Opioid toxicity and alternative opioids

Palliative care fixed resource session
Opioid toxicity and alternative opioids - aims

- Know the symptoms of opioid toxicity
- Understand which patients are at higher risk of opioid toxicity
- Know how to assess a patient with possible opioid toxicity
- Know the principles of managing opioid toxicity
- Understand the rationale for using alternative opioids
What is opioid toxicity?

- Build up of an opioid and/or its active metabolites in a patient’s body producing significant functional and cognitive impairment
- Different to a side effect
Spotting opioid toxicity

• What are the symptoms of opioid toxicity?
  – (think Train Spotting.....)
Spotting opioid toxicity – Mr P

• Mr P is a 65 year old man with prostate cancer which has metastasised to bone. He has a background of type 1 diabetes and has moderate renal impairment.

• He is complaining of severe back pain unrelieved by cocodamol 30/500 at maximum dose and his GP starts him on long acting morphine (MST)
Spotting opioid toxicity – Mr P

• Initially his pain is better, but a month later he complains of severe pain on movement.
• His GP doubles his MST with an improvement in his pain, but unfortunately 3 days later he becomes confused and drowsy.
Spotting opioid toxicity – Mr P

• You see Mr P in the medical ward. He struggles to give you a clear history and his AMT is 6/10. He complains of seeing shadows and spiders out of the corner of his eye and thinks there’s someone standing next to him.

• On examination he’s apyrexial. Every so often his limbs jerk and when he’s sleeping he reaches for things that are not there.
Spotting opioid toxicity

- **Acute** opioid use (A&E; post-op) can produce toxicity with drowsiness, hypotension and respiratory depression.

- **Chronic** opioid use can produce toxicity, but respiratory depression is a late complication *unless* something else is making things worse (eg severe sepsis; renal or liver failure).
<table>
<thead>
<tr>
<th>Spotting opioid toxicity – progression (usually…)</th>
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<tbody>
<tr>
<td>• Subtle agitation</td>
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<tr>
<td>• Sleepiness Confusion</td>
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<td>• Vivid dreams</td>
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<td>• Hallucinations</td>
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<td>• Myoclonus</td>
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<td>• Respiratory depression</td>
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<td>• Hypotension</td>
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<td>• Bradycardia</td>
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<td>• Coma</td>
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<td>• Death</td>
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Assessment

• Consider other things that may mimic opioid toxicity
  – Disease progression
  – Sepsis
  – Other drugs
  – Other causes of tremor
  – Electrolyte disturbance (hypercalcaemia)

• Consider things that make toxicity more likely…
Opioid toxicity is more likely when...

- Impaired excretion – renal or liver failure
- Old age
- Co-existing pathology that make confusion more common (e.g., dementia, CVD)
- Rapidly increasing dose
- Movement related pain
- Neuropathic pain
GFR < 30ml/min greatly increased risk of drug induced toxicity
Recommended Drugs

- Alfentanil
- Transdermal buprenorphine
- Fentanyl
- Appear to be the safest opioids of choice
Prescribing guidance

- GFR = 90-60 ml/min 100% dose
- GFR = 60-30 ml/min 50%
- GFR = 30-15 ml/min = recommended drugs
- GFR = <15 ml/min = recommended drugs
Excretion of opioids

- Codeine and dihydrocodeine – converted to morphine
- Morphine – converted in the liver to active and inactive metabolites and excreted by the kidney
- Oxycodone and hydromorphone – metabolised in the liver then largely excreted by the kidney
- Fentanyl – mainly metabolised by the liver (minimal (10%) renal excretion)
- Alfentanil – metabolised by the liver (minimal renal excretion)
Which means….

- Care with codeine and morphine in patients with any renal impairment (lower dose; longer dose interval)
- Care with Oxycodone and hydromorphone in mild renal impairment (lower dose; longer dose interval)
- Other opioids may be safer in patients with moderate or severe renal impairment (eg fentanyl or alfentanil)
- Care with *all* drugs in liver failure (INR)
- Ask!!!
Managing opioid toxicity 1

- End of life…. What’s appropriate?
- Make sure there’s nothing else going on
- Reduce the dose
  - 30-50% if mild
  - Stop MR forms
  - use NR PRN alone if severe
- Fluid support
  - Increases excretion
  - Drowsy patients don’t drink
Managing opioid toxicity 2

- Treat agitation
- Switch opioid?
- Other ways for treating the pain
  - Adjuvant analgesics, radiotherapy, etc
- Get help from seniors/PCT
Alternative opioids – why?

• High risk of toxicity – see above
• Some people do better on one than another
  – Balance of side effects to effect
  – Specific side effects (eg fentanyl possibly less constipating than morphine)
Alternative opioids - how

• One isn’t “better” than another – it’s about individuals
• Conversion ratio based on potency compared to morphine
• Aim low and ensure they have breakthrough medication
Conclusions

- **Attention to choice of opioid**

- Consider dose reduction and/or an increase in dosage interval

- Change from modified release to immediate release

- Carry out frequent clinical monitoring and review
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• Any questions?