Cisatracurium besylate

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Functional Sub-Group: Clinical
Summary: This guideline has been developed to ensure standardized preparation and administration of cisatracurium throughout the SWSLHD.

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1. Introduction:

Cisatracurium besylate is used to facilitate intubation and mechanical ventilation in a select group of patients who require skeletal muscle relaxation (e.g. major ventilatory difficulty, unstable ICP, major cardiovascular instability). To facilitate surgical intervention where muscle relaxation is required (e.g. emergency reopening of sternotomy).

The risk addressed by this policy: Patient Safety
2. The Aims / Expected Outcome of this policy:

Cisatracurium besylate will be administered safely and appropriately with minimal adverse effects

Related Standards or Legislation

- NSQHS Standard 1 Governance
- National Standard 4 Medication Safety

Related Policies (if relevant)
PD2013_043 Medication Handling in NSW Public Hospitals

3. Principles

- All care provided within SWSLHD will be in accordance with infection control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer/authorised nurse practitioner (NP) unless required during an emergency.
- All drugs administered during an emergency (under the direction of a medical officer/authorised nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
- Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require ‘same time’ administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritised) and are to be signed by the administering nurse.
- Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The “rights of drug administration” must be followed: right: patient, drug, dose, route, administration, time, reason for the drug and documentation.
- Adverse drug reactions are to be documented and reported to a medical officer.
- Medication errors are to be reported using the hospital electronic reporting system: IIMS.
- Guidelines are for adult patients unless otherwise stated.
- Patients are to receive concurrent sedation/anaesthesia when a neuromuscular blocking agent is in use, unless their neurological state does not require it.
- Paralysis is preferably maintained using bolus doses of a neuromuscular blocker as infusions increase adverse effects.
- When an infusion is prescribed the reason for using an infusion rather than bolus dosing should be documented.
- A nerve stimulator must be used for determining on-going neuromuscular blockade; with the aim of achieving 2 finger twitches with ‘train-of-four’ assessment. (See Educational material below).
- **This guideline is for administration of drugs in critical care areas only.**

Actions

- Cisatracurium besylate, a stereoisomer of atracurium, is an intermediate duration, nondepolarising benzylisoquinolinium skeletal muscle relaxant.
- Cisatracurium besylate binds to cholinergic receptions on the motor endplate to antagonise the action of acetylcholine, resulting in a competitive block of neuromuscular transmission. This action is readily reversed by anticholinesterase agents such as neostigmine
- Onset of action: I.V.: 2-3 minutes
- Peak effect: 3-5 minutes
- Duration: Recovery begins in 20-35 minutes when anesthesia is balanced

**Indications**

- During surgical procedures and other procedures that require relaxation of the skeletal muscles.
- To facilitate intubation and, in some cases, mechanical ventilation.
- An adjunct to general anaesthesia or sedation in the ICU

**Contraindications**

- Known hypersensitivity to cisatracurium besylate, atracurium or benzenesulfonic acid.

**Precautions**

- Cisatracurium paralyses the respiratory muscles as well as other skeletal muscles but has no effect on consciousness or pain threshold.
- Should only be administered under the supervision of intensive care clinicians or anaesthetists familiar with its use and effect.
- Facilities for intubation, ventilation and oxygenation must be available.
- Patients with myasthenia gravis or other neuromuscular diseases have increased sensitivity to non-depolarising neuromuscular blocking agents.
- Severe acid-base and/or electrolyte abnormalities may increase or decrease the sensitivity of this drug.
- Should not be administered into the infusion line of a blood transfusion due to being hypotonic.
- Maintenance of adequate ventilation.
- Hypotension.
- Hypothermia – prolonged paralysis may occur.

