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)

Spotting opioid toxicity – progression (usually…)

- Subtle agitation
- Sleepiness Confusion
- Vivid dreams
- Hallucinations
- Myoclonus
- Respiratory depression
- Hypotension
- Bradycardia
- Coma
- Death

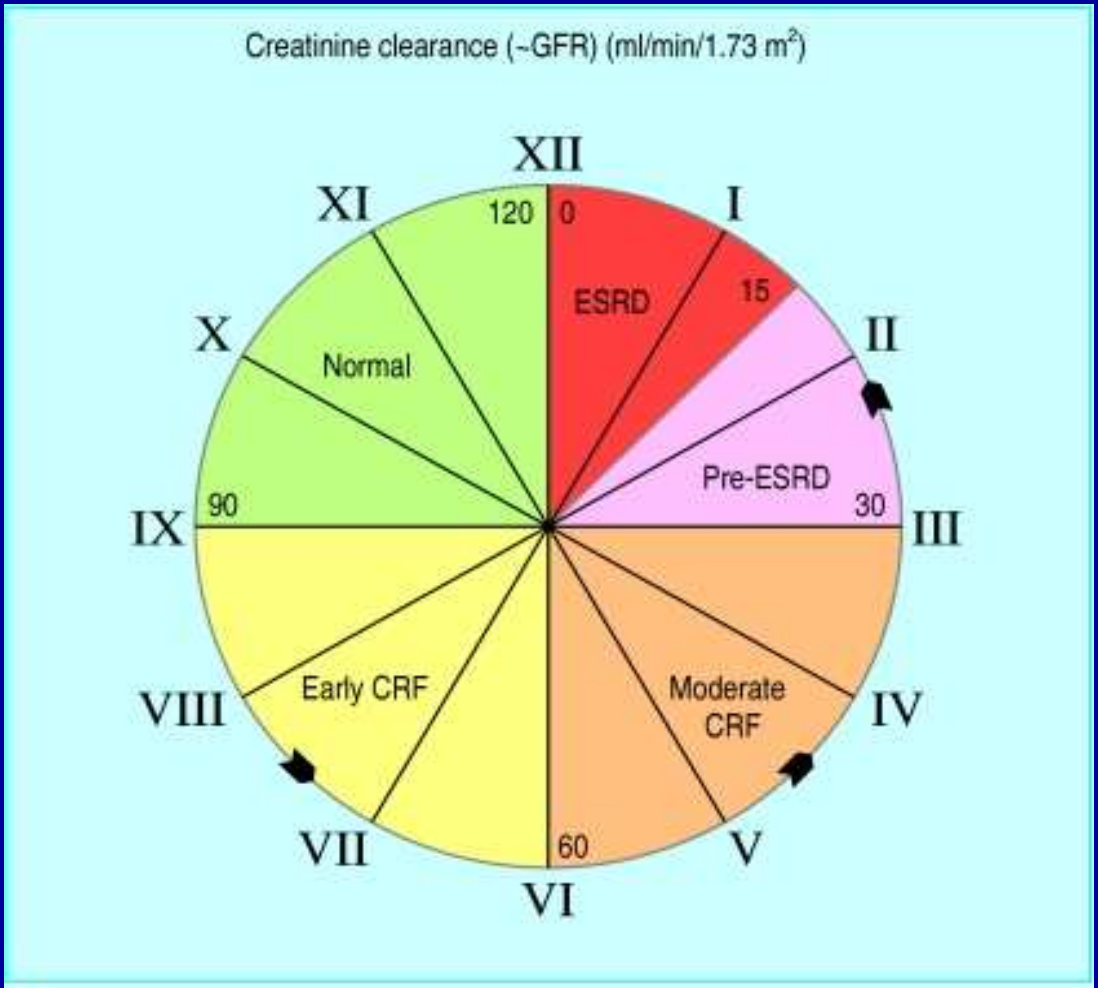
Assessment

- 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 (eg 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 – its 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?