

# Prescribing opioids

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James talks to Joanne Rimington about prescribing opioids.

Joanne works as a senior pharmacist for education and training, South East Sydney Local Health District. She previously worked as a clinical pharmacist at Prince of Wales Hospital. Joanne's main areas of interest are improving inter-professional education opportunities, strategies to improve management of high risk medicines including narcotics, as well as improving knowledge and understanding by patients of their own medicines to enhance medication safety.

## Prescribing opioids

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*With Joanne Rimington, Senior Pharmacist for education and training in South Eastern Sydney Local Health District*

### Introduction

Opioids are amongst the most commonly used medications in hospital. With a range of types, routes and formulations, safe opioid dosing may be challenging for junior doctors. Errors in prescribing of opioids can be severe and even life-threatening due to their high risk side effect profile. Joanne Rimington talks to us about the important factors to consider when prescribing opioids.



### 1. What are your general thoughts on prescription of opioids in the hospital?

- There is no 'one size fits all' rule for opioids - important to balance analgesic effects with potentially serious side effects
- Opioids are high risk medications and should always be used with care and awareness of the risks
- Assess the pain
  - A good pain history is important
  - Regular pain assessment leads to improved treatment of acute pain
  - Self reporting of pain should be used whenever possible as pain is a subjective experience
  - Determine the type of pain you are treating e.g., opioids not first line for neuropathic pain
- What analgesia has already been trialled?

- Are they opioid naïve or taking additional sedatives? This increases risk of opioid overdose.
  - What other analgesics have been trialled?
  - Multi-modal approach (combination of medications from different classes of analgesics targeting different pain pathways) may be more effective and reduce the need for opioids
- ‘Start low and go slow’
  - Gradually titrate the dose until pain controlled or side effects limit treatment (e.g. sedation)
- Adjust dose based on age and weight
  - Children – use an appropriate paediatric reference
  - Elderly – use smaller doses, usually 25-50% of usual adult dose and titrate slowly. Elderly patients usually have reduced renal function, are more sensitive to analgesic effects and are at greater risk of adverse effects.
  - Weight – may need to adjust dose
- Do not crush slow release medications as it increases the risk of dose dumping (premature and exaggerated release of the drug) which could greatly increase opiate concentration leading to adverse effects or opiate toxicity
- Assess co-morbidities
  - Higher risk of complications e.g. respiratory depression in some patients e.g. severe COPD
  - Use cautiously and monitor closely in patients with head injuries. Sedation may be confused with a deteriorating neurological condition.
  - Renal and liver impairment can affect both drug choice and dosing – some drugs may be contraindicated due to accumulation of active or toxic metabolites
- Review current medications and look for potential drug interactions e.g. central nervous system depressants such as benzodiazepines may increase risk of side effects or potential for falls
- If pregnant or breastfeeding, seek further information from MotherSafe, CIAP or pharmacist

## 2. What routes of administration are available for opioids?

- Choice will depend on the type and severity of pain and how quickly you require the drug to work
- Be very clear about the route, to avoid drug administration errors
- Doses are not equivalent across all routes
  - Remember that the dose may be different when switching between different routes of the same drug e.g. hydromorphone 1.5-2mg subcutaneously is equivalent to 6-7.5mg orally

- Ensure you prescribe only one route OR you prescribe different routes on a different order and are very clear when each should be used to avoid double dosing
- Oral
  - Can they swallow tablets whole? Are they nil by mouth?
  - Important to specify immediate or slow release when prescribing
    - Don't use slow release formulations for acute pain
    - Hydromorphone implicated in many significant errors due to a potential mix up between immediate release (Dilaudid) and slow release (Jurnista). Prescribe using both the generic and brand name for this drug to help distinguish formulations.
- Intravenous
  - Give a rapid predictable effect in severe pain e.g. after surgery, but need appropriate monitoring. Often not appropriate for PRN dosing on the wards.
- Subcutaneous
  - More appropriate if ongoing parenteral administration required on the ward
- Transdermal
  - All opioid patches are not recommended for the management of acute pain as there is delayed onset of action and it is difficult to titrate doses
  - Do not use transdermal patches, particularly fentanyl, in opioid naïve patients with non-cancer pain as there is an increased risk of serious side effects including respiratory depression and death
  - Buprenorphine patches, a weaker opioid with partial agonist activity, have been used in opioid naïve patients, but should be started at the lowest dose possible as long acting

