KETAMINE SEDATION FOR ADULT BURN DRESSING CHANGES

SUMMARY

Ketamine is a nonbarbiturate anesthetic/analgesic agent which produces a "dissociative" effect as well as an analgesic effect. The use of ketamine as adjunctive or primary sedative/analgesic agent for dressing changes in adult burn patients may result in improved compliance with both the dressing change and accompanying physical and occupational therapy.

RECOMMENDATIONS

- **Level 1**
  - **None**
- **Level 2**
  - **Ketamine should be given with concurrent benzodiazepine therapy to minimize emergence reactions**
  - **Ketamine is contraindicated in patients with the following conditions:**
    - **History of or current myocardial ischemia or arrhythmias**
    - **Severe pulmonary secretions**
    - **Concurrent closed head injury**
    - **History of or current glaucoma**
    - **Psychiatric history**
- **Level 3**
  - **For patients with > 20% TBSA Burns, consider ketamine if adequate analgesia cannot be obtained**
  - **Recommended dosing:**
    - **Ketamine 0.5 mg/kg (or 50 mg maximum) IV bolus over 3-5 minutes**
    - **Ketamine 20-50 mg/hr continuous infusion; titrate in 10 mg/hr increments to SAS 2-3 during procedure, discontinue at the end of the procedure**
    - **Midazolam 2 mg IV at induction and 2 mg IV at the conclusion of the procedure just prior to discontinuation of the ketamine infusion**
    - **Midazolam and fentanyl may be administered as needed during the procedure in addition to the ketamine per the Burn Service dressing change protocols**
    - **Emergency equipment (bag-valve-mask, oxygen, and suction) should be in the patient's room during the dressing change**

INTRODUCTION

Burn patients undergo frequent, extensive, and painful dressing changes. As a result of these dressing changes, burn patients develop tolerance to both opioid and benzodiazepine agents. Tolerance to the analgesic and sedative agents results in the need for progressive dosages in order to maintain adequate

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

sedation and analgesia during the procedure. For patients with significant burns (>20% total body surface area) two problems emerge: 1) prolonged recovery after each dressing change due to high opioid and benzodiazepine doses, and 2) heterotopic ossification as a result of pain-limited mobility. The addition of ketamine to a regimen of opioids and benzodiazepines for dressing changes may not only decrease the opioid and benzodiazepine requirements, but also facilitate improved compliance with physical and occupational therapy leading to a decreased incidence of heterotopic ossification (1).

Ketamine is a nonbarbiturate anesthetic/analgesic agent which is structurally related to phencyclidine and cyclohexamine (2). Ketamine produces a "dissociative" anesthetic response (which prevents high brain centers from perceiving auditory, visual or painful stimuli) as well as analgesia (2). Ketamine's effects are mediated through both opioid and non-opioid mechanisms. The use of anesthetic-level doses of ketamine results in a trancelike, cataleptic state without respiratory depression. The patient may be awake, but is disconnected from their environment, immobile, and unresponsive to pain. Overall, ketamine results in sensory blockade with amnesia and analgesia (2). Other clinical effects of ketamine include elevated intraocular and intracranial pressure, cerebral vasodilatation, and bronchodilatation (2,3).

Ketamine exhibits a pharmacokinetic profile that makes it ideal for procedural sedation. It has a rapid onset of 30-40 seconds following IV administration. Duration is as short as 5-10 minutes after a single IV dose up to 30-45 minutes with repeat dosing. Recovery time following continuous infusion may be as long as an hour. No dosage adjustments are required for renal impairment, but may require lower doses in hepatic insufficiency. Dosing for adult procedural sedation should include a bolus dose (administered by a physician) with either a supplemental bolus dose or a continuous infusion for the duration of the procedure. Suggested initial dosing: ketamine 0.5 mg/kg IV over at least 1 minute followed by either a repeat in dose in 5-15 minutes or a continuous infusion of 5-20 mcg/kg/minute (2,5,6-9). Continuous infusion doses up to 45 mcg/kg/min have been described in the burn population (6). Patients who require repeat administration of ketamine may develop tolerance leading to increased doses (2,3,5).

There are multiple adverse effects associated with the administration of ketamine in adult patients. The most common adverse events include hypertension, tachycardia, and emergence reactions (characterized by vivid dreams, out-of-body experiences, floating sensations, hallucinations, delirium, confusion or "weird trips" which occur in up to 50% of adults receiving ketamine) (2-5). Skeletal muscle hyperactivity including twitching, extensor spasms, myoclonus, random extremity movements, fasciculations, and rigidity have also been described – these are more frequent at higher doses (2). Other common side effects include increased upper airway secretions, nystagmus and diplopia (2,3,5). The majority of the adverse events are mitigated by the concurrent use of benzodiazepines – especially midazolam (2).

LITERATURE REVIEW

[Class II] MacPherson et al. conducted a prospective study on the use of a combination ketamine/midazolam PCA for burn dressing changes. Each PCA contained ketamine 200mg/midazolam 10mg/normal saline 20 mL. The PCA was programmed to provide demand doses of ketamine 20mg/midazolam 0.5mg every three minutes; there was no basal rate. The PCA was controlled either by the patient or the nurse performing the dressing change. Other oral or intravenous opioid analgesics could be administered prior to the start of the dressing change only. Forty-four patients were evaluated during 95 procedures which lasted 78 ± 33 minutes and used a mean of 9 mL per procedure (~ketamine 180mg/midazolam 4.5mg). At the end of the procedure, patients and staff rated the effectiveness of the treatment on a scale of 1 to 10, with 1 being the worst. The average score was an 8.5/10 for both patients and staff (calculated median = 9/10). Adverse events were noted in 15/44 patients with the most frequent being hallucinations (11/44) and desaturations < 95% (5/44). The authors concluded that this PCA provided adequate and effective analgesia (11).

