Naloxone for Reversal of Opiate Toxicity - Full Clinical Guideline

Reference no.: CG-ANAES/2015/003

1. Introduction

Opiate toxicity can be a result of inappropriate high dosing, high patient sensitivity, accumulation (particularly in renal failure) and intentional overdose.

Opioid toxicity manifests as sedation, slow respiratory rate with large tidal volumes, and pin-point pupils, leading to respiratory failure and arrest.

Naloxone is a competitive antagonist to opioid drugs and is used in the treatment of opioid overdose. Its half-life is shorter than all opioid drugs, so repeat doses or an infusion may be required to maintain clinical effect.

Abrupt reversal of opioid drugs in the context of chronic use has been reported to precipitate symptoms of withdrawal (e.g. restlessness, nausea and vomiting, sweating, tremor, abdominal pain, tachycardia, hypertension and tachypnea). There is danger of completely reversing opioids in patients who will otherwise have significant pain.

2. Aim and Purpose

This guidance document should be used in association with the clinical context, to achieve safe reversal of opioid analgesia, whilst minimising adverse effects of abrupt cessation of opioids.

3. Clinical context:

The characteristics of opiate overdose are typically: sedation/loss of consciousness, slow respiratory rate with large tidal volumes, and pin-point pupils. It should be in the context of significant opiate use/suspected overdose or accumulation. Other causes of unconsciousness should be considered also.

In the event of suspected opioid overdose or accumulation:

A doctor (and Critical Care Outreach Team (CCOT) if occurring outside of the Emergency or Critical Care Department) should be called immediately to assess the patient if there is a depressed level of consciousness Neuro AVPU (alert, voice, pain, unresponsive) <A, or respiratory rate (Respiratory Rate (RR) ≤ 8 bpm).

Commence high flow oxygen (15 litres) immediately, and if necessary provide airway support using a chin lift/jaw thrust maneuver, +/- oropharyngeal airway. If possible place the patient in the recovery position.

All opioid medications (including opioid containing epidural infusions) should be ceased immediately.

Once opioid overdose has been identified, patients should have respiratory rate and conscious level (AVPU) recorded every 15 minutes. National Early Warning Scores (NEWS) should be calculated every 30 minutes, and escalated as appropriate.

Naloxone administration should occur as soon as possible and be stocked on all wards and departments where opioid drugs are used. Intravenous access should be gained as soon as possible but if delayed, intramuscular and subcutaneous doses may be given. The onset of action may be slower via these routes.

4. Initial Bolus Doses:

Reversal of respiratory depression and reduced conscious level from medicinal use of opiates

Naloxone 100 micrograms as a slow IV bolus over 30 seconds repeated every 1-2 minutes until a satisfactory rise in respiratory rate/ improvement in conscious level is achieved.

(Prepared as 400 micrograms diluted to 10 ml with sodium chloride 0.9% and administered in 2.5 ml (100 microgram aliquotes)

Deliberate opioid overdose or respiratory arrest

Naloxone 400 micrograms as a slow IV bolus over 30 seconds repeated every 1-2 minutes until satisfactory respiratory rate and conscious level obtained, to a maximum of 4 mg.
The dose maybe further diluted to 10ml with sodium chloride 0.9%. If no response to 4 mg naloxone then the diagnosis of opioid toxicity should be questioned.

If no IV access then naloxone 200 – 400 microgram boluses can be given intramuscularly or subcutaneously whilst IV access if obtained (neat).

5. Monitoring:

In the event of adequate clinical response to naloxone (aim for RR>10 bpm, AVPU=A), observations every 15 minutes should be maintained for 2 hours. Hourly NEWS should be calculated for at least 6 hours after the last dose of naloxone. This maybe continued longer at the discretion of the medical team.

In the event of further deterioration, further boluses of naloxone at previously therapeutic doses should be given and close patient monitoring continued.

If 3 repeat boluses of naloxone are required to maintain clinical effect, transfer to a critical care area should occur. A doctor and/or CCOT nurse should remain with the patient until they arrive on critical care and are handed over to the critical care team.

Note: Patients receiving haemodialysis on renal HDU who require a naloxone infusion should be discussed with Critical Care and referred to CCOT but, if deemed appropriate, may remain on the renal HDU for ongoing renal replacement therapy.

6. Naloxone Infusion

An IV naloxone infusion may be useful where repeated IV doses are required; particularly if patients have taken opioids with a long half-life (e.g. methadone, buprenorphine, dextropropoxyphene, MST or zomorph).

Naloxone infusions should ONLY be used in a monitored bed where the patient is visible to medical or nursing staff. This would typically be restricted to Critical Care, ED Resus, MAU monitored beds or Renal HDU.

7. Infusion regimen

Infusion preparation

Naloxone 4 mg (10 x 400 micrograms) made up to 20ml with Dextrose 5% or Sodium Chloride 0.9% *(resulting solution 200 micrograms per ml).*

Please contact pharmacy as soon as possible as they will normally make up the infusion for everywhere except ICU.

The infusion must be administered through an electronic rate controlled device (e.g. syringe pump), preferably via a large peripheral vein (or central venous catheter) to avoid potential venous irritation due to the preparation's low pH.

Prescription

The initial hourly starting rate should equal **0.6 x resuscitative cumulative bolus dose** that gave an adequate clinical response. *(see table1)* This should then be adjusted according to clinical condition.

The resuscitative dose is described as that dose that was sufficient to maintain the patient with satisfactory ventilation for at least 15 minutes.

Table 1

Initial cumulative bolus dose producing response (mcg)	Initial hourly rate of naloxone likely to be necessary (mcg/hr)	Rate to set pump (4mg in 20ml concentration) (ml/hr)
400	240	1.2
600	360	1.8
800	480	2.4
1000	600	3.0
1200	720	3.6
1400	840	4.2
1600	960	4.8
1800	1080	5.4
2000	1200	6

Further bolus doses may be required whilst titrating the infusion.
In this case; half the initial bolus dose should be given at 15 minutes into the infusion.

e.g. Initial cumulative bolus producing response was: naloxone 800 micrograms

Infusion is now set up and running at 2.4 mls per hour

Response is not satisfactory after 15 minutes

Another bolus does of 400 micrograms should be given

Review with medical staff after 4 hours, or prior to preparing a new infusion to determine if the infusion is still required.

8. Adverse Effects

Abrupt reversal of opioid drugs in the context of chronic use has been reported to precipitate symptoms of withdrawal (e.g. restlessness, nausea and vomiting, sweating, tremor, abdominal pain, tachycardia, hypertension and tachypnoea). There is danger of completely reversing opioids in patients who will otherwise have significant pain. These patients will need to have an analgesic plan made post

administration of naloxone. Please contact the acute pain team for advice in this instance.

9. Key References:

Support to minimise the risk of distress and death from inappropriate doses of naloxone 26 October 2015: NHS/PSA/Re/2015/009

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Toxbase http://www.toxbase.org/Poisons-Index-A-Z/N- Products/Naloxone-antidote/

10. Documentation Controls:

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