**Significant Interactions**

- The following drugs have been shown to increase the effects of non-depolarising neuromuscular blocking agents: volatile anaesthetics such as isoflurane and sevoflurane; ketamine; other non-depolarising neuromuscular blocking agents; antibiotics, including the aminoglycosides, tetracyclines, lincomycin and clindamycin; antiarrhythmic drugs, including propranolol, calcium channel blockers, lignocaine, procainamide and quinidine; diuretics, including frusemide and possibly thiazides, mannitol and acetazolamide; magnesium salts and lithium salts.
- Decreased effect of non-depolarising neuromuscular blocking agents with prior chronic administration of phenytoin or carbamazepine.
- Prior administration of suxamethonium has no effect on the duration of neuromuscular block following bolus doses of cisatracurium injection or on infusion rate requirements. Administration of suxamethonium to prolong the effects of non-depolarising neuromuscular blocking agents may result in a prolonged and complex block which can be difficult to reverse with anti cholinesterases.
- Rarely, certain drugs may aggravate or unmask latent myasthenia gravis or actually induce a myasthenic syndrome. Increased sensitivity to nondepolaring neuromuscular blocking agents might result. Such drugs include various antibiotics, beta-blockers (propranolol, oxprenolol), antiarrhythmic drugs (quinidine), antirheumatic drugs (chloroquine, penicillamine), chlorpromazine, steroids, phenytoin and lithium.
- Compatibility in syringe: Incompatible with Ceftriaxone.

**Adverse Effects**

- <1%: Effects are minimal and transient, bradycardia and hypotension, flushing, pruritus, rash, bronchospasm, acute quadriplegic myopathy syndrome (prolonged use), myositis ossificans (prolonged use)
Presentation
- Cisatracurium 5mg in 2.5ml ampoule (refrigerated at 2-8°C).
- Cisatracurium has organ independant degradation based upon pH and temperature and requires refrigeration.

Administration Guidelines

Bolus Dose
- Administer an initial dose of 0.15mg /kg.
- Neuromuscular blockade can be extended with a maintenance dose of 0.03mg/kg bodyweight. This provides approximately 20 minutes of additional clinically effective neuromuscular blockade during opioid sedation or propofol anaesthesia.

IV Infusion
- Draw up the infusion neat to equal a total concentration of 100mg in 50mL (2mg/ml). Draw up 20 ampoules of (5mg /2.5ml) undiluted, which will equal 100mg in 50mL.
- An initial infusion rate of 3 microgram/kg/minute (0.18 mg/kg/hour) is recommended. There may be wide inter-patient variation in dosage requirements and these may increase or decrease with time. After initial period of stabilisation of neuromuscular blockade, a rate of 1-2 microgram/kg/min (0.06 – 0.12 mg/kg/hour) should be adequate to maintain neuromuscular blockade.
- Titrate infusion to achieve 2 finger twitches of the train-of-four response of the adductor pollicis muscle following supra maximal electrical stimulation of the ulnar nerve using a nerve stimulator (refer to educational material below).

Infusion rate of Cisatracurium in mL/hr according to concentration, patient weight and dose of 3mcg/Kg/min

<table>
<thead>
<tr>
<th>Concentration of infusion</th>
<th>Patient weight</th>
<th>Infusion rate (ml/hr) according to dose (3microgram/kg/minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2mg/mL</td>
<td>40kg</td>
<td>3.6 mL/hr</td>
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<tr>
<td>2mg/mL</td>
<td>50kg</td>
<td>4.5 mL/hr</td>
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<td>2mg/mL</td>
<td>80kg</td>
<td>7.2 mL/hr</td>
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<tr>
<td>2mg/mL</td>
<td>90kg</td>
<td>8.1 mL/hr</td>
</tr>
<tr>
<td>2mg/mL</td>
<td>100kg</td>
<td>9 mL/hr</td>
</tr>
</tbody>
</table>

