Pharm-06A7 Briefly outline the pharmacology of naloxone

Background

Naloxone is a competitive antagonist at MOP >> DOP and KOP, with minimal intrinsic activity (seen only at high doses)

Mainly used to reverse opioid induced sedation and respiratory depression (e.g. during opioid overdose)
Also used to reverse opioid side effects – e.g. nausea/vomiting, pruritis, urinary retention, biliary spasm and rigidity

Physicochemical and Pharmacetic Properties

N-alkyl derivative of oxymorphone
Clear colourless solution
Vials containing 400 microg in 1 mL of naloxone hydrochloride
Also in Minijets containing 2 mg in 2 mL

Bolus dose 1 ~ 4 microg/kg
Infusion dose 5 microg/kg/hr

Onset of action 1 ~ 2 minutes
Duration of action 30 ~ 40 minutes
Note: duration of action is shorter than most opioids → if naloxone offset before opioid then re-sedation is possible

Pharmacokinetics

Absorption: IV main, also IM or intratracheal
Minimal oral bioavailability (2%, extensive first pass metabolism)

Distribution: pKa 8.0 → 25% unionised at pH 7.4
Vd = 2 L/kg
45% protein bound
Highly lipid soluble
Crosses placenta

Metabolism: hepatic glucuronidation to naloxone-3-glucuronide
Minimal N-dealkylation

Elimination: High clearance (25 mL/kg/min with HER 1.0)
Short elimination t1/2β (60 ~ 90 min)

Pharmacodynamics

CVS: rapid injection → SNS activation → ↑HR, ↑BP, ↑arrhythmias

RESP: reverses opioid induced respiratory depression
CNS: antanalgesic; reverses opioid-induced sedation and analgesia
GIT: reverses opioid induced sphincter of Oddi spasm

Reversal of tramadol minimal (~ 30%)

**Examiner’s comments**

The majority of answers were well organized. The main points to include were

Pharmaceutics
Pharmacokinetics
- IV and IM administration
- High clearance, short half life
- High lipid solubility
- Clinical implications
Pharmacodynamics
- Competitive mu opioid receptor antagonist
- Clinical applications
- Adverse effects

Common problems included lack of organization, failure to discuss the important pharmacokinetic properties or the potential serious adverse effects of naloxone.