Pain management

Opioids

Helen Imseeh
**Tolerance**  
Physiologic phenomenon resulting in progressive decline in potency of an opioid with continued use.  
- It takes a higher dose of the drug to achieve the same level of response achieved initially.

**Dependency**  
Physiologic state characterized by symptoms upon abrupt discontinuation of reduction of narcotic therapy.

**Abuse**  
Physiological and behavioral syndrome manifested by drug seeking behavior, loss of control of drug use and continued use despite adverse effects.  
- Dependence is characterized by the symptoms of tolerance and withdrawal. While it is possible to have a physical dependence without being addicted, addiction is usually right around the corner. Addiction is marked by a change in behavior. Substance use becomes the main priority of the addict, regardless of the harm they may cause to themselves or others.
Morphine

- Mechanism of action:
  - is a strong mu receptor agonist & also acts at κ
  - It decreases the release of substance P, which modulates pain perception in the spinal cord.
  - inhibit the release of many excitatory transmitters from nerve terminals carrying nociceptive (painful) stimuli.
- Used to treat moderate- severe acute and chronic pain
- It is characterized by being least the least lipophilic of the common opioids & Only a small percentage of morphine crosses the blood–brain barrier (duration of action 4 to 6 hours when administered systemically to morphine-naïve individuals)
- Morphine should be used with caution in patients with asthma, liver disease, or renal dysfunction
- Actions:
  - Analgesia
  - Euphoria
  - Respiratory depression by reduction of the sensitivity of respiratory center neurons to carbon dioxide.

  (most common cause of death in acute opioid overdoses.)

Tolerance to this effect does develop quickly with repeated dosing, which allows the safe use of morphine for the treatment of pain when the dose is correctly titrated

- Morphine increases growth hormone release/enhances prolactin secretion/increases antidiuretic hormone and leads to urinary retention.

- Morphine and other opioids produce constipation, with little tolerance developing.
- Morphine can also increase biliary tract pressure due to contraction of the gallbladder and constriction of the biliary sphincter
- **Miosis**, Emesis
- Morphine has no major effects on the blood pressure or heart rate at lower dosages. With large doses, hypotension and bradycardia may occur. Respiratory depression → carbon dioxide retention → cerebral vessels dilate and increase cerebrospinal fluid pressure. Therefore, morphine is usually contraindicated in individuals with head trauma or severe brain injury

Histamine release: Morphine releases histamine from mast cells causing urticaria, sweating, and vasodilation.

*It can cause bronchoconstriction, morphine should be used with caution in patients with asthma.*
USES IN CHRONIC PAIN

• **Moderate to severe cancer pain** is usually treated with an immediate-release oral morphine preparation (10–30mg every 1–4h). These preparations have an effective half-life of 2 to 4h.

• Once the patient’s daily requirements are determined, the same dose can be given in the form of a sustained-release morphine preparation which is dosed every 8 to 12h.

• The immediate-release preparation is then used only as needed for breakthrough pain.
Morphine pump

- Totally implanted, programmable morphine pump is an intrathecal drug delivery system (IDDS) with externally programmable pumps can also be used for continuous infusion.
- The reservoir of the implanted pump is periodically refilled percutaneously.
- Intraspinal opioids is an excellent alternative for patients obtaining poor relief with other analgesic techniques or who experience unacceptable side effects.
- Morphine delivered directly into the intrathecal space is particularly effective because it does not have to circulate systemically to reach the CSF and the dorsal horn of the spinal cord and may provide a good option for pain relief.
Fentanyl

- synthetic opioid chemically related to meperidine
- has 100-fold the analgesic potency of morphine and is used for anesthesia.
- The drug is highly lipophilic and has a rapid onset and short duration of action (15 to 30 minutes)
- administered IV, epidurally, or intrathecally

An oral transmucosal preparation and a transdermal patch are also available
transdermal patches

- It creates a reservoir of the drug in the skin. Hence, the onset is delayed at least 12 hours, and the offset is prolonged duration (48 to 73 hrs)
- Rate of absorption is dependent on a number of factors. Body temperature, skin type, amount of body fat, and placement of the patch can have major effects.
- Use is contraindicated in opioid-naïve patients, and patches should not be used in managing acute and postoperative pain.
- It must be used with caution because death resulting from hypoventilation has been known to occur
Pethidine (Meperidine)

- Meperidine is a lower-potency synthetic opioid structurally unrelated to morphine.
- Acts primarily as a \( \kappa \) agonist, with some \( \mu \) agonist activity also.
- It is used for acute pain.
- Meperidine is very lipophilic and has anticholinergic effects, resulting in an increased incidence of delirium as compared to other opioids. The duration of action is slightly shorter than that of morphine and other opioids.
- Meperidine also has an active metabolite (normeperidine) that is renally excreted. Normeperidine has significant neurotoxic actions that can lead to delirium, hyperreflexia, myoclonus, and possibly seizures. Due to the short duration of action and the potential for toxicity, meperidine should only be used for short-term (≤48 hours) management of pain. Other agents are generally preferred.
- Meperidine should not be used in elderly patients or those with renal insufficiency, hepatic insufficiency, preexisting respiratory compromise, or concomitant or recent administration of MAOIs. Serotonin syndrome has also been reported in patients receiving both meperidine and selective serotonin reuptake inhibitors (SSRIs).