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Outline the pharmacology of an opioid injected into the spinal intrathecal space.

Pharmaceuticals

- Intrathecal morphine available as 500mcg/mL solution
- Fentanyl available as 50mcg/mL
- Intrathecal opioids must be preservative free
- If in a glass vial, must be drawn up through filter tip needle
- Indications: intra/post-operative analgesia

Pharmacodynamics

- Mechanism of action:
  - Bind to G-protein-coupled pre and post synaptic receptors in the dorsal horn
  - Causes G-protein-mediated K^+ channel opening (mu and delta receptors) → hyperpolarises cell
  - Causes G-protein-mediated Ca^{2+} channel receptors (kappa receptors)
    - Causes reduction in intracellular Ca^{2+}
    - Leads to decreased release of excitatory transmitters, glutamate and substance P
    - Consequent reduction in nociceptive transmission
- Side effects:
  - Pruritus
  - Nausea and vomiting
  - Urinary retention
  - Respiratory depression

Pharmacokinetics

	Lipophilic e.g. fentanyl	**Hydrophilic e.g. morphine**
Absorption	• Highly potent • Rapid onset • Limited duration of action	• Slower onset • Longer duration of action
Distribution	• Bulk flow in caudal → cephalad direction • Fluctuating thoracic pressure changes (due to respiration) facilitate this flow • Uptake into posterior radicular artery means opioids can travel to brainstem	
	• Rapidly redistributes into other areas, including epidural fat, myelin, white matter • High volume of distribution in spinal cord • High pKa means less un-ionised molecule is available in receptor sites in grey matter • Rapid decreased in CSF concentration • Increased epidural and plasma concentrations	• Slow diffusion into the epidural space • Less redistribution into myelin and white matter (non-receptor sites) • Small volume of distribution in spinal cord • Sustained high concentration in CSF
Metabolism		• Removal from CSF facilitated by glycoprotein carrier transport in choroid plexus
	• Opioids metabolised in liver to both active and inactive metabolites • Some extra-hepatic metabolism → kidney conjugate morphine	
Excretion	• In urine and bile • Water soluble glucuronides excreted in bile may be metabolised by gut flora back to parent opioid, and reabsorbed (enterohepatic recirculation)	