Guideline for Ketamine Subcutaneous Infusion for Acute Pain

Please note that this guideline has been prepared by the Pain-Management Team and should only be used for patients upon their guidance. No other patients should be initiated on subcutaneous ketamine infusions without their advice.

Description	Ketamine is an anaesthetic with significant analgesic properties. It is an n-methyl-d-aspartate (NMDA) receptor antagonist and may be beneficial in reducing "wind up" of the pain pathway in response to ongoing pain.
Indications	Subcutaneous ketamine infusions, in patients with acute pain, should ONLY be instituted under the guidance of the Pain-Management Team. • Patients with acute pain, in whom multimodal therapy with local anaesthesia (including epidurals), opioid, paracetamol and NSAID as appropriate, are not providing adequate pain relief. • Patients with acute pain who are developing neuropathic pain. In some situations ketamine infusions may be used in chronic pain management and in palliative care. This will be under the direction of specialists in these areas and are **not** included in this protocol.
Contra-indications and cautions	Known or suspected allergy to ketamine. At the doses recommended in this protocol, contraindications are relative. Caution should be used in prescribing a ketamine infusion for patients who either are or have: • Uncontrolled hypertension, • Ischaemic heart disease, • Cardiac failure • Cerebrovascular disease • Increased intracranial pressure • Prone to hallucinations • History of seizures • History of psychosis • Receiving other sedating medications as the effect will be cumulative.
Drug Interactions	Ketamine interacts with: • Theophylline (tachycardia, seizures) • Levothyroxine (monitor for hypotension, tachycardia) • Diazepam (increases the plasma concentration of ketamine) In addition, patients on ketamine receiving regular high doses of opioid (immediate or sustained release formulations) should be reviewed with a view to reduce dose while receiving concomitant ketamine.
Side effects	All of these side effects should be minimal at the lowest dose, but may limit a patient's ability to tolerate higher infusion rates: • Sedation • Cardiovascular stimulation resulting in hypertension and tachycardia (bradycardia and hypotension have also been seen) • Increased intracranial pressure • Hallucinations, dysphoria, and vivid dreams • Respiratory depression • Laryngospasm • Diplopia and nystagmus (1) Subcutaneous ketamine may cause skin irritation at the site of the infusion and sites should be reviewed regularly and rotated **at least every 24hrs** or as necessary if any sign of redness and or swelling (5).

Dosage and Administration	**<u>Dosage</u>** Initial rate 2.5 to 5mg/hour, increasing in increments of 2.5mg to 5mg every two hours until adequate pain control is achieved or intolerable side effects occur; to a maximum of 15 to 20mg/hour. Caution required with elderly and frail patients. Normal infusion rate in adults is 1 to 4 mL/hour (based on standard concentration of 5mg/ml – see preparation section below) A loading dose is not recommended. The pain-management team will advise on rate of titration **<u>Administration</u>** Syringe prepared every 24 hours or more frequently, as per monograph (Appendix 1). Check the syringe is not cloudy and protect it from light. Infused through a subcutaneous cannula (21 gauge Wallace Y-CAN cannula with syringe valve) and single lumen anti-syphon line using an Omnifuse lockable PCA pump, handset remains attached to pump but is non functional. Ideally a new ketamine infusion should be commenced before 2pm, so that patients can be closely monitored for side effects, particularly opioid toxicity during day time hours.
Patient Observation and monitoring	As with all drug infusions the infusion and the pump must be checked **hourly** and a standard infusion chart completed. Monitoring required during administration include: 1) Respiratory rate 2) Heart rate 3) Blood pressure 4) Mental status and level of sedation 5) Pain score Evaluation must be carried out just prior to initiating infusion, then every 20 minutes for first hour; and after each dose titration monitor every 30 minutes. Once required dose of ketamine is reached routine monitoring hourly or more frequently if the patient's condition requires it. **Patient will be reviewed regularly throughout the day by pain team whilst ketamine infusion in progress.**
Duration of infusion and discontinuation	Duration of infusion will be determined by clinical effect and ongoing symptoms. Usually 3 to 4 days is the normal duration, and will be discontinued as instructed by the pain-management team. When stopping ketamine infusion, the nurse must notify the responsible pain team/anaesthetist if: 1) Systolic blood pressure drops by 30% 2) Respiratory rate drops to less than 8/minute 3) Patient has profound sedation

For further Information or any questions please contact the Pain-Management Team:
RIE: page 5247 or the anaesthetic SHO on call via page 2140
WGH: page 8292 or the anaesthetic SHO on call via page 5112
SJH: page 3934 or on call via page 3561

Appendix 1 – Ketamine Subcutaneous Infusion for Acute Pain Monograph

Please note that this monograph has been prepared for the Pain-Management Team and should only be used for patients upon their guidance. No other patients should be initiated on subcutaneous ketamine infusions without their advice.

Presentation	Vials containing a solution for injection or infusion of ketamine hydrochloride 1g in 10mL (100mg/mL) (1).
Reconstitution	Not applicable.
Concentration of final solution	5mg/mL **<u>Special note:</u>** *The Standard solution (recommended by the Pain-Management Team) is 2mL of ketamine 100mg/mL solution diluted to 40mL with sodium chloride 0.9% in a 50mL syringe*
Preferred method of administration	Subcutaneous infusion.
Infusion fluids	Sodium chloride 0.9% IV infusion (1,2).
Stability in solution	Prepare immediately before use (1). For single use only. Discard any unused product (1).
Drug admixture compatibility	No other medicines should be added to ketamine. The **exception** to this is when infusion site inflammation is a problem. In this case 0.5mg to 1mg of dexamethasone may be added to the infusion to help reduce inflammation (3).
Special notes Stability: Sodium content: Hazards:	Do not store above 25^0C (1). Negligible (4). ***This is an unlicensed indication and route of administration for this medicine but there is evidence in the literature to support safety and possible efficacy (6). Clinicians should advise patients accordingly.***

References

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6 Macintyre P, Schug S, Scott D, Visser E, Walker S. Acute pain management: scientific evidence 2nd edition Updates. Australia: Australian and New Zealand College of Anaesthetist and Faculty of Pain Medicine (December 2007).

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