[Class II] Newton et al. conducted a prospective, observational study on the use of intravenous ketamine for procedural sedation in adult patients (age > 16 years). Patients were excluded if they had an abnormal airway, current respiratory infection, TBI, ocular injury, increased intraocular pressure, cardiac disease, psychotic illness, uncontrolled HTN, hyper- or hypothyroidism, porphyria, or an allergy to

ketamine. Patients received an initial dose of ketamine 0.5 mg/kg IV which was repeated in 5 minutes if adequate sedation not achieved. Patients were on continuous ECG and pulse-oximetry and blood pressure was checked every 5 minutes. They enrolled 92 patients and achieved adequate sedation in 91 of the 92 patients (98.9%). Twenty of the 92 patients experienced adverse events, 12 of which were emergence-related reactions (12).

[Class III] Ward et al. evaluated ten adults (ages 24-74 years) who received ketamine as a part of their burn dressing change sedation. These patients were kept NPO for 4 hours prior to sedation. Ketamine (concentration ketamine 400 mg / atropine 0.6 mg) was administered by an anesthetist. Their protocol consisted of an induction dose of ketamine 2 mg/kg IV followed by ketamine 4 mg/kg IM. Subsequent IM doses of ketamine were administered when the patient made purposeful movements or nystagmus reappeared. At the end of the dressing change, ketamine 1 mg/kg IV was administered and then the patient was left to recover under nursing supervision. Ketamine was found to provide adequate analgesia (9).

[Class III] Demling et al. described the use of ketamine for anesthesia during tangential excision of burn eschar in the burn unit. They used a dose of ketamine 4 mg/kg IM which provided adequate sedation and analgesia for approximately 20 minutes. A repeat dose was given if the patient started to emerge prior to completion of the procedure. For patients who underwent repeated procedures, doses as high as 6 mg/kg IM were administered. Only 10% of their patients developed emergence reactions – all of which were mild (13).

[Class III] San Francisco General Hospital has developed a protocol for the use of ketamine during dressing changes in burn patients. Dosing of 0.5-1 mg/kg IV for dressing changes can produce analgesia for 5-30 minutes. The protocol is described below (3):

- Emergency equipment should be immediately available (oxygen, suction and crash cart)
- Preferred route of administration is IM 2-3 mg/kg with MD present during administration. IV administration by anesthesia or anesthesia resident only – 0.5-1 mg/kg
- Contraindications: psychiatric history, h/o HTN, elderly patients, h/o MI, increased ICP or IOP, respiratory difficulties, eclampsia

[Class I] Yamauchi et al. conducted a prospective, randomized study comparing the addition of ketamine or placebo to fentanyl for post-operative analgesia in patients undergoing cervical or lumbar spine surgery. Group 1: ketamine 1 mg/kg bolus, then ketamine 42 mcg/kg/hr x 24 hours. Group 2: ketamine 1 mg/kg bolus, then ketamine 83 mcg/kg/h x 24 hours. Group 3: normal saline placebo. All patients were placed on a fentanyl PCA and were prescribed diclofenac 50 mg suppositories every 8 hours as needed. Two hundred patients were enrolled in the study. Patients with cervical spine surgery in Group 2 had significantly lower pain scores compared to Group 1 at 24 hours and compared to placebo at 48 hours. There were fewer differences in the lumbar spine surgery groups. Patients who received ketamine after undergoing cervical spine surgery were more satisfied with their pain control than those patients undergoing lumbar spine surgery (10).

Study	No. of Patients (age range)	Route of Administration	Ketamine Dosing	Adjunctive Medications
Edrich (6): Ketamine long-term sedation and analgesia in burn patient	1 (28 yrs)	IV – continuous	Ketamine 2.7 mg/kg/h IV infusion	IV morphine, versed, valium, propofol – all of which were weaned when ketamine started
Ward (8): Ketamine for dressing change or STSG	6 (age 9 mon-8 yrs)	IV IM	Ketamine 2 mg/kg IV induction then Ketamine 4 mg/kg IM (may repeat PRN), then Ketamine 1mg/kg IV at the end of the procedure	Ketamine/Atropine 400 mg/0.6 mg for induction
MacPherson (11): Burn dressing changes	49 (age 16-76 yrs)	IV-PCA	Ketamine 10 mg/Versed 0.5 mg/mL per PCA 1 mL q 3 min (administered by patient or RN)	Pre-treat w/po or IV opioids only
Newton (12): Emergency Department sedation for procedures	92 (age 16-89 yrs)	IV	Ketamine 0.5 mg/kg IV then 0.5 mg/kg IV q 5 min prn	No information provided
Demling (13): Ketamine for bedside escharotomy	45 (age 18 mon-71 yrs)	IM	Ketamine 4 mg/kg IM x1 May repeat x1 if needed Max dose in study 6 mg/kg IM	No information provided
Slogoff (14): Burn dressing changes	40 (age 3-55 yrs)	IM	Ketamine 1.5 mg IM x 1 (average of 3.75 doses/patient)	No information provided
Sage (15): Ketamine for burn anesthesia	62 (age 11 mon-10 yrs)	IV IV – continuous	< 35 kg Ketamine 10 mg/kg IV induction (later changed to 4 mg/kg), then 2 mg/kg IV prn, then 350-658 mcg/kg/min > 35 kg Ketamine 2 mg/kg IV induction, then 1 mg/kg prn **OR** then ketamine 1 mg/mL in D5W at 67-360 mcg/kg/min	< 35 kg (premed) Trimeprazine 2 mg/kg po Atropine 0.6 mg po > 35 kg (premed) Pethidine (narcotic) Atropine Promethazine 25 mg IV (