Dose Intervals (cont)

- Morphine is the least lipid soluble and has the longest delay (15 min plus for max effect IV).
- IV Fentanyl 5 mins max effect IV.
- Duration of action of any given opioid dose also depends on several factors.

Titration of IV Opioids

- Dose ranges based on AGE of patient.
  - <70 yrs 1mg, 2mg or 4mg
  - >70 yrs 0.5mg, 1mg or 2mg
- Appropriate dose interval 3-5 mins (remember a less lipid soluble drug like morphine may take 15 mins to exert max effect on CNS post admin IV)

Titration (cont)

- However 15 min is too long an interval to obtain rapid analgesia.
- Balance between peak effect and efficacy.
- 3-5 min titration is safe and effective with appropriate monitoring.

ALLERGY TO OPIOIDS

- A true allergy to opioids is VERY uncommon. The term “allergy” is often mistakenly applied to an intolerance to the drug, a common side effect, or a dose related effect.
Adverse Effects of Opioids

- The most common side effects of opioids are sedation, pruritis, nausea, slowing of G.I. function and urinary retention.
- Most (but not all) side effects are dose dependant. One option may be to reduce dosage providing satisfactory analgesia is maintained.
- Another option is pharmacological treatment of side effects (eg antiemetics for nausea)
- May be efficacious to switch to a different opioid (opioid rotation)

NAUSEA AND VOMITING

- Is a side effect not an allergy
- Common post op. (particularly opioid related)
- ? Genetic predisposition (hx travel sickness)
- Risk significantly reduced by use of antiemetics (Droperidol, Dexamethasone, Ondansetron are all equally effective.
- Maintain hydration and BP
- Excessive movements in immediate post op period can trigger nausea/vomiting

PONV (Multiple causes)

- Give antiemetics before emetic stimulus is expected (easier to prevent than to stop)
- Emesis coordinated by Vomiting Centre in the medulla
- Another important source of stimulation in the brain is the Chemoreceptor Trigger Zone (CTZ).
- CTZ is not protected by blood/brain barrier so can be stimulated by toxins or drugs.

Nausea + Vomiting (cont)

- There are a number of different classes of antiemetic drugs that act at different receptor sites involved in the emetic response.
- Dopamine, Seratonin, 5HT3 (5-hydroxytryptamine), histamine, acetylcholine.

PONV - RECEPTORS

- CTZ possesses many dopamine (D2) receptors.
- CTZ also possesses 5ht3 receptors.
- D2 and 5ht3 antagonists are ineffective in reducing n+v of motion sickness.
- Anticholinergic drugs or antihistamines may be effective although side effects are common.

Nausea+vomiting (cont)

- Several different types of antiemetic drugs have antidopaminergic actions including butyrophenones (eg droperidol, haloperidol).
- Phenothiazines (eg prochlorperazine stemetil).
- Metoclopramide (G.I. prokinetic)
**Nausea+vomiting (cont)**

- Droperidol may be effective as 5HT3 inhibitors, may cause extrapyramidal reactions, restlessness, apprehension.
- Prochlorperazine (stemetil) Potential side effects same as any phenothiazine and include extrapyramidal reactions. (may occur after single dose)

**Nausea+vomiting(cont)**

- Metoclopramide (Maxalon) acts centrally at dopamine receptors and has prokinetic action on gut to increase drug absorption. (useful in migraine)
- Also has some effect at 5HT3 receptor sites.
- Most commonly used and least effective antiemetic(some studies indicate little better than placebo).

**Antiserotonergic (eg: ondansetron)**

- Inhibit actions of 5HT3 receptors, most effective antiemetics to date.
- No extrapyramidal side effects, long duration of action.
- Expensive.

**Antihistamines**

- Cyclizine, hydroxyzine and promethazine (phenergan) are commonly used as antiemetics and may be particularly effective for movement induced PONV.
- Sedation may be a problem.

**Anticholinergic**

- Scopolamine (hyoscine) patch, particularly effective for movement induced nausea and vomiting.
- May have significant anticholinergic side effects eg sedation, dry mouth, visual disturbances, and confusion.

**PRURITIS**

- Mechanism not fully understood. Some opioids may cause histamine release from mast cells.
- May also be centrally mediated by Mu receptor activation.
- Is a side effect of the opioid not an allergy.
- More common with morphine than pethidine or fentanyl.
- Small IV doses of naloxone is an effective Rx for opioid induced itch.
- Anti histamines can add to risk of sedation and resp. depression. (avoid)
Respiratory depression

- Fear of resp. depression and hypoxia often lead to inadequate dosing with opioids.
- Resp. depression can usually be avoided with careful titration and individualisation of dose against effect.
- Opioid naive patient is at greater risk.
- Resp. depression may occur due to incorrect dose by any route, accumulation during inadequately monitored continuous infusion or inappropriate use of long acting drugs (eg MST, methadone).
- Co administration of other sedative agents including benzodiazepines, antihistamines (eg phenergan), and some anti emetics (eg cyclizine).
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Physical Dependence

- Physiological phenomenon that manifests in the development of withdrawal syndrome after sudden discontinuation or substantial reduction of therapy or administration of an antagonist drug such as naloxone.
- Physical dependence indicates neither the presence nor the absence of addiction.

Tolerance to opioids

- Opioid will decrease in analgesic effect over time (will need dose increased to maintain effect).
- Tolerance to side effects of opioids will also develop over time (except for one).
- Tolerance should not be confused with addiction and is not a predictor of abuse.

Addiction

- There is no evidence that the use of opioids for treatment of severe pain leads to opioid addiction in the opioid naive patient.
- Addiction is more a type of psychological dependence as opposed to a physical dependence.
- The taking of opioids for pain relief is not addiction no matter how long or at what doses the person takes opioids for (NHMRC Guidelines 2005).
- Behaviours indicative of uncontrolled pain or fear of uncontrolled pain are often misinterpreted as addiction.

Intercurrent disease states such as hypovolemia, hepatic dysfunction, resp disease or raised ICP.
- Obstructive sleep apnoea or intermittent airways obstruction. (Overnight O2 oximetry may identify pts at risk of post op airway obstruction. O2 at 2lt is recommended in first 48-72hrs following major surgery.) (NHMRC Guidelines 2005)
- A decrease in resp. rate has been found to be a late and unreliable clinical indicator of resp. depression. (NHMRC Guidelines 2005)
- Sedation is a better indicator and should be monitored using a sedation score.
- This method has limitations if a patient who is deeply sedated is assessed as being in “normal sleep.”
- “Normal sleep” means patient is asleep but rousable, (eg responds when pulse is taken)