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# **Clonidine for Pain Management**

## Dosing, Administration and Monitoring Guidelines

## Clinical documents related to this guideline

• Intensive Care Unit – Clonidine Guideline

## **Prescribing requirements and restrictions**

- Epidural Clonidine: should only <u>prescribed and the first dose given</u> by an Anaesthetist or the Acute Pain Service (APS).
- Oral/IV administration: There are no restrictions on who can prescribe, however caution should be undertaken if using IV dosing in non-monitored environment.

## **Pharmacokinetics and Pharmacodynamics**

- Clonidine is an alpha-2 adrenoreceptor agonist.
- IV/ Epidural: hypotensive effect occurs within 5mins achieving a peak effect within 30mins and may last 3 to 6 hours (1).
- Up to 50% of Clonidine is metabolised in the liver to inactive metabolites. Mainly renal excretion as unchanged drug (2).
- Half-life in normal renal function is 12 to 20 hours. Half-life is prolonged to 41 hours in end stage renal failure (3).

#### **Indications**

- Clonidine may be used for neuropathic, postoperative or chronic pain, however is generally an inadequate analgesic when used alone.
- Clonidine can be used for anxious patients who also have significant pain.
- Clonidine can also be used to manage opioid withdrawal symptoms (shivering, sweating, anxiety, diarrhoea)
- As an additive to standard epidural analgesia solutions to improve the quality of analgesia when:
  - There is breakthrough pain despite high doses of standard epidural infusion solution (local anaesthetic +opioid)
  - There is intolerance to fentanyl, morphine or other opioids.
  - Incomplete sensory block across dermatomes (patchy).
  - Adjunct analgesic particularly with coexisting anxiety or opioid abuse/withdrawal. Can reduce severity of opioid withdrawal symptoms.

#### **Contraindications**

- Hypersensitivity to clonidine
- Severe bradycardia or hypotension

#### **Precautions**

- Caution when ceasing after prolonged treatment with high doses: Abrupt withdrawal may cause rebound hypertension. Symptoms include agitation, nervousness anxiety, restlessness and headache. Patients discharged on clonidine should be warned to not discontinue abruptly (See Discharge Section).
- TGA Medication Safety Update: April 2021. Clonidine importance of dosing compliance and safe storage:
  - Health professionals are reminded that serious adverse events can occur in children who are accidentally overdosed with clonidine either when receiving treatment for behavioural disorders, or obtaining access to a family member's medication. Health professionals are advised to counsel patients and their parents/carers to pay close attention to dosing and remind them of the need for safe storage and other safety precautions.

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## **Dosage and Administration**

#### **Epidural dose** (4,5):

- Loading dose: 150 microg with 5 mL local anaesthetic only to be administered by an anaesthetist.
- Maintenance dose: 300 microg to 450 microg in a 200 mL epidural infusion bag (i.e. Clonidine 1.5 to 2.25 microg /mL)
  - o infused at normal epidural infusion rates of 4 to 15 mL/hour.
- Compatible Solutions for epidural administration of clonidine (at above final concentrations):
  - o Ropivacaine 0.2% (2mg/mL) (11), bupivacaine 0.125% (1.25mg/mL) (12)
  - o Ropivacaine 0.2% (2mg/mL) with fentanyl 200 or 400 microg/mL (13)
  - Other combinations (e.g. with morphine (12)) may be possible discuss use with your ward or the Medicines information Pharmacist ext 14359.

**Note**: The <u>Pharmacy Department</u> can make specific epidural analgesia solutions containing clonidine, provided the order is received <u>during working hours</u>. Outside Pharmacy Department hours, contact the <u>on-call anaesthetist</u> (ext 14522) who will prepare the solution.

#### Oral/IV:

- Usual starting dose 50 microg TDS.
  - o The dose may be titrated to 75 microg TDS <u>OR</u> 1 microg/kg TDS.
  - If higher dose required for pain management seek APS advice.
- Do not give if systolic blood pressure is less than 100mmHg.
- When switching formulations note that oral and IV doses are considered equivalent.
- IV injection is unlikely to be necessary for chronic pain relief.
- When administering by IV Infusion: add dose of clonidine to a convenient amount of sodium chloride 0.9% or glucose 5% (normally 50-100mL) and infuse over 10-15 minutes.
- Compatible solutions for IV administration: sodium chloride 0.9% (6) or glucose 5% (7).

