Clonidine: Use as a Sedative in Adult Intensive Care [Unlicensed Indication]

Unlicensed Milrinone is at Consultant Intensivist Request Only

Background

Clonidine is an alpha$_2$ receptor agonist which is licensed for the treatment of hypertension.
Due to its sedative and antihypertensive effects, clonidine may also be used (unlicensed) with the consent of a **Consultant Intensivist** for:

- Alcohol withdrawal reactions
- Opiate withdrawal reactions
- Agitation with tachycardia and hypertension, especially during weaning from the ventilator.
- Autonomic storm after traumatic brain injury.
- As an additional sedative when adequate sedation cannot be maintained using standard drugs.

The half-life of clonidine is 10 – 20 hours, rising to up to 41 hours in end stage renal failure.

Contra-Indications

Known hypersensitivity, Severe bradyarrhythmia due to 2nd or 3rd degree AV block or sick sinus syndrome.

Cautions

Extreme caution should be exercised with hypotension, bradycardia, low cardiac output or impaired left ventricular function.
Enhanced hypotensive effects will be seen when other hypotensive drugs are given concurrently.
Concurrent use with haloperidol may produce QT prolongation.
Raynaud's syndrome or other occlusive peripheral vascular disease.
Caution in patients with a history of depression as it can worsen the condition (with prolonged use).
Unsafe for use in porphyria.

Adverse Effects

Bradycardia, hypotension, AV block (rare), fluid retention, depression, dry mouth, dry eyes (rare), constipation.

Administration

Continuous Intravenous Infusion

Dilute 750micrograms of clonidine (5 ampoules of 150micrograms/mL) to 50mL with sodium chloride 0.9% to produce a solution of 750micrograms in 50mL (15micrograms in 1mL). Can be administered peripherally or centrally.

However, a higher concentration of 1500 micrograms in 50 mL has been used in fluid-restricted patients
N.B this will change the infusion rate calculation.

Dose

Initiation: initial dose of 75 micrograms (5mL of the 150microgram in 1mL solution) may be given by slow intravenous injection over 10 minutes followed by a continuous infusion of 0.5 – 2 microgram/Kg/hour. The dose should be titrated up quickly, as the patient's blood pressure and heart rate allows.

Higher doses may occasionally be needed in some patients (local practice)*, up to a maximum 4microgram/Kg/hr. This must be discussed with the consultant intensivist.*

Discontinuation: When no longer required, gradually wean off the infusion by reducing the rate by 0.25 - 0.5 micrograms/Kg/hr every hour to minimise rebound hypertension and agitation.
A slower rate of dose reduction may be required in some patients.

Compatible diluent

Compatible with sodium chloride 0.9% or dextrose 5% and 10%.
Refer to Medusa injectable medicines guide for further compatibility information.

Example calculation
The **infusion rate** can be calculated from the following equation:

$$\text{Clonidine infusion rate (mL/hour)} = \frac{\text{Dose (micrograms/Kg/hr) x Patient weight (Kg)}}{\text{Concentration (micrograms in 1mL)}}$$

For example: To administer a dose of 2 micrograms/Kg/hr of clonidine to a 70Kg patient using a standard solution of 750microgram in 50mL (15 microgram in 1mL), the calculation would be as follows:

$$\text{Clonidine infusion rate} = \frac{\text{2(micrograms/Kg/hr) x 70(Kg)}}{\text{15(micrograms in 1mL)}} = 9.33\text{mL/hr}$$

Using a 750microgram in 50mL (15micrograms/mL) clonidine solution the following specifies the infusion rate (mL per hour) required for different patient weights

Dose →	**0.5micrograms/Kg/hr**	**1 microgram/Kg/hr**	**2 micrograms/Kg/hr**	**4 micrograms/Kg/hr**
Patient weight ↓	Infusion Rate (mL/hour)*			
40Kg	1.3 mL/hour	2.7 mL/hour	5.3 mL/hour	10.7 mL/hour
60Kg	2 mL/hour	4 mL/hour	8 mL/hour	16 mL/hour
80Kg	2.7 mL/hour	5.3 mL/hour	10.7 mL/hour	21.3 mL/hour
100Kg	3.3 mL/hour	6.7 mL/hour	13.3 mL/hour	26.7 mL/hour
120Kg	4 mL/hour	8 mL/hour	16 mL/hour	32 mL/hour
140Kg	4.7 mL/hour	9.3 mL/hour	18.7 mL/hour	37.3 mL/hour

*Infusion rates (mL/hour) have been rounded to 1 decimal place for ease of administration
N.B this table does not apply for other concentrations and thus calculations will need to be recalculated- contact ward pharmacist for assistance if needed:

Intravenous Bolus
Method of administration
Appropriate in acute agitation in a hypertensive, tachycardic patient.

Dilute dose to 10mL with sodium chloride 0.9% to facilitate slow administration and give by slow IV injection over 10-15 minutes to avoid a possible transient hypotensive effect.

Ideally administer centrally due to low pH. If central venous access is unavailable, administer via a large peripheral vein monitoring insertion site closely. Resite cannula at first signs of inflammation.

Initiation: Usual starting dose is 50micrograms tds. This may be titrated to a maximum of 250micrograms tds. Clonidine should not be stopped suddenly.
Discontinuation: Wean off gradually to minimise rebound hypertension and agitation.

Enteral Route / Via Enteral Feeding Tube
Method of administration
It is well absorbed in the gastrointestinal tract within 30 minutes of administration. Peak plasma concentration is reached 1 to 3 hours after oral administration

First choice is 150microgram/mL injection which can be given enterally as this is easier to administer NG. Either give neat or dilute with water prior to administration. If unavailable disperse 100microgram tablets in 10mL water. Allow 2 minutes for tablet to disperse, shaking if necessary. Administer immediately after dispersion, via NG. A prolonged break in feeding is not required.
25microgram tablets are film coated and do not readily disperse. Avoid if possible.

Initiation: Usual starting dose of 50micrograms tds may be titrated gradually to a maximum 400micrograms tds. If converting from the intravenous route, divide the current total daily dose into 3 doses (capped at the maximum enteral dose of 400micrograms tds) and administer enterally.

Discontinuation: Should not be stopped suddenly. Wean off gradually to minimise rebound hypertension and agitation.

Renal adjustments

AKI:
Dose titrated to effect

CKD not on RRT:
CKD (GFR less than 30 mL/minute/1.73m^2) patients are at greater risk of drug accumulation. Prescribe smaller infusion and intermittent doses.

Continuous veno-venous haemofiltration (CVVHF) or haemodiafiltration (HDF):
No dose adjustment; titrate to effect. Caution during periods of RRT greater than 4 hours.

Note: Toxicity is difficult to discern based on titration to sedation alone.
Consider accumulation of clonidine when either heart rate or blood pressure drops inexplicably, or in excess noradrenaline requirements or, occasionally, paralytic ileus.

References

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