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PLEASE NOTE: This statement is currently being reviewed following recent changes to the TGA approved indications for prescription opioids and the recent updates to the FPM document PS01(PM) *Statement regarding the use of opioid analgesics in patients with chronic non-cancer pain.*

Statement on principles for identifying and preventing opioid-induced ventilatory impairment (OIVI)

Statement on principles for identifying and preventing opioid-induced ventilatory impairment (OIVI) in the acute pain setting.

Introduction

Opioids are high-risk drugs that continue to be associated with preventable harm, including death, due to opioid-induced ventilatory impairment (OIVI). In the acute pain setting, monitoring that includes regular assessments of a patient's level of sedation, with appropriate early responses and interventions when excessive sedation is noted, can reduce the risk of harm. Identification of potentially avoidable risk factors is also important.

It has been suggested that all postoperative patients prescribed opioids should be monitored using continuous pulse oximetry, with the addition of continuous capnography in those patients receiving supplemental oxygen (Gupta & Edwards, 2018). It is acknowledged that provision of continuous electronic monitoring for every patient given an opioid for management of acute pain (including but not limited to postoperative pain) in every Australian and New Zealand hospital, although highly desirable, is currently not possible. Therefore, in the absence of this, detection and monitoring of OIVI can and must be improved through sedation score monitoring.

This statement represents a resource to assist in defining and promoting a minimum standard of clinical care for patients administered opioids in the hospital environment, and to support clinicians in implementing appropriate recommendations for care. It applies in particular to situations where there is an acute escalation in opioid dose, or the initiation of opioid therapy.

Background

1. OIVI may result from three main and interlinked mechanisms:
   - Depression of respiratory drive with a reduction in respiratory rate and/or depth of breathing – "central respiratory depression"
   - Depression of consciousness (and therefore arousal) – "sedation"
   - Depression of supraglottic airway muscle tone – "obstruction" (Macintyre et al, 2011).
2. The true incidence of OIVI in the acute setting is unclear as most publications commonly rely on surrogate measures such as respiratory rate (usually arbitrarily defined as less than 10 or 8 breaths/min), which may remain within a 'normal' range even in the presence of significant OIVI (as measured by carbon dioxide levels), or measures of oxygen saturation (Macintyre et al, 2011). These surrogate measures are not direct indications of adequacy of ventilation.
3. In many published reports of patient deaths resulting from OIVI, undue reliance has been placed on respiratory rate as a unidimensional measure of OIVI, either without formal assessment of patient sedation, or without recognising the significance of excessive sedation (Macintyre et al, 2011; Schug et al, 2015).

4. In some cases where patients have come to harm from OIVI, snoring was reported prior to the event. Patients who are snoring should not be assumed to be sleeping normally and their level of sedation should still be assessed on a regular basis.
5. OIVI continues to cause patient harm in the acute pain setting, including death and hypoxic brain damage (Overdyk et al, 2014; Lee et al, 2015). The peak risk is within 24 hours of surgery and the majority of events are preventable (Lee et al, 2015; Gupta et al, 2018).
6. Risk factors for OIVI have been identified and include (Overdyk et al, 2014; Lee et al, 2015; Gupta et al, 2018):

- Patient factors such as obesity, sleep-disordered breathing (SDB), chronic obstructive pulmonary disease, renal disease, cardiac disease, neurological disorders, ASA status 3 or 4, and age > 65 years. Note that a significant proportion of patients who have been shown not to have SDB before surgery, may develop moderate to severe SDB in the postoperative period (Chung et al, 2015).
- External factors such as coadministration of sedatives (including benzodiazepines, gabapentinoids and antipsychotics), administration of opioids by multiple routes (this does not refer to verified doses of opioids taken for management of chronic pain, where the patient has developed a tolerance to and physical dependence on these medications), continuous infusions of opioids, multiple prescribers, and inadequate nursing assessments or responses. Use of slow-release opioids carries similar risks as the use of a continuous opioid or patient-controlled analgesia (PCA) 'background' infusion in opioid-naïve patients (Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine, 2018).

Importantly however, many patients who come to harm have no identifiable comorbidities that would predict an increased risk of OIVI (Overdyk et al, 2014; Lee et al, 2015; Gupta et al, 2018). The focus must therefore be on better assessment and monitoring of *all* patients, especially in the high-risk period, rather than only patients deemed to be high risk.

Practice points

"OIVI can usually be avoided by careful titration of the dose against effect and careful observation and monitoring." (Schug et al, 2015). This applies to all opioids administered for the management of acute pain, regardless of route or technique of administration.

Recognition of OIVI

Significant OIVI is almost always accompanied by excessive sedation. Therefore, regular assessment of a patient's level of sedation in all patients receiving any opioid for management of their acute pain, using a sedation score, is a more reliable clinical indicator of early OIVI than a decrease in respiratory rate (Macintyre et al, 2011; Schug et al, 2015). One example of a commonly used sedation scoring system is in Table 1 (Macintyre & Schug, 2015; Macintyre et al, 2011)

Table 1 SEDATION SCORES
0 = wide awake 1 = easy to rouse 2 = easy to rouse but unable to remain awake 3 = difficult to rouse
1. A score of 2 is taken to indicate early OIVI and therefore the aim should be to titrate an opioid so that a patient's sedation score is always less than 2. 2. Note that a sedation score (e.g. 'sedation score less than 2') may be specified in the 'Max Dose/24 hrs' in the PRN section of the ACSQHC National Inpatient Medication Chart (NIMC) to indicate the maximum amount to be administered in 24 hrs when prescribing opioids in (Australian Commission on Safety and Quality in Health Care, 2016).

