Ketamine for Pain Management

Medication Protocol

Areas Applicable: St Vincent Hospital Melbourne
Areas Not Applicable: N/A
Related DocumentsContinuous Subcutaneous Drug Infusion with a Niki T34 Syringe Driver – Oct 2013

Medication Information

Prescribing Requirements and Restrictions
Ketamine should only be commenced in consultation with an anaesthetic, pain or palliative care specialist as part of a multi-modal management plan. Patients with acute, escalating or chronic pain may have different clinical priorities and ketamine’s efficacy and toxicity profile may vary across these patient groups. Thus there may be variation in the rationale for using ketamine and in the way it is administered in this hospital.

Action / Pharmacology
Ketamine is a non-competitive NMDA (N-methyl D-aspartate) receptor antagonist, which blocks glutamate, interrupts cholinergic transmission and inhibits the reuptake of noradrenaline and serotonin. Direct action on the cortex and limbic system produces a cataleptic-like state in which the recipient is dissociated from the surrounding environment. Ketamine modulates central pain sensitization, hyperalgesia and opioid tolerance.

Ketamine can be used as a rapid-acting non-barbiturate dissociative anaesthetic but this is not the focus of this protocol. At sub-anaesthetic doses ketamine can be used as a non-opioid analgesic agent.

Indications

Anaesthetic
1. Induction of anaesthesia (not the subject of this protocol)
2. Maintenance of anaesthesia (not the subject of this protocol)

Analgesic
1. Severe acute peri-operative pain or exacerbation of chronic pain, including:
   a. refractory neuropathic pain
   b. phantom limb pain
   c. severe cancer pain
2. ‘Wind-up’ pain (rapidly escalating opioid requirements)

Contraindications
Ketamine is contraindicated in those who have shown hypersensitivity to the drug or its components.
### Precautions
- Conditions that may be worsened by an elevation of blood pressure or heart rate (eg poorly controlled hypertension, stroke, intracerebral haemorrhage, angina, recent MI, stenotic valvular heart disease, tachyarrhythmias, chronic heart failure)
- Psychiatric disorders
- Raised intracranial or intraocular pressure
- Epilepsy

### Side Effects
Factors such as advanced age, poor health status, frailty and progressive cancer must be taken into consideration when considering the likelihood and impact of adverse reactions.

**Common**
- **Dermatologic:** irritation at injection site (due to low pH) may require re-siting cannula daily or more often
- **Gastrointestinal:** nausea, vomiting, hypersalivation
- **Psychiatric:** hallucinations, delirium (often hypoactive), dysphoria, feeling ‘spacey’ or disconnected, vivid unpleasant dreams

**Uncommon (although may be problematic in frail patients)**
- **Cardiovascular:** hypertension, elevation of heart rate
- **Musculoskeletal:** increased muscle tone (may resemble tonic-clonic seizures)
- **Ophthalmological:** lacrimation

**Serious**
- **Cardiovascular:** arrhythmias
- **Neurological:** sedation, amnesia, intracranial pressure elevation, diplopia, nystagmus
- **Ophthalmological:** intraocular pressure elevation
- **Psychiatric:** hallucinations, delirium (often hypoactive), dysphoria, feeling ‘spacey’ or disconnected, vivid unpleasant dreams
- **Respiratory:** respiratory depression (with rapid infusion but may also be due to pre-existing high levels of opioid)

### Drug Interactions
- Any drug that raises blood pressure or heart rate – will increase adverse effects

### Use in Pregnancy/Lactation
- Ketamine crosses the placenta with potential for causing respiratory or central nervous system depression in the foetus. Limited data exists regarding use whilst breast-feeding.
- Australian category B3.
**MEDICATION PROTOCOL**

**Ketamine for Pain Management**

### Dosing, Administration and Monitoring

<table>
<thead>
<tr>
<th>Product Presentation</th>
<th>Ketamine (as hydrochloride) 200 mg per 2 mL vial (Ketalar®).</th>
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<tbody>
<tr>
<td></td>
<td>• contains 0.1 mg/mL benzethonium chloride as preservative</td>
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<td></td>
<td>• pH = 3.5 to 5.5</td>
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<thead>
<tr>
<th>Product Storage</th>
<th>• Schedule 8 drug (ordering, storage and recording as for drugs of addiction)</th>
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<tbody>
<tr>
<td></td>
<td>• Store below 30°C and protect from light</td>
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<table>
<thead>
<tr>
<th>Product Location</th>
<th>Normal business hours: Central Pharmacy (Fitzroy)</th>
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<tbody>
<tr>
<td></td>
<td>After hours: EMG, OPS, SM6.</td>
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#### Compatibility

- **Intravenous infusions:** Department of Anaesthesia preferred method is to use continuous ketamine infusion plus patient controlled (PCA) fentanyl or morphine analgesia as a separate infusion.
- **Continuous subcutaneous infusions:** Ketamine is preferably administered alone due to low pH.
- **Compatible fluids:** sodium chloride 0.9% (preferred), glucose 5%, water for injection.
- **Compatible Drugs:** midazolam, morphine sulfate
- **Compatible in syringe only drugs:** morphine sulphate, morphine tartrate, fentanyl, hydromorphone, pethidine, bupivacaine, midazolam, haloperidol, dexamethasone
- **Incompatible drugs:** barbituates, diazepam, methylprednisolone

