

**St Joseph's Mercy Hospice
Auckland NZ**

Guidelines for Ketamine Use

Ketamine is a dissociative anaesthetic agent which has analgesic properties in sub-anaesthetic doses¹

Its principal site of action is in the dorsal horn of the spinal cord where it blocks the N-methyl D-aspartate (NMDA) receptor complex.

Ketamine is used in palliative care settings primarily for neuropathic pain which is unresponsive or poorly responsive to first-line analgesics (which may include one or more of opioid drug, NSAID, tricyclic antidepressant, or anticonvulsant)
It has also been used for phantom limb and ischaemic pain and for intractable incident pain or prior to procedures such as dressing changes.

Potential side effects Ketamine

Routine use of ketamine is limited by its cost and potential side effects which may occur in up to 40% of patients; These may include:

- Psychotomimetic phenomena – “feeling strange” - dysphoria, vivid dreams, nightmares, hallucinations, altered body image. These effects may be minimised or treated by concurrent use of haloperidol or a benzodiazepine
- Delirium
- Hypertension, tachycardia
- Diplopia, nystagmus
- Erythema and pain at injection site

Contraindications to ketamine use

Ketamine has the potential to increase intra-cranial and intra-ocular pressures.
It is contraindicated in patients with a history of hypertension, cerebrovascular disease or epilepsy and should be used with caution in patients with raised intra-cranial pressure and/or known cerebral metastases.

Dosage regimens for Ketamine use

1. “Burst ketamine”²

Ketamine is prescribed as a ‘burst’ or ‘pulse’ course for a maximum of 5 days. The dose is titrated up, in a stepwise fashion, and once the lowest effective dose is achieved it is continued for 3 days at that dose then stopped.

This method has the advantages of an adequate trial of treatment (with discontinuation if analgesia is ineffective or significant side effects occur) and minimisation of the logistics of longer term ketamine use. (cost, syringe driver monitoring and sc site irritation)

Burst ketamine protocol

- Starting dose 100 mg per 24 hrs via syringe driver
- If effective continue for three days then cease

- If 100 mg ineffective after 24 hrs, increase to 300 mg
- If 300 mg effective, continue three days then cease

- If 300 mg ineffective after a further 24 hrs increase to 500 mg
- Cease ketamine at day 5 whether effective or not, or earlier if significant side effects occur

See appendix for protocol sheet to include in drug chart

¹ Fallon MT and Welsh J. The role of ketamine in pain control. European Journal of Palliative Care, 1996;3: 143- 146

² Jackson K et al. Burst Ketamine for refractory cancer pain: An open label audit of 39 patients. J Pain and Symptom Management 2001;22:834-842

2. **Continuous Subcutaneous ketamine**³

- Starting dose 1 – 2.5 mg/kg per 24 hrs
- Increase by 50 – 100 mg per 24 hrs. Maximum reported dose 3.6 G /24 hrs
- Duration of administration determined by clinical response

3. **PRN ketamine for incident pain or prior to procedures**³

- 10 – 25 mg sc prn (0.5 mg per Kg approx)

4. **Oral ketamine**³

- May be used directly from the vial or diluted to 50 mg /5 ml with flavour of choice added
- Starting dose 10 – 25 mg tds – qid and prn
- Increase dose in steps of 10 mg up to 50 mg qid
- Maximum reported dose 200 mg qid
- Use a smaller dose more frequently if psychotomimetic phenomena or drowsiness occurs which does not respond to a reduction in opioid dose (see below)

Concurrent opioid use⁴

- The current dose of opioid may need to be reduced when starting ketamine or if excessive drowsiness or psychotomimetic phenomena occur.
- If opioid dose is stable with minimal breakthrough requirements, consider reducing the opioid dose by 25 – 50%
- If pain is unstable and frequent breakthrough analgesia is required, consider reducing the opioid dose by 10%
- Reassess opioid and ketamine dose every 24 hrs
- Note if ketamine is used with methadone, be alert to the possibility of opioid toxicity developing over several days as a consequence of the long and variable half-life of methadone.

Minimising side effects³

- If patients develop psychotomimetic phenomena, consider concurrent use of haloperidol (2.5 mg bd) or benzodiazepine (clonazepam 0.5 – 1 mg nocte; midazolam 2.5 – 5 mg stat and 10 – 15 mg per 24 hrs via syringe driver)
- In patients at risk of dysphoria, the above may be started prior to the ketamine infusion
- Erythema and pain at injection site – dilute with normal saline in 20 or 30 ml syringe

Use with other medications³

Ketamine is miscible with morphine, haloperidol, metoclopramide, levomepromazine, midazolam and low dose dexamethasone.

It should be diluted with normal saline.

Addition of 0.5 – 1 mg of dexamethasone may reduce sc site inflammation

³ www.palliativedrugs.com/book.php?*ketamine

⁴ www.palliativedrugs.com bulletin board discussion 06/01/05 to 13/01/05

Appendix

To be placed in drug chart of patients prescribed "Burst ketamine"

"Burst" ketamine dose escalation protocol

Starting dose 100 mg per 24 hrs via syringe driver

If effective continue 3 days then cease

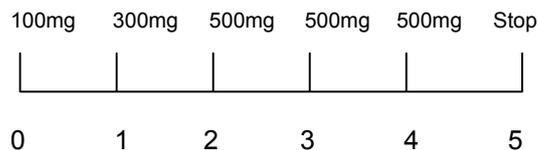


If 100 mg ineffective after 24 hrs, increase to 300 mg

If 300 mg effective, continue three days then cease



If 300 mg ineffective after 24 hrs increase to 500 mg



Cease ketamine at day 5 whether effective or not, or earlier if ineffective and/or significant side effects

Potential side effects of ketamine

Routine use of ketamine is limited by potential side effects which may occur in up to 40% of patients. These may include:

- Psychotomimetic phenomena – "feeling strange" - dysphoria, vivid dreams, nightmares, hallucinations, altered body image. (see below)
- Delirium
- Hypertension, tachycardia
- Diplopia, nystagmus
- Erythema and pain at injection site – dilute with normal saline in 20 or 30 ml syringe

Minimising side effects

- If patients develop psychotomimetic phenomena, consider concurrent use of haloperidol (2.5 mg bd) or benzodiazepine (clonazepam 0.5 – 1 mg nocte; midazolam 2.5 – 5 mg stat and 10 – 15 mg per 24 hrs via syringe driver)
- In patients at risk of dysphoria, the above may be started prior to the ketamine infusion
- Concurrent opioid use – be alert to the possibility of opioid toxicity developing over several days and consider opioid dose reduction. (see guideline)

Contraindications to Ketamine use

Ketamine has the potential to increase intra-cranial and intra-ocular pressures.

It is contraindicated in patients with a history of hypertension, cerebrovascular disease and epilepsy and should be used with caution in patients with raised intra-cranial pressure and/or known cerebral metastases