

Ketamine for Acute Pain in Adults - Full Clinical Guideline

Reference No: CG-STEP/2019/004

Contents:

Introduction:	2
Aim and Purpose:	2
Background:	2
Indications for use:	3
Exclusion Criteria:	3
Prescribing Regulations:	4
Route of Administration:	4
Preparation:	4
IV Dosing Recommendations (including "test dose"):	5
Oral Ketamine:	6
Side Effects:	7
Paper Prescription Chart:	8
Management of Toxicity:	9
References:	10
Documentation Controls:	11

Introduction

Ketamine is an anaesthetic agent with analgesic properties when used at sub anaesthetic doses. This guideline has been developed to offer an alternative or supplemental analgesic option for patients whose pain is not sufficiently controlled by an opiate PCA or infusion, or an epidural.

Adverse effects at low doses are usually minimal but the occurrence of unpleasant hallucinations should prompt cessation of treatment.

Prescriptions of Ketamine for Acute Pain MUST only be made with the DIRECT INVOLVEMENT OF A CONSULTANT ANAESTHETIST.

Aim and Purpose

The aim of this guideline is to provide an additional option for the management of complex acute pain patients whose pain is not sufficiently managed with more routine analgesic options. This provides guidance on the indications for ketamine use in acute pain, how to choose between oral and intravenous ketamine, and where and how patients should be managed and monitored while being treated with ketamine.

Background

Ketamine exerts the majority of its analgesic effect by non-competitively antagonising the N-Methyl D Aspartate (NMDA) receptor. This is a different mechanism of action to opiates so both ketamine and opiates can be used together to provide a combined analgesic effect. Ketamine can also be used as an opiate sparing agent. This has the benefit of reducing unpleasant opiate effects such as nausea and vomiting, sedation, and the potential for tolerance and addiction.

Indications for use:

- As an alternative to epidural analgesia when this is not an option (e.g. coagulopathy, technical difficulties, patient refusal)
- Opioid tolerant patients
- Severe pain poorly responsive to opioids
- Uncontrolled adverse side effects with opioids
- Acute neuropathic pain e.g. phantom limb pain
- Hyperalgesic states

Exclusion Criteria:

Ketamine is contraindicated in patients with:

- Threatened airway obstruction
- Raised intracranial pressure or closed head injury
- Malignant hypertension
- Pregnancy
- Current Psychosis
- History of significant adverse reaction to Ketamine (psychosis / hypersensitivity)

Ketamine is relatively contraindicated in:

- History of psychosis
- Ischaemic heart disease or severe cardiac failure
- Raised intraocular pressure
- Myasthenia Gravis
- Porphyria

Prescribing Regulations:

Ketamine is a Controlled Drug and its storage, prescription and administration is subject to the misuse of drugs act 1971 (Schedule 2, Class B)

Ketamine intravenous infusions must be prescribed on the EPMA system and on the separate paper Ketamine Infusion Prescription chart (see page 8). Infusions should only be delivered via a trust approved lockable infusion device using a dedicated Ketamine infusion programme. Oral Ketamine should be appropriately prescribed on EPMA.

Route of Administration:

Ketamine may either be given as an intravenous infusion or orally. Intravenous infusions of ketamine are restricted in location to critical care areas only (including ICU/HDU, SDU, Theatre recovery and Theatres.) Oral ketamine may be administered on any surgical ward.

Preparation:

Intravenous Ketamine infusions should be drawn up as 100mg in 10mls (half of a standard vial) added to 40ml 0.9% sodium chloride in a 50ml luer lock syringe (making a total volume of 50ml in a syringe with a concentration of **2mg/ml**). Only pharmacy or an anaesthetist may prepare these syringes. Registered nurses working within an approved area may change the empty syringe for a pre-prepared one.

The infusion should ideally be attached to a dedicated peripheral cannula or a central line alongside intravenous fluids with a non-return valve. Ketamine solutions are compatible with morphine, fentanyl and oxycodone and therefore can be administered through the same access point as any infusions of these agents, as long as appropriate non-return valves are used.

Oral ketamine comes as an oral specific preparation with a concentration of 10mg/ml. Care should be taken to double check the concentration of oral ketamine prior to administration - the normal volume of solution for an adult patient will range between 1-3 mls (equivalent to 10-30mg). An alert to double check this is included within the EPMA prescription of oral ketamine to reduce the risk of dosing errors.

