OPIOID TOXICITY, OPIOID INDUCED ADVERSE EVENTS AND SPECIAL CIRCUMSTANCES

Keywords: Palliative pain management, opioid toxicity

AIM

- The recognition and management of opioid toxicity and opioid induced events.

KEY POINTS

1. In palliative care, the preferred routes of administration are either orally or subcutaneously.
2. In certain situations e.g. shock or coagulopathic states the intravenous route of administration is preferable. Contact the Palliative Care Team in these circumstances.

OPIOID TOXICITY

- Respiratory depression is very unlikely if opioids are titrated appropriately. If it occurs, withhold the morphine or other opioid and check for other causes of respiratory depression e.g. hypercapnia.
- Use of Naloxone to reverse opioid analgesia should only be considered in significant respiratory compromise i.e. respiratory rate < 8 per minute.
- Naloxone should not be used diagnostically to exclude opioid toxicity in women with ongoing requirements for opioid analgesia.
- When commencing opioids, discuss the possibility of adverse effects with the woman. Apart from constipation, most of the effects are self limiting and can be easily managed with antiemetics, adequate hydration and appropriate titration.
- If an adverse effect fails to settle, repeat biochemistry and exclude other contributing factors. A change of opioid may be required.

OPIOID INDUCED ADVERSE EFFECTS

- Opioid induced adverse events may be numerous and include toxicity presenting in a variety of ways. Toxicity may include confusion, drowsiness, delirium, hallucinations, nausea, vomiting, myoclonic jerks, seizures, pruritis, respiratory depression and constipation.
- It occurs when:
  - Either the parent drug or its metabolites accumulate.
  - Other medications have synergistic or cumulative adverse reaction or alter the metabolism of opioids.
  - Other patient related factors mimic opioid toxicity.

Common Causes of Changes in Cognitive State in Advanced Gynaecological Malignancies

- Metabolic
  - Liver failure
  - Renal failure
  - Adrenal failure
  - Hypercalcaemia of malignancy
  - Hypoxia
  - Electrolyte disturbance
  - Dehydration
• Endocrine
  ➢ Hyper / hypoglycaemia
  ➢ Hypo / hyperthyroid

• Sepsis

• Cerebral disorders
  ➢ Cerebral metastases
  ➢ Vascular accidents
  ➢ Paraneoplastic (cerebellar, limbic encephalitis).

• Iatrogenic
  ➢ Opioids
  ➢ Antidepressants
  ➢ Benzodiazepines
  ➢ Corticosteroids
  ➢ NSAIDs
  ➢ Anticholinergics
  ➢ Serotonin syndrome

• Substance withdrawal
  ➢ Alcohol
  ➢ Benzodiazepines
  ➢ Illicit drugs

• Physical discomfort
  ➢ Acute retention of urine
  ➢ Constipation

• Psychological distress
• Impending death.

Management

• Tailor the management to the clinical situation.
• Distinguish the most likely cause of the problem (reversible vs. irreversible).
• Reduce the background dose of the opioid medication if there is adequate analgesia.
• Treat the distressing symptoms.
• Ensure adequate hydration.
• In some situations change of opioid may be beneficial.

• Opioid antagonists i.e. naloxone
  ➢ Should not be used ‘diagnostically’ to exclude opioid toxicity in women with an ongoing requirement for opioid analgesia.
  ➢ Should only be considered in the circumstance of significant respiratory compromise.
  ➢ The most appropriate measure of impending airway compromise is rousability in conjunction with respiratory rate.
  ➢ Confusion and pinpoint pupils are unreliable signs.
  ➢ Naloxone should not be given unless clinically indicated as it will reverse the opioid analgesia and may prompt a drug withdrawal and uncontrolled pain.
  ➢ If naloxone is clinically indicated it is recommended that it is given in increments until the woman’s respiratory status is satisfactory.
  ➢ Naloxone has a short duration of effect when compared to most opioid formulations in use. Close monitoring is mandatory and repeated increments of naloxone may be required.
  ➢ Ensure that opioids are charted at either a lower dose or use an appropriate alternative opioid.
PRESCRIBING OPIOIDS IN SPECIAL CIRCUMSTANCES

**Impaired Renal Function**
- Caution must be exercised if renal function is impaired as an increased accumulation of the parent drug and metabolites may occur.
- Be aware that elderly and cachexic women may have impaired renal function (decreased glomerular filtration rate) even when serum creatinine is within ‘normal’ range.
- Codeine should **not** be used.
- Extreme caution should be used when prescribing morphine, hydromorphone and oxycodone. They should be dose reduced with extended dosing frequency.
- Fentanyl and methadone are considered safe, but should be prescribed with caution and specialist advice.

**Impaired Liver Function**
- Women with severe liver disease should be prescribed lower doses of opioids, with an extended dosing frequency.
- Codeine and methadone should not be given.
- Use morphine, hydromorphone and oxycodone very cautiously with close supervision.
- Fentanyl is considered safe, but specialist advice is recommended.

REFERENCES / STANDARDS

Greater Metropolitan Clinical Taskforce. 2008. *Gynaecological Cancer Palliative Care*. NSW Department of Health, Australia

| National Standards | 1- Care provided by the clinical workforce is guided by current best practice  
|--------------------| 4- Medication Safety |
| Legislation        | *Poisons Act 1964* |
| Related Policies   | Nil |
| Other related documents | KEMH Clinical Guidelines Palliative Care |

RESPONSIBILITY

OGCCU / Palliative Care Team

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<th>Policy Sponsor</th>
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