

DRUG-INDUCED RESPIRATORY DEPRESSION IN ACUTE PAIN MANAGEMENT – THE SLEEPING CHALLENGE

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Opioids form the backbone of most analgesic strategies, yet their use in acute post-operative pain is associated with an unappreciated degree of morbidity and mortality. The use of an unbalanced strategy for pain management, which emphasises the need for better pain management and lower pain scores without stressing the need for appropriate patient assessment and monitoring, can and does lead to an increase in adverse events. In the Lee Moffatt Cancer Centre, aggressive adoption of PCA analgesia in response to the US JCAHO call for pain to be assessed as a "5th Vital Sign," resulted in a significant increase in opioid overdosage events and ICU admissions.¹ While some studies have indicated that neuraxial opioids pose a much higher risk than intravenous opioids (up to 7.9 times; 95% CI 1.4 – 40.3),² other comprehensive reviews have identified that PCA opioids, and even IM opioids, also carry a significant risk of adverse events.³ Data from our own institution supports this, with event rates of 0.8% for epidural opioids, 1.1% for IV PCA opioids and 2.2% for intrathecal morphine. However, a significant problem with all such analyses is that the definition of what constitutes respiratory depression is highly variable.

Opioid Induced Ventilatory Impairment (OIVI) more appropriately describes the impact of opioids on patients than the term 'respiratory depression,' because opioids affect consciousness (sedation), airway tone, and central respiratory drive.⁴ Postoperatively, the addition of sedatives, residual anaesthetic agents and fatigue further adds to these risks. Finally, individual patient factors may contribute as well – especially advanced age, obesity and a history of sleep disordered breathing (such as obstructive sleep apnoea). Any strategy to reduce the risk of OIVI in patients receiving parenteral opioids needs to address all these areas. It should be noted however, that the risk in a given individual is difficult to predict and many of the tragic cases of postoperative death related to the use of parenteral opioids occur in relatively young, apparently healthy individuals. Coroner's reports frequently identify a failure to adequately monitor patients postoperatively as a major contributing factor to adverse outcomes.

Monitoring strategies for OIVI should address all three of the above mentioned effects of opioids – sedation, depression of respiratory drive and loss of airway tone. Patient clinical observations should therefore include a standardised sedation score (perhaps the 6th vital sign), respiratory frequency and some assessment of airway patency. The latter is difficult by observation alone but includes training in identification of obstructive patterns of ventilation and an awareness of the risks of the 'snoring' patient. Probably the most controversial area is the clinical assessment of sedation. Assessment of simple arousal does not appear to be sufficient – and the ability to remain responsive for, say, 10 seconds or more seems to be important.⁵ Thus a sedation scale might be: 0 – awake, alert; 1 – mild sedation, easy to rouse by voice (10 second eye opening); 1S sleeping, easy to rouse; 2 – moderate sedation, easy to rouse BUT unable to remain awake (<10 second eye opening); 3 – difficult to rouse / unrousable. With such a scale a level of 2 or more would require a clinical intervention of some sort. The question of the sleeping patient is a vexed one, but overall the stakes are too high to 'ignore' sedation assessments in a patient who is apparently asleep.

The ideal frequency and duration of monitoring is uncertain, however most events occur within 24 to 36h of surgery.⁶ Assessment frequency should also be influenced by patient factors and changes in therapy. Many factors limit the ability of people to reliably perform clinical assessments; these include fatigue, distraction and inadequate training. Therefore to reliably care for these patients, monitoring for OIVI should be enhanced by electronic systems. This is a process that has been promoted by the Anesthesia Patient Safety Foundation (APSF) in the US.

Oxygen saturation monitoring (SpO₂) has been advocated as a requirement for all patients receiving parenteral opioids. The APSF summarised the sensitivity, specificity, reliability, response times and costs of a number of methods of monitoring ventilation and / or oxygenation – respiratory rate, tidal volume, continuous measurement of oxygen saturation and end-tidal CO₂, blood gas analysis, minute ventilation and chest wall impedance.⁷ Despite recognising the limitations of currently available monitors, and despite the low sensitivity of continuous pulse



oximetry in patients given supplemental oxygen (common in many countries), the recommendation of the APSF was for “the use of continuous monitoring of oxygenation (generally pulse oximetry) and ventilation in non-ventilated patients receiving PCA, neuraxial opioids or serial doses of parenteral opioids.”⁷ This approach has been questioned by the American Society of Anesthesiologists with respect to neuraxial opioids.⁸ In any case, if the patient is receiving supplemental oxygen, the added oxygen may mask deterioration in respiratory function and there can be reasons other than opioids for hypoxaemia, especially in the postoperative setting.⁹ Therefore, although useful for patient care, SpO₂ should not be relied upon on its own.

Sedation can be assessed electronically by BIS or Entropy, but these may be too sensitive and not specific enough for monitoring the unattended patient.¹⁰ They are also not very responsive to opioid induced sedation per se. Therefore sedation needs to be assessed by clinical response (arousal) in response to stimulation using a standardised scale (see above).

For measuring adequacy of ventilation, PaCO₂ should ideally be continuously monitored – the most reliable non-invasive current technology uses transcutaneous devices but they are not well-suited for longer-term use.^{11,12} Expiratory capnography has the advantage of monitoring actual ventilation and respiratory rate. Nasal sampling devices are more comfortable to wear and allow supplemental oxygen to be administered, but may dislodge. This is however, currently the most reliable monitor of OIVI. Respiratory rate may reflect the central respiratory effects of OIVI but non-capnographic assessments are unreliable.

Bedside-only alarm systems have the advantage that tones may serve as local arousal mechanisms, thus providing a safety reserve. All electronic systems have the disadvantage of causing ‘alarm fatigue’ and therefore being ignored by clinical staff. The best way to avoid frequent false alarms is not to rely on threshold based triggers but to intelligently monitor multiple parameters as well as analysing for patterns or trends in measured values, similar to the monitoring strategies used in anaesthesia. Consistent recording or charting of trends must be undertaken either electronically or manually.

Finally and importantly, strategies for intervention must be clearly defined to ensure that when a patient does show signs of deterioration, clinical staff have established responses that they can implement and unambiguous reporting and clinical care escalation pathways. The risks of OIVI are real and the frequency is higher than most clinicians expect. We need to detect problems at an early stage to increase the chance of avoiding significant and permanent patient harm.

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