### Monitoring

• Epidural – See Special Analgesia Nursing Observations Policy

#### **Adverse Effects**

- Sedation, hypotension, bradycardia, dry mouth, dizziness, constipation, weakness and fatigue (1)
- Avoid using clonidine in haemodynamically unstable patients
- Caution when using 12 to 18 hours post operatively because hypotension can be more marked due to hypovolaemia

#### Interactions (1,8)

- CNS depressants may enhance sedation bradycardia and hypotension monitor and titrate dose carefully.
- Tricyclic Antidepressants may reduce hypotensive effect of clonidine. Avoid or monitor BP and titrate clonidine dose.
- Beta-blockers may enhance bradycardia and hypotension. May rarely cause paradoxical increase in blood pressure.
- Sympathomimetics increased risk of hypertension
- Antihypertensives may further lower blood pressure
- Haloperidol high IV doses of clonidine may increase arrhythmogenic potential of high IV does of haloperidol

## Weaning and Discharge (10)

- Stopping clonidine abruptly may precipitate a severe withdrawal syndrome. Taper dose over at least 7 days to weeks if patient has been taking for more than a few weeks.
- Ideally, if started in hospital, clonidine should be weaned off before the patient is discharged home.
  - This can be achieved by reducing the dose by a third each day (i.e. 50 microg TDS can be reduced to 50 microg BD then 50 microg daily then cease)
- If the patient is discharged home on clonidine they should be advised not to abruptly cease the medication as this can cause a rebound hypertension, headache, flushing, insomnia, agitation and tremor.
- Notify the GP of clonidine weaning plan by ensuring this information is added into the Discharge Summary.

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## Use in pregnancy and lactation (9)

- Clonidine crosses the placenta however maternal use has not been associated with an increased risk of birth defects or adverse pregnancy outcomes. Monitoring is required. Discuss use with the Medicines information Pharmacist ext 14359.
- Clonidine is excreted into breast milk, but is considered safe to use in nursing mothers at the lowest effective dose.
   Observe the breastfed infant for adverse effects and avoid use in the early postpartum period as the reduction in prolactin secretion may reduce breast milk production.

## Presentation and Storage (1)

- Clonidine hydrochloride (Catapres®) 150 microg per 1 mL ampoule
- Catapres® 100microg and 150microg tablets (100 tablets per box)
- Store Catapres® ampoules below 30° C and tablets below 25° C

#### References

- 1. MIMS® Online, Catapres® (Clonidine hydrochloride) 150 microg/mL ampoules Product Information, MIMS Australia, 2023 accessed online on 4/10/2023 via Clinicians' Health Channel.
- 2. Micromedex® (electronic version) IV Index. IBM Watson Health, Greenwood Village, Colorado, USA. Accessed online on 4/10/2023 via Clinicians' Health Channel.
- 3. Martindale: The complete drug reference [online] London: The Pharmaceutical Press, accessed online on 4/10/2023 via Clinicians' Health Channel.
- 4. ASHP. Handbook on injectable drugs. Accessed in Lexi-Comp online on 4/10/2023 via Clinicians' Health Channel.
- 5. Chan A, Cheung C, Chong Y. Alpha-2 agonists in acute pain management. Expert Opin Pharmacother. 2010 Dec;11 (17):2849-68
- 6. SHPA, Australian Injectable Drug Handbook, 9th Edition Melbourne: The Society of Hospital Pharmacists of Australia: accessed online on 4/10/2023 via Clinicians' Health Channel.
- 7. Gray, A. Injectable drugs guide, London: Pharmaceutical Press. 2011 accessed online on 4/10/2023 via EBSCO HOST.
- 8. Baxter K, Preston CL (eds), Stockley's Drug Interactions. [online] London: Pharmaceutical Press, accessed online on 4/10/2023 via Clinicians' Health Channel.
- 9. Loke, Tan, et al. The Women's Pregnancy and Breastfeeding Medicines Guide, The Royal Women's Hospital, accessed online on 4/10/2023 via Clinicians' Health Channel.
- 10. Rossi S. editor. Australian medicines handbook. Adelaide: Australian Medicines Handbook Pty Ltd; accessed online on 4/10/2023 via Clinicians' Health Channel.
- 11. Öster Svedberg K, et al. Compatibility of ropivacaine with morphine, sufentanil, fentanyl, or clonidine. J Clin Pharm Ther,2002;21:39-45.
- 12. Bianchi F, et al. Stability and compatibility of drug mixtures in an implantable infusion system. Anaesthesia. 2008 Sep;63(9):972-8
- 13. J. G. Förster, P. H. Rosenberg. Small dose of clonidine mixed with low-dose ropivacaine and fentanyl for epidural analgesia after total knee arthroplasty. Br J Anaesth, 2004 Nov;93(5):670–7.

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