### 3. What types of opioids are available to prescribe in the hospital setting?

- Codeine
  - Weak opioid but still potentially high risk as unpredictable effects due to variations in metabolism
  - Usually in combination with paracetamol
  - Prodrug therefore needs conversion to an active morphine metabolite. Some people can't metabolise it effectively and so may get no or limited analgesic effect, some people can rapidly metabolise the drug and are more at risk of toxic effects.
- Oxycodone

- Strong opioid commonly used in acute and chronic pain
- Common post-op if prolonged pain expected - stepwise de-escalation should be in place
- Immediate release tablet (Endone or OxyNorm) or liquid (OxyNorm)
- Slow release tablet (Targin = oxycodone with added naloxone which is reported to reduce gastrointestinal side effects particularly constipation)
- Morphine
  - Potent opioid and is the standard against which potency of other opioids is compared
  - Many formulations available Oral: Immediate release tablets (variable bioavailability). Slow release tablets used for treatment of chronic pain. Liquid formulation available. Intravenous (injection or PCA) and subcutaneous used for severe acute pain
  - Active metabolites can accumulate in renal failure - caution with use
- Hydromorphone
  - Strong opioid
  - Lots of medication errors associated with this drug so ensure you are familiar with its use
    - NSW Health have recently issued a safety alert regarding hydromorphone
    - Prescribe using trade name and generic name to also help distinguish between slow and immediate release forms
    - Tallman prescribing could also be used to minimise risk of errors with prescribing e.g. HYDRORmorphone
  - **Five to seven times more potent than morphine** so smaller doses are required
  - Not usually first line but is an alternative if morphine inappropriate e.g. in the elderly and patients with renal impairment
- Tramadol
  - Weak opioid
  - Also a serotonin and noradrenaline reuptake inhibitor - may develop associated
    - serotonergic side effects e.g. sweating, nausea
    - Multiple drug interactions can occur
- Fentanyl
  - Very potent opioid with fast onset of action used in severe pain
  - Useful in renal impairment
  - Available as intravenous, transdermal patch and lozenges/buccal tablets
  - Oral formulations used in cancer pain only - used mainly for breakthrough or 'incident' pain
  - Transdermal patch only for chronic or cancer pain - do not use in opioid naïve patients with non-cancer pain
  - If patch is exposed to a heat source (e.g. heat pack, sitting in front of a fire, a sauna or if patient febrile) the rate of drug release from the patch increases and can cause toxicity, due to skin vasodilation leading

to increased absorption. Conversely, if peripherally shut down or grossly oedematous may not absorb the patch in the manner that you would expect.

- Other opioids
  - Such as tapentadol and buprenorphine – check your resources and ensure you are familiar with each one, including relative potencies and precautions, before prescribing
  - Pethidine rarely used anymore

#### 4. What resources are available to assist junior doctors in prescribing opioids?

- CIAP has many useful resources
  - AMH – good information on dosing and side effects for individual drugs
  - eTG – analgesic guidelines, therapeutic options, what drugs and doses to use in different pain scenarios
  - UpToDate
- Analgesic Ladder by World Health Organisation – principles and key concepts are applied in chronic pain with a stepwise approach to pain depending on severity
- Acute or Chronic Pain Team in your hospital – important for complex or opioid-dependent patients
- Drug and Alcohol Team – issues with pain management in opioid-dependent patients
- Palliative care team
- Pharmacists
- Renal Drug Handbook – dosing in renal disease and dialysis