<table>
<thead>
<tr>
<th>Infusion Stability</th>
<th>• 24 hours if stored 2-8°C</th>
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<td>• If prepared by Sterile Pharmacy and kept refrigerated, refer to expiry date on Pharmacy infusion label</td>
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### Pre-treatment and Monitoring Requirements

<table>
<thead>
<tr>
<th>Nursing observations</th>
<th>Acute and Chronic Pain Service Patients</th>
<th>Palliative Care Service Patients</th>
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<tbody>
<tr>
<td></td>
<td><em>Intravenous Infusions</em></td>
<td><em>Continuous Subcutaneous Infusions</em></td>
</tr>
<tr>
<td>Pain Assessment</td>
<td>Hourly for the first 12 hours, then 2 hourly whilst patient is awake using pain score (0-10)</td>
<td>Two hourly whilst patient awake plus at commencement of shift – use pain score (0-10) as appropriate</td>
</tr>
<tr>
<td>Functional Activity Score</td>
<td>Hourly for the first 12 hours, then 2 hourly whilst patient is awake</td>
<td>Only required if part of usual care or in consultation with medical staff</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>Hourly for the first 12 hours, then 2 hourly whilst patient is awake</td>
<td>Only required if part of usual care or in consultation with medical staff</td>
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<tr>
<td>Sedation Score</td>
<td>Hourly for the first 12 hours, then 2 hourly whilst patient is awake</td>
<td>Only required if part of usual care or in consultation with medical staff</td>
</tr>
<tr>
<td>Blood pressure, pulse &amp; temperature</td>
<td>4 hourly after routine post-anaesthetic observations (RPAO)</td>
<td>Only required if part of usual care or in consultation with medical staff</td>
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<tr>
<td>Dose administered</td>
<td>Hourly</td>
<td>At change of syringe</td>
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<tr>
<td>Pump function &amp; infusion site</td>
<td>At commencement of new bag and once per shift</td>
<td>30 minutes after commencement of new syringe, two hourly thereafter plus at commencement of shift</td>
</tr>
<tr>
<td>Adverse events*</td>
<td>Hourly until pain control achieved, then 2 hourly whilst patient awake</td>
<td>Two hourly whilst patient awake plus at commencement of shift</td>
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* *sedation, respiratory depression, hallucinations, confusion, injection site irritation: must be reported to medical staff immediately for review of dosage – for pain service patients report to Pain Unit or anaesthetics registrar on call if out of hours, for palliative care service patients report to Palliative Care Team or Palliative Care registrar on-call if out of hours.*

The **Special Analgesia Observation Chart (SV167)** must be used to record observations for intravenous infusions for Acute Pain Service patients. The **Syringe Driver Cannula Checklist** must be used to record observations for continuous subcutaneous infusions for Palliative Care Service patients (use ‘Comments’ column for pain assessment and adverse events).
### Dosage/Administration: Acute Pain Service (APS) Protocol

**Continuous Intravenous (or occasionally subcutaneous) Infusion via a pump with a locked box (Gemstar or Alaris)**

- Ketamine MUST be ordered by the Department of Anaesthesia on the **Analgesia Infusion Treatment Sheet**.
- A dedicated line or IV giving set with one way valve in the main line must be used.
- **Initial rate** = 0.05 mg/kg/hour.
- **Optimal rate** usually = 0.1 to 0.15 mg/kg/hour.
- Prepare a 2 mg/mL solution: 200 mg ketamine/100 mL sodium chloride 0.9%
  
e.g. 60 kg person = 6 mg to 9 mg/hour = 3 to 4.5 mL/hour of a 2 mg/mL solution.
- Dose is titrated to effect - decreasing if hallucinations or other adverse effects occur.
- Midazolam may be added to the infusion to reduce the incidence of hallucinations (only when prescribed by APS).
- Dose adjustments are made every two to four hours.
- Bolus doses ordered on **Analgesia Infusion Treatment Sheet** can be administered by two Registered Nurses (Division 1).
- Concurrent intravenous or subcutaneous opioids / epidural analgesia can be given.
- In rare circumstances the subcutaneous route may be used – seek guidance from the Acute Pain Service team.

### Dosage/Administration: Palliative Care Service Protocol

**Continuous Subcutaneous infusion via Niki T34 Syringe Driver**

- See [Continuous Subcutaneous Drug Infusion with a Niki T34 Syringe Driver – Oct 2013](#)
- Ketamine can be ordered alone or in combination with an opioid.
- The order must specify the dose, total volume, diluent (see compatibilities) and rate in ml/hour.
- Dexamethasone given at the site prior to administration may reduce redness and irritation caused by the low pH of ketamine.
- Standard infusion:
  - **Initial daily dose**: 100 mg to 200 mg over 24 hours.
  - **Subsequent days**: increase by 50-100 mg per day to a maximum of 500 mg subject to adverse reactions.
- ‘Burst’ regimen:
  - For some patients a continuous subcutaneous infusion for 3 to 5 days followed by cessation (without weaning) may control pain and improve opioid sensitivity. During this time, opioid doses may need to be reduced
  - **Initial daily dose**: 100 mg over 24 hours.
  - **Subsequent days**: titrate to effect by daily increments of 100-200 mg to a maximum of 500mg over 24 hours subject to adverse reactions.
# MEDICATION PROTOCOL
Ketamine for Pain Management

## References


## AUTHOR(S)/CONTRIBUTORS

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### Medication Protocol Review Group

### Medicines and Therapeutics Advisory Committee

### Head of Department/Unit Responsible for Guideline:

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## Keyword search: Ketamine, Ketalar