A 36-year-old ASA Physical Status II man presented for resection of a liver mass. Preoperatively, the patient was given a 250 mcg dose of intrathecal morphine. 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 400 mcg 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 ventilated 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 an important topic in anesthesia safety, which is why we are revisiting the topic after this column first looked at the above case in 2012.

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 2013 was 6.49 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. Using this definition, 3.1 percent of NSQIP patients in 2007 developed PRF. Of those patients, 30-day mortality was 25 percent. A risk model developed using NSQIP data identified type of surgery, emergency case, poor (dependent) functional status, sepsis and ASA Physical Status as predictors of PRF.² A similar study published in 2011 examined predictors of postoperative intubation in noncardiac surgery patients and concluded that half of PRF events occurred in the first three days after surgery.³ Requirement for re-intubation was associated with a nine-fold increase in mortality. A third study to develop a respiratory failure risk score using only history and physical variables developed a model with 12 variables.⁴ The highest weight came from procedure type, recent ascites and dependent functional status.

Submissions to the AIRS database that describe postoperative respiratory depression cite multiple causes, including excessive opioid administration, inadequate recovery from neuromuscular blockade, laryngospasm and pulmonary edema. Postoperative respiratory depression is a risk in patients who have received large amounts of intravenous opioid or neuromuscular blockade. Once the excitement of emergence has passed, and the patient is tucked away into a darkened PACU bay, the patient may become “re-sedated.” The route, frequency and quantity of opiates administered during the case will influence the risk of postoperative respiratory depression.

Intrathecal opioids provide long-duration analgesia and are particularly useful for obstetric and major abdominal surgery. The goal of intrathecal opioid use is to provide improved analgesia with fewer side effects, which can lead to better postoperative respiratory effort. In some studies, intrathecal morphine has been found to offer more intense analgesia than intravenous PCA morphine,⁵ and it provides for more continuous and less labor-intensive analgesia once the initial dose is given.

When administered intrathecally, opioids will travel cephalad within the CSF, spread inward to the spinal cord, and spread outward toward 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 will migrate to the plasma and be removed and metabolized quickly, providing fast-onset, brief-duration analgesia for a narrow band of spinal levels near the level of injection. Hydrophilic opioids will remain largely confined to the CSF, 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.
Intrathecal opioid is much more potent than intravenous opioid. For example, morphine has a 1:200 IT:IV potency ratio. The duration of intrathecal morphine is so long that the peak analgesic effect does not occur until approximately six hours after administration. The peak respiratory 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 intrathecal 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 action of 30 to 45 minutes. A continuous infusion may be required to sustain narcotic reversal. 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 dyspnea or apnea should be placed on a continuous naloxone drip (5 mcg/kg/hr) and should remain in a closely monitored setting.

**ASA Neuraxial Opioid Guideline Update**

The ASA Task Force on Neuraxial Opioids recently updated its practice guideline on the management of respiratory depression associated with neuraxial opioids:

- For a single injection of neuraxial lipophilic opioid (e.g., fentanyl), monitoring should be done for a minimum of two hours: continuously for 20 minutes, then at least once per hour.
- For a continuous infusion of neuraxial lipophilic opioid, monitoring should be done continuously for 20 minutes, then at least once per hour to 12 hours, then at least every two hours to 24 hours, and at least every four hours 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 continuous infusion of neuraxial hydrophilic opioid, initial monitoring should be done as for a single injection. After 24 hours, monitoring should be done at least once every four hours.

Prevention of postoperative respiratory depression after intrathecal opioid treatment can be achieved through an understanding of the relative potency and half-life of the agents involved. A hospital-wide policy for postoperative monitoring of patients who have received intrathecal opioid should be established. Nursing units that routinely receive patients with neuraxial medication should receive extra training on when to expect respiratory depression in these patients. Patients receiving intrathecal morphine should receive only small amounts of intravenous narcotic. Patients should be monitored in the immediate postoperative period with attention given to the timing of peak effect. If intrathecal morphine has been used, advise the PACU nursing staff when the six-hour peak will occur and insist on monitoring the patient in accordance with the task force guidelines. 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 should be kept in a monitored setting (i.e. ICU, PACU or step-down unit).

Supplemental oxygen should be used in patients showing signs of respiratory depression or altered level of consciousness. However, oxygen can make it more difficult to detect hypventilation and hypercarbia.

Targeted use of intrathecal opioid can improve postsurgical recovery by reducing the patient’s overall opioid requirement. However, anesthesiologists and PACU staff need to be aware of the unusual properties of intrathecal medication and be prepared for episodes of postoperative respiratory failure.

**References:**

4. Johnson AP, Altmark RE, Weinstein MS, Pitt HA, Yeo CJ, Cowan SW. Predicting the risk of postoperative respiratory failure in elective abdominal and vascular operations using the National Surgical Quality Improvement Program (NSQIP) participant use data file [published online September 6, 2016]. Ann Surg.