Clinical Considerations
- Sedation if required should be provided prior to administration of cisatracurium.
- Cisatracurium may be administered by bolus dose or infusion to adult patients in ICU.
- Assess neuromuscular blockade every 30 minutes – 1 hour to ensure adequate blockade. Please refer to Appendix 1 for how to use nerve stimulator to assess neuromuscular blockade.
- Reversal of the drug may be achieved with neostigmine. As neostigmine can cause bradycardia, atropine may need to be used as well.
- A patient receiving cisatracurium should receive sedation if there is a potential for awareness.
- The time to onset of paralysis decreases and the duration of maximum effect increases with increasing Cisatracurium doses.
4. References and links

5. [emedicine.medscape.com](http://emedicine.medscape.com)
6. [www.teleflex.com](http://www.teleflex.com)
7. Liverpool Hospital Intensive Care Unit Guidelines. 2013. Adrenaline, SWSLHD.

5. Background Information/Educational Material

**Peripheral Nerve Stimulator**

- The neuromuscular blockade is assessed by using a nerve stimulator.
- The peripheral nerve stimulator (PNS) is used to monitor impulse transmission across the neuromuscular junction. This allows assessment of the depth of neuromuscular blockade (NMB).

**Indications for Use**

- All patients in critical care areas who are receiving muscle relaxants by infusion should have the depth of neuromuscular blockade formally assessed at least 2nd hourly by peripheral nerve stimulation. They may be given a scheduled “drug holiday” (i.e. cessation of NMB until movement and deep tendon reflexes return, normally once a day).
- “Train of Four” – this term describes four “twitches” delivered 0.5 sec apart. Because these stimuli are delivered so closely together, there is a fade in muscular response when neuromuscular blocking agents have been given.

**Procedure.**

1. Position two surface electrodes (ECG electrodes suffice) over the ulnar aspect of the patient's forearm 2-3cm apart. This ensures that the nerve is stimulated and avoids direct electrical stimulation of the muscle.
2. Connect to the leads marked “proximal” (red, +ve) and “distal” (black, -ve).
3. Turn unit on (and test battery if appropriate)
4. Select current output using wheel button (20-40mA is usually sufficient, although 50-80mA may be necessary in oedematous or obese patients).
5. You should be aware that nerve stimulation can be painful, and only the lowest output necessary should be selected.
6. Press “Play/start button” whilst carefully feeling the patient’s thumb. Stimulation of the ulnar nerve results in contraction of the adductor pollicis brevis muscle, resulting in twitching (flexion) of the thumb.
7. With “ideal” neuromuscular blockade using a NMB infusion, the rate should be adjusted so that only one or two twitches of a TOF are felt. Reassessment of the depth of blockade should be made 10-15 minutes following any rate change.
8. With “intense” neuromuscular blockade, there will be no obvious twitch. In such circumstances, the neuromuscular infusion should be decreased and the patient reassessed in 30-60 minutes. If in doubt, the test may be repeated with either an increased output or following a tetanic stimulation. The infusion rate is titrated to achieve 1-2 twitches. Decrease the infusion rate further if the return of one to two twitches has taken >60 minutes.
9. If on initial testing there is normal twitch strength, the patient is inadequately blocked at the neuromuscular junction, and the infusion will need to be increased (+/- following bolus).
Electrode Placement

**Ulnar nerve:**
Place negative electrode (black) on wrist in line with the smallest digit 1-2cm below skin crease and the positive electrode (red) 2-3 cm proximal to the negative electrode

**Response:** adductor pollicis muscle - thumb adduction

**Facial Nerve:**
Place negative electrode (black) by the ear lobe and positive (red) 2cm from eyebrow (along facial nerve inferior and lateral to eye)

**Response:** Orbicularis occuli muscle – eye lid twitching

**Sural (posterior tibial) nerve:**
Place negative electrode (Black) over the medial malleolus (palpate posterior tibial pulse and place electrode there) and positive electrode (Red) over flexor hallucis brevis muscle

**Response:** Planter flexion (curl of big toe)

*Note: This is an example of one nerve stimulator – you will need to refer to local guidelines and manufacturer’s instructions depending on the nerve stimulator available in your critical care area.*
Peripheral nerve stimulator
www.teleflex.com

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