AFFIX PATIENT LABEL

GUIDELINES FOR USING KETAMINE

Agreed at Meeting of Northern Regional Palliative Care Physicians March 1999

(Revised December 2002, March 2005, May 2006, August 2008).

INDICATIONS

Neuropathic pain: Following a trial of strong opioids, anti-convulsants and Tricyclic anti-depressants +/- trial of high dose Dexamethasone.

Other pains: Which may respond to Ketamine:

- Movement related pain.
- Skin pain.
- Mucosal pain.

Patients should be given the appropriate conventional analgesics before Ketamine.

PREPARATION FOR STARTING KETAMINE

1. Ketamine should only be prescribed by or in conjunction with a doctor experienced in Pain Management or Palliative Care.

2. Adjustment of opioid regime:

- Switch patient from long to short acting opioids.
- Reduce total daily opioid dose by 30%. *This may not always be necessary, for example patients on low doses of morphine or patients with incident pain but this should always be discussed with a doctor experienced in prescribing ketamine*
- Prescribe usual opioid rescue medication (ie 1/6th of total daily dose).
- As a guide the lag time for MST – 12 hours
  Oxycodone m/r (Oxycontin) – 12 hours
  MXL/Morcap – 24 hours
  Transdermal Fentanyl – 48 hours
  SR Hydromorphone – 12 hours

Patients should always be observed for opioid toxicity.

3. Relative contraindications (Please document in notes if no CI)

Ketamine should be avoided in patients with:

- Raised intracranial pressure.
- Severe systemic hypertension.
- Raised intra-ocular pressure.
- Recent history of epilepsy.
- Recent history of psychosis.

4. Ketamine should be used with caution in patients with:

- Intracranial space occupying lesion.
- Cardiac arrhythmia.
- On long-acting opioid.

SIDE EFFECTS

Dysphoria, hallucinations, drowsiness, vivid dreams, dizziness, palpitations, hypertension, nausea and features of opioid toxicity. Symptoms of cystitis, haematuria and supra-pubic pain have been linked to ketamine especially in doses over 400mg/24 hours. Specialist review should be sought.

PRESCRIBING KETAMINE

- Ketamine may ordinarily be given by the oral or subcutaneous route.
- Ideally treatment with Ketamine should be commenced before 2:00 pm so that patients can be monitored for side effects particularly opioid toxicity before bedtime.

Starting Dose – Oral route:

All patients: 10 mg QDS

Rate of Increase – Oral route:

10-45 mg QDS: 50-100% daily

45-100 mg QDS: 25-33% daily

> 100 mg QDS: 20-25% daily

Example. Day 1 10mg qds

Day 2 20mg qds

Day 3 40mg qds

Day 4 60mg qds

Day 5 80mg qds

Day 6 100mg qds

- *Analgesia may be acheived at low doses and higher doses may not be needed.*
- *Delay dose increases if side effects a problem*
- *Dose increases should be stopped at 100mg qds and response assessed over the next few days as the active metabolite norketamine will start to contribute to analgesia*
- *Doses above 100mg qds are only occasionally required*

Starting Dose – Subcutaneous route:

Frail patient - 25-30 mg subcutaneous infusion / 24 hours.

Fit patient - 50-100 mg subcutaneous infusion / 24 hours.

Maximum dose in the region of 500 mg/24 hours depending on patient, side effects and response.

Rate of Increase – Subcutaneous route:

Severe uncontrolled pain - 50-100% 8 hourly.

Other patients - 50-100% daily.

Rescue Medication: The usual 4 hourly opioid dose.

Observations: Pain score, pulse and BP should be recorded at 0 mins, 30 mins, 1 hour and 4 hours on Day 1 for all patients.

Thereafter patients with the following should have 4 hourly observations until dose titration is complete.

a) Patients with a relative contra-indication to Ketamine.

b) Where Ketamine is started while patient is on long acting opioid.

c) Patients where rapid dose titration of Ketamine is needed.

For all other patients daily Pain Score, pulse and BP is recommended during titration and monthly thereafter.

- There should always be an awareness for potential opioid toxicity (ie respiratory, depression, drowsiness, jerking) during titration, especially for those patients on high and long-acting opiates, however in most circumstances it is rare.
- Modest BP rises need no action, significant rises should prompt a medical review.

Clinical review of patient: Should be carried out within 24 hours of starting Ketamine and documented in case notes.

Conversion ratio: subcutaneous to oral Ketamine – unknown, probably equi-analgesic. In practice clinicians use anything from 1:1 to 1:3. Norketamine, the active metabolite of oral Ketamine, is an analgesic agent.

Once Analgesia is achieved:

a) Consider reducing regular opioid daily dose by 33% and gradually reduce further if possible.

b) Review need for concurrent analgesics (eg NSAIDS, Paracetamol, anti-convulsants and Tricyclic anti-depressants) one week after achieving stable pain control with Ketamine and gradually optimise medications as deemed appropriate.

If analgesia is not achieved consider stopping Ketamine.

Review need for ongoing Ketamine treatment at one month.

Need for concurrent sedation?

Central side effects (hallucinations) are less common with oral Ketamine usage and slow upward dosage titration. Prophylactic sedation is not needed. Low dose oral Diazepam / Lorazepam / Haloperidol is effective if hallucinations occur. If using Ketamine SC, Midazolam 10 mg SC / 24 hours will abolish hallucinations.

OPIATE OVERDOSAGE

If respiratory rate > 8/min and patient not cyanosed, no action other than observation is necessary.

If life threatening respiratory depression, dilute NALOXONE 400 mcg in 10 ml saline for injection and give I.V. 1 ml per min. Repeat until patient's condition improves or if no response after 3200 mcg reconsider diagnosis.

If relapse occurs (likely after about 20 mins.) give further 400-800 mcg I.V. and consider commencing an I.V. drip with 400 mcg per 100ml saline and titrate rate according to response.

N.B. most opioids used in palliative medicine have a longer half life than Naloxone and therefore relapse is likely. With sustained release preparations there may be relapses for 24 hours or more.

Bear in mind that total reversal of opioid action will result in recurrence of pain. The aim is to reverse respiratory depression to safe levels and not necessarily total abolition of opioid effects.

Appendix

March 2006

Ketamine Prescribing for Palliative care specialists only

- **Sublingual or buccal ketamine.**

Indication. Movement or procedure related pain. E.g painful dressing changes or pathological fractures

Dose 2.5mg- 5mg of ketamine oral solution 50mg/5ml

Sublingual ketamine has a rapid onset peak blood level (similar to parenteral ketamine), therefore it may be useful for rapid analgesic effect. However there is also the potential for dysphoric type side effects.

For buccal administration deliver the solution in a syringe to the space between the teeth and cheek.

- **As Required Ketamine**

The duration of action of oral ketamine is 4-6 hours. Therefore it would appropriate to prescribe a PRN dose of oral ketamine equivalent to the current regular dose, especially at night.

However repeated extra doses will result in a rapid increase in the total daily dose of ketamine and will increase the chances of dysphoric symptoms. Therefore on non specialist wards/units there should be clear instructions regarding PRN ketamine.

References

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