Intravenous Dosing Recommendations:**Intravenous test dose:**

An intravenous test dose should be considered for patients being considered for ketamine due to poorly managed acute pain. This helps to identify those patients who have accessible NMDA receptors. This should only be administered by an anaesthetist. The test dose should consist of up to 15mg IV ketamine, given incrementally in doses of 2.5-5mg with at least a 2 minute gap between increments. Patients who do not gain analgesic benefit from this test dose are unlikely to see a noticeable improvement in symptoms from ongoing treatment with ketamine, and other options should be considered.

Intravenous Loading and Infusions: Theatres, Recovery, ITU / HDU, SDU

Intravenous use is only recommended if there are doubts about oral absorption. As soon as the patient has a reliable enteral route of administration, this should be used.

- Loading / intraoperative dose: A dose of 0.5mg/kg may be given by the anaesthetist during the course of anaesthesia.
- Loading dose with conscious patient: The test dose described above should be used as a loading dose prior to commencing a ketamine infusion in patients who have not already received ketamine intra-operatively.
- Infusion dose:
 - Start the infusion at 4mg/hr (consider reducing to 2mg/hr if age >70)
 - The infusion rate may be increased by 2mg per hour to a maximum of 12mg/hr.
- Patient Monitoring:
 - Monitoring is as per the opiate PCA / infusion protocols.
 - Respiratory rate, sedation score, oxygen saturation, heart rate, pain score, nausea and vomiting score should all be recorded every **15 minutes for the first hour** then **HOURLY** whilst the ketamine infusion is in progress.
 - Following any increase in infusion rate go back to recording observations every 15 mins for the next hour.
 - If the patient is asleep, use discretion but ensure the respiratory rate is counted visually every hour and is greater than 8 breaths per minute. If less than 8, wake the patient and assess.

Opiate weaning while on ketamine:

Patients who are receiving significant opiate doses prior to ketamine being commenced should have their opiate levels steadily reduced once their pain is better controlled on the ketamine infusion. The target should be to get the patients down to a relatively low level of opiate consumption prior to stopping the ketamine. If this is not achieved there is an increased risk of rebound pain once the ketamine is stopped, which can be difficult to treat if the patient remains on higher doses of opiates.

Oral Ketamine:

Once a patient has reliable enteral absorption the intravenous infusion should be replaced with oral ketamine. Ketamine oral suspension 50mg in 5ml is available for oral administration, equating to a concentration of 10mg/ml. Typical oral doses of ketamine are 10-30mg, so only 1 to 3 mls of this oral preparation are required. This has previously led to significant dose administration errors as this is a relatively small volume compared to other oral liquid medications.

It is not necessary to wean the intravenous ketamine infusion when changing to oral ketamine. The infusion should be stopped as the first dose of oral ketamine is given.

Patients on oral ketamine do not need to be nursed in a high dependence setting. As such once the intravenous infusion has stopped (and if there are no other indications for on-going high dependency care) they may be transferred back to a normal ward.

It may occasionally be appropriate to start oral ketamine for a ward-based patient with acute pain who has not been through critical care. **This may only be prescribed after consultation with an anaesthetic consultant from the acute pain team or step down unit.**

Oral dosing guidelines:

- An intravenous test dose (as per the IV ketamine section above) may be considered prior to starting oral ketamine - alternatively the first oral dose may be used as a guide to the efficacy of ketamine in individual patients
- Ketamine 20mg four times a day initially. In elderly / frail patients reduce to 10mg four times a day. In particularly robust patients it may be appropriate to start at the higher dose of 30mg.
- As with IV ketamine infusions, patients on significant opiate doses should have these steadily reduced while on ketamine. If this is not done there is a higher risk of rebound pain once the ketamine is stopped.
- Oral ketamine **MUST NOT** be included in the patients discharge medication.

Side Effects:

Common (>10%) side effects include:

- Hypertension
- Increased cardiac output
- Emergence phenomena (dissociative symptoms)
- Raised intracranial pressure
- Tachycardia
- Vivid dreams
- Hallucinations
- Increased muscle tone

Less common (1-10%) side effects include:

- Bradycardia
- Double vision
- Hypotension
- Increased intraocular pressure
- Nystagmus

Rare (<1%) side effects include:

- Anaphylaxis
- Cardiac Arrhythmias
- Hypersalivation
- Respiratory depression

Serious or unpleasant side effects should prompt dose reduction or stopping treatment with ketamine.

University Hospitals of Derby and Burton NHS Foundation Trust

INTRAVENOUS KETAMINE PRESCRIPTION CHART for ADULTS

For use in Theatre Recovery, SDU or ICU only

Name	
Address	
DOB	Hosp. No.

Ward Date

Prescriber Signature:

Print Name:

Preparation:

Ketamine 100mg in 50ml 0.9% Sodium Chloride (2mg/ml) in 50ml luer lock syringe. Infuse alongside IV fluids via giving set with anti-siphon and non-reflux valves.