#### 5. In what situations is advice from the Pharmacist or Acute/Chronic Pain Team useful?

- Frequently the pain team is already aware of the patient and therefore a more nuanced or a more efficient approach to adequate analgesia may be possible
- In complex pain patients, a chronic pain team (multi-disciplinary) approach to dealing with pain including both pharmacological and non-pharmacological modalities is important to consider. These patients need consistency of management of their analgesic and psychological needs.
- Renal or liver dysfunction
- Opioid-dependent patients
- Elderly or paediatric patients
- Drug interactions
- Opioid de-escalation and switching between opioids

- Post-op pain - if not ceased prior to discharge, a weaning plan (usually of oxycontin or Targin) must be in place and communicated to the GP if further weaning required on discharge.

## 6. One of the roles of the pharmacist is to help with calculating equivalent doses of opioids with different potencies. What are some resources to assist with this?

- Opioid equivalency table from AMH or eTG
- Some hospitals have their own clinical business rules outlining this
- Generally opioids are compared to morphine in assessing equivalent doses
  - **10mg IM/SC morphine = 1.5 - 2mg IM/SC hydromorphone**
- Changing between opioids
  - There may be incomplete cross tolerance when swapping from one opioid to another
  - Start at approximately 50% of the equivalent dose if switching to a different opioid to take this into consideration and re-titrate dose as needed until pain controlled - potentially use a breakthrough dose if needed while titrating the dose
- Changing the route of an opioid
  - Doses are not necessarily equivalent depending on the drug's oral bioavailability e.g. hydromorphone oral doses is less than half of the subcutaneous dose
  - **Important to use separate order on the medication chart for different routes of a drug where doses are not equivalent - try and only prescribe one route if possible**

## 7. What are some of the common drug interactions with opioids?

- CNS depressants e.g. sedatives, hypnotics such as benzodiazepines - lead to an increased risk of respiratory depression and sedation, so use with caution
- Serotonin toxicity
  - Some opioids can contribute to serotonin toxicity e.g. tramadol and fentanyl
  - Care should be taken with drugs that may also affect serotonin e.g. selective serotonin reuptake inhibitors (SSRIs)
  - Useful table in AMH highlights drugs that can contribute to serotonin toxicity
- Methadone has many drug interactions and can cause QT prolongation especially if used in combination with other drugs that have a similar effect - a useful table

available in the AMH

- Some opioids e.g. fentanyl are metabolized in liver by CYP450 system and may be affected by drugs that inhibit or induce these enzymes
  - CYP3A4 inhibitors e.g. fluconazole and voriconazole can increase fentanyl in circulation
  - If patient is taking a CYP3A4 inducer, you may get a reduced analgesic effect
  - Useful table in AMH of drugs that are substrates, inhibitors and inducers of CYP450 enzymes
- Fentanyl and buprenorphine patches – effects of drug interactions may last longer than expected due to slow reduction in plasma levels as drug can remain in system 24-48hrs after patch removal

**Case – You are a junior doctor asked to review a 65 year old female patient who is day 2 post elective hip replacement. She has a history of minor renal impairment and has been on regular oxycodone for 2 days. You would like to prescribe ongoing analgesia and discharge analgesia.**

## 8. What other information is important to know about this patient?

- Allergies
- Is she taking any other analgesics e.g. regular paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) – multimodal analgesia using drugs from different classes is usually the best approach
- Current medications – any drug interactions?
- Current dose of oxycodone
- Current level of sedation
- Adequacy of pain control
- Current side effects e.g. constipation, urinary retention, nausea and vomiting
- Baseline renal function compared to current renal function

Oxycodone would still be appropriate if patient had mildly impaired renal function – may need to reduce dose and add paracetamol.

