Naloxone

Naloxone is a competitive opioid receptor antagonist at mu, kappa and delta receptors and is used for Rx of opioid-induced respiratory & CNS depression

Primary aim in opioid intoxication: ***restore*** adequate respiration ***without*** precipitating withdrawal

Avoid in opioid dependence unless: RR ≤ 12 and SpO2 < 92% on room air

Can be trialed in clonidine/imidazoline overdose to avoid intubation in children (variable response)

Pharmacokinetics:

Low oral and sublingual bioavailability

Onset of action depends on route:

IV: 1-2 minutes; IM: 5-6 minutes; IN: 3-4 minutes: Neb/SC: 5 minutes

Duration of action: 20-90 minutes

Adverse effects:

- In non-opioid dependence, naloxone has no adverse effects, even in large doses
- In opioid dependence a dose-dependent withdrawal syndrome occurs and should be avoided - vomiting (risk of aspiration) and a catecholamine surge can lead to dysrhythmias, AMI, APO, stroke
- If the patient is agitated, they do not need naloxone

Dose and Administration: IV route preferred to allow titration (can also be administered IM, SC, IN, IO, Neb)

Dose: Extremely variable. Depends on the amount & type of opioid taken, & existing opioid tolerance

Use the lowest dose possible to reverse respiratory depression – start low and titrate

- Place 400 mcg naloxone in 10 mL syringe and make up to 10 mL with N/saline (40 mcg per mL)
- Titrate IV every 60 seconds to response – 1 mL, 2 mL, 3 mL, 4 mL
- Further 200 – 400 mcg increments may be required to total dose of 2000 mcg (then consider other DDx)

Paediatric naloxone dose – bolus 10 mcg/kg up to 400 mcg, repeat as required every 60 seconds

Larger initial doses (400 mcg every 60 seconds) may safely be used if the patient is not opioid dependent

Doses > 400 mcg IV are rarely required for heroin overdose. Larger doses may be required for other opioids and buprenorphine overdoses as response is less predictable. If no IV access is available, administer 800 mg naloxone IM. If the pre-packaged IN preparation (1.8 mg/ 0.1 mL) is available, this can also be used.

Therapeutic Endpoint:

- In **non-opioid dependence**: awake and maintaining SpO2 > 92% on room air
- In **opioid dependence**: maintenance of airway, AND SpO2 > 92% on room air - not full reversal NOTE: if hypoxia persists despite normalizing respiratory rate, then seek senior advice
- If re-sedates: administer total naloxone bolus dose that was initially required to restore respiration and commence naloxone infusion at 2/3 of this dose per hour (more likely with long-acting & MR/SR opioids)

Naloxone infusion is not a substitute for continual vigilance. Must occur in HDU setting. Never cease at night

Observation for re-sedation: at least 2 hours after last bolus dose & 4-6 hours post cessation of infusion

Pregnancy: safety not been established. Should not be withheld if required to Rx life-threatening toxicity