To be run concurrently with opiate PCA or continuous infusion unless significant opiate side effects preclude this.

Loading dose givenmg Date..... Time..... Signature.....

Standard Adult Prescription

Adult > 70 years old

Starting Infusion Rate: 4mg/hr

Starting Infusion Rate: 2mg/hr

Maximum Infusion Rate: 12mg/hr

Maximum Infusion Rate: 6mg/hr

Clinician Bolus Via Pump:

If pain score 7 or more consider clinician bolus 2ml (4mg) and / or increase infusion rate.

4mg; Given by Signature.....Time.....

4mg; Given by Signature.....Time.....

4mg; Given by Signature.....Time.....

4mg; Given by Signature.....Time.....

Changes to Infusion Rate:

Date	Time	Pain Score	New Rate	Signature

Management of Toxicity:

Toxicity during administration may be secondary to ketamine itself or (more probably) related to concurrent opioid administration. The degree of response required is dependant upon the clinical presentation. There is no reversal agent specific to ketamine and the focus should be on reversing any serious opioid toxicity whilst attempting to maintain analgesia in all but the most serious of cases.

If Respiratory Arrest or Respiratory Rate 5/min or less:

- Stop ketamine infusion and any on-going opioid administration
- If senior anaesthetic support not immediately available call 2222 – “Adult Respiratory Arrest”
- Give oxygen 15L via non-rebreathe mask
- If on concurrent opioids give naloxone in doses of 100mcg until respiratory rate is > 8 breaths per minute and sedation score is 1.

If Respiratory Rate 6-8/min and only responding to Pain on AVPU:

- Stop ketamine infusion and any on-going opioid administration
- Arrange URGENT medical review
- Give oxygen 15L via non-rebreathe mask
- Consider lower dose incremental naloxone if on concurrent opioids (increments of 40mcg with one minute intervals), titrated to achieve a respiratory rate of >8 breaths per minute and a sedation score of 1.

If Respiratory Rate is >6/min and Alert or responding to Voice on AVPU

- Arrange routine medical review
- Continue ketamine infusion
- Review opioid requirements:
 - Is it appropriate to reduce opioid dose
 - Has renal function deteriorated

References

- Low Dose Ketamine for the treatment of complex pain in adult inpatients - Imperial College Healthcare NHS Trust Guideline - Chumbley et al.
- Schwenk et al. vol 43, No5, July 2018. Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists; Regional Anaesthesia and Pain medicine
- Aitkenhead, A.R, Rowbotham, D.J, Smith,G. Textbook of Anaesthesia. 4th Edition.p178-179. Churchill Livingstone.
- Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine (2010) Acute Pain Management: Scientific Evidence. 3rd Edition
- Bell, R.F , Dahl J.B, Moore, R.A, Kalso, E.A (2006) Cochrane Review- Perioperative Ketamine for Acute Pain Management.
- Choiniere, M (2004) Pain of Bums. In Wall, P.D, Melzack,R Textbook of Pain. New York,Churchill Livingstone
- Hocking, G, Cousins, M.J (2003) Ketamine in Chronic Pain Management: An Evidence Based Review. Anaesthesia/ Analgesia 97: 1730-1739
- McIntyre, P (2005) Acute Pain Service, Royal Adelaide Hospital, Guidelines for Anaesthetists
- Notcutt, W.G (1994) Transporting Patients with overwhelming pain. Anaesthesia.49:147-149
- Peck, T.E, Hill, S.A, Williams,M (2004) Pharmacology for Anaesthesia and Intensive Care.
- 2nd Edition. P96- 98.www.greenwich-medical.co.uk
- Subramaniam, K, Sibramaniam, B, Steinbrook, R.A (2004) Ketamine as an adjuvant analgesic to opioids: A quantitative and qualitative systematic review. Anaesthesia/Analgesia 99: 482-495
- C. Harber, S Arunachalam, Nottingham University Hospitals NHS Trust: Low dose Ketamine guidelines for Acute Pain in adult patients.

Documentation Controls

Development of Guideline:	Authors: Dr. Nagendra Prasad, Consultant Anaesthetist Dr. Stefan Valdinger, Consultant Anaesthetist Acute Pain Team
Consultation with:	Clinical Guidelines Group
Approved By:	April 2023 - Surgery Division
Review Date:	April 2026
Key Contact:	Dr Stefan Valdinger, Consultant Anaesthetist Clinical Nurse Specialists Acute Pain
Date of Upload: Version 2	11/05/2023