## 9. Are there any particular precautions in use of opioids in patient with renal or hepatic dysfunction?

- Renal failure
  - Check biochemistry – urea and creatinine and work out renal function
  - If need to determine dosing in renal dysfunction, can use Cockcroft-Gault formula (preferable for critical dosing), or EGFR-CKD
  - Some drugs should be avoided in patients with renal dysfunction due to accumulation of active metabolites e.g. morphine

- May use fentanyl as has no active metabolites, or hydromorphone
- Oxycodone may be used in moderately impaired renal function but using a reduced dose
- Renal drug handbook available for dosing in dialysis patients
- Liver failure
  - Most opiates are metabolized by liver, so caution advised when dosing
  - Avoid slow release preparations in patients with extensive liver disease
  - Can be complex so check references or discuss with the pharmacist
  - Paracetamol doses need to be reduced

## 10. What are some of the common low risk side effects associated with opioids?

- All opioids are associated with gastrointestinal side effects
  - Nausea and vomiting common but may lessen over time
  - Constipation is very common
    - Can be limiting factor to use of opioids over long period
    - Little tolerance develops to constipation
    - Always use a laxative for patients needing regular opioids e.g. Coloxyl and Senna (stimulant and stool softener) or Movicol (osmotic laxative). Avoid bulk forming laxatives which can worsen situation.
  - Targin (oxycodone and naloxone combination): naloxone is an opioid antagonist which has poor oral bioavailability and extensive first pass metabolism, which works predominantly on opioid receptors in the GI tract and reduces risk of constipation without affecting analgesia - be aware that this may not be the case if high dose Targin is used
- Pruritis
- Urinary retention
- Cognitive issues in particular in elderly patients - can precipitate delirium, contribute to falls
- Postural hypotension
- Opioid tolerance - physical dependence may be common

## 11. What are the serious and life threatening side effects that junior doctors should be aware of?

- Respiratory depression is most serious adverse effect
- Higher risk of respiratory depression if:
  - Starting with large doses of opioids or increasing doses too rapidly



- Pre-existing compromised lung function e.g. COPD, sleep apnoea
- Using CNS depressant such as benzodiazepines in combination with opioid
- Start low and go slow to minimize the risk
- Check sedation scores – early predictor of respiratory depression – aim for score <2
- Respiratory rate alone is a late and unreliable predictor of respiratory depression
- When increasing doses of opioids, increase the frequency of observations as well
- Be cautious with use of IV opioids, rapid rates of infusion can cause bradycardia, vasodilation and hypotension – would usually only be used in a high dependency area

## Take home messages

- Make sure you treat patients on a case by case basis – be compassionate, check if opioid naïve and what other analgesics have been tried
- Start cautiously with small doses and increase slowly in elderly patients, until patient is pain free (or comfortable) or you are limited by side effects
- Respiratory depression is important to look for but does not preclude use of opioids – need to be very careful and monitor sedation scores
- Know your drugs and their inherent risks
- Be aware of different opioid potencies e.g. hydromorphone is 5 – 7 times more potent than morphine and the two are easily confused
- Be aware of different doses for different routes of the same drug and prescribe different routes on different individual medication orders where doses are not equivalent e.g. hydromorphone
- Reduce your doses before switching from one opioid to the other – cross tolerance between opioids does not always occur
- Transdermal patches should not be used for acute pain or in patients who are opioid naïve
- (can lead to a significantly increased risk of severe side effects)
- Prescribe a laxative to minimise constipation
- Opioids and especially hydromorphone are high risk medications and the consequences of incorrect prescribing are severe – so always ask for help if unsure
- **Have a clear post-operative weaning plan for patients started on opioids – make sure the plan is clearly communicated to the GP or Pain Clinic (if required). Think about whether patients really need the opioid when they go home and don't prescribe more opioids than is absolutely necessary.**

## References

- Gupta A, Rosenquist R. Use of opioids in the management of non-cancer pain. UpToDate August 2016.
- eTG (Therapeutic Guidelines Limited). Approximate relative potencies of various opioids used in chronic pain. eTG July 2016.
- Australian Medicines Handbook. Opioid analgesics. Australian Medicines Handbook 2016.

## Related Blogs

- [Prescribing for Interns by Dr Sally Bath](#)
- [Top 10 podcasts listened to in 2017](#)

## Related Podcasts

- [Opioid dependence](#)
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