraxial medication should receive extra training on when to anticipate respiratory depression in these patients. Patients receiving intrathecal morphine should receive only small amounts of short-acting intravenous narcotic. Patients should be monitored in the immediate postoperative period with attention given to the timing of peak drug effect. If intrathecal morphine has been used, the PACU nursing staff should be advised when the six-hour peak will occur. Supervising anesthesiologists should resist administrative pressure to transfer these patients prematurely to less-monitored settings, even if they appear comfortable and hemodynamically stable.

If a patient does experience respiratory depression, a bolus of naloxone is appropriate for initial resuscitation, but a continuous infusion is indicated even if the patient appears to have recovered. A patient on a naloxone drip for respiratory depression should be kept in a monitored setting (e.g., ICU, PACU or step-down unit).

References:

1. Agency for Healthcare Research and Quality, National Healthcare Quality Report 2011. Accessed at <http://www.ahrq.gov/qual/nhqrl1/chap3txt.htm#fig38> on July 26, 2012.
2. Gupta H, Gupta PK, Fang X, Miller WJ, Cemaj S, Forse RA, Morrow LE. Development and validation of a risk calculator predicting postoperative respiratory failure. *Chest*. 2011 Nov;140(5):1207-1215.
3. Rathmell JP, Lair TR, Nauman B. The role of intrathecal drugs in the treatment of acute pain. *Anesth Analg*. 2005 Nov;101(5 Suppl):S30-43.
4. American Society of Anesthesiologists Task Force on Neuraxial Opioids. Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration. *Anesthesiology*. 2009; 110:218-230.