- The use of supplemental oxygen to help prevent hypoxaemia (which is often indicated depending on factors such as type of surgery or injury and patient comorbidities), makes the measurement of oxygen saturation levels an unreliable method for the early detection of OIVI; there may also be reasons other than opioids for hypoxaemia (Schug et al, 2015). In addition, hypoxemia is commonly worse while the patient is asleep and may be missed if pulse oximetry is used only intermittently, because the patient is roused during measurement (Sun et al, 2015).
- Continuous monitoring of carbon dioxide levels is the most reliable way to detect OIVI at an early stage. Currently, the ability to measure carbon dioxide is generally limited to settings such as postoperative recovery, intensive care, and some high dependency units.
- Patients prescribed opioids to take at home, and their family or carers, should be educated about the significance of sedation and the steps to take should excessive sedation be noted.

Potential risk factors for OIVI

- Note potentially avoidable risk factors as listed above.
- Sensitivity to the effects of opioids increases as patient age increases, therefore, in opioid-naïve patients, initial doses of opioid for moderate to severe acute pain should be based on patient age (Macintyre & Jarvis, 1996).

Appropriate responses and interventions

- Acute Pain Services usually use 'standard orders' when prescribing analgesic techniques such as PCA, epidural or regional analgesia, to maximise the effectiveness of pain relief as well as patient safety. These orders aim to guide selection of medicines and their concentrations, dose and dose intervals, monitoring requirements, choice of equipment, and responses to inadequate or excessive analgesic doses, including excessive sedation, or other complications (Schug et al, 2015). Similar standard orders that accompany prescriptions for immediate-release opioids administered on a PRN basis orally or by injection are used in some centres and may reduce patient risk. Examples of suggested inclusions in 'standard orders' are available (Macintyre & Schug, 2015). All patients given any opioid by any route in the acute pain setting require regular assessment of their levels of sedation.

- Opioids should not be titrated to pain scores alone as there are many reasons why patients may report high pain scores. In addition, in some patients, the pain may not be opioid-responsive. An assessment of the patient's functional activity may give a better indication of analgesic efficacy (Schug et al, 2015).
- In a patient who has become sedated but is still in pain, adjuvant analgesics including NSAIDs and ketamine (low dose) may be helpful opioid-sparing measures. Note that atypical opioids may have enhanced analgesic effect if pain does not seem responsive to conventional opioids, with less risk of OIVI. It is important to recognise that patients who have already been administered opioids are at increased risk of OIVI once pain is more effectively treated as the pain drive for respiration has been reduced.
- Opioid prescriptions must be linked to monitoring and recording of sedation in a robust way. This is of particular importance with the current development of electronic prescribing and documentation systems.

Table 2 - Summary of practice points

Recognition of OIVI

1. Sedation scores should be monitored and documented in all patients receiving any opioid for management of their acute pain - increasing sedation is a more reliable indicator of early OIVI than respiratory rate.
2. The use of supplemental oxygen to help prevent hypoxaemia (which is often indicated depending on factors such as type of surgery or injury and patient comorbidities), makes the measurement of oxygen saturation levels an unreliable method for the early detection of OIVI; there may also be reasons other than opioids for hypoxaemia.
3. Monitoring of carbon dioxide levels is the most reliable way to detect OIVI, but the ability to do this is currently limited.
4. Education of patients and their families about the significance of sedation when a patient is discharged with an opioid prescription is important.

Potential risk factors for OIVI

1. Avoid, or use with extreme caution, the administration of more than one opioid regardless of route, continuous infusions of opioids, and slow-release opioids (especially fentanyl patches).
2. Avoid, or use with extreme caution, sedatives and sedating analgesic adjuvants.
3. In opioid-naïve patients, initial doses of opioid for moderate to severe acute pain should be based on patient age.

Appropriate responses and interventions

1. The development of 'standard orders' for the safe prescription and administration of all opioids used in acute pain management, including PRN opioids, is likely to add an extra safety dimension by emphasising monitoring of sedation and promoting quicker recognition and treatment of opioid-related side effects.
2. All opioids should be carefully titrated, but not to pain scores alone; an assessment of functional activity may be a better indicator of analgesic efficacy. Titration includes consideration of side effects. In some patients, pain may not be opioid-responsive.
3. If a patient is sedated and still in pain, adjuvant analgesics may be helpful opioid-sparing measures; atypical opioids may be of benefit with less risk of OIVI.

Note: The term "slow-release" is used by the Australian Commission on Safety and Quality in Health Care in its National Inpatient Medication Chart10 and covers all medications that may be referred to as slow-release, sustained-release, extended-release, modified-release and long-acting. For the purposes of this statement, 'slow-release' will also refer to transdermal opioid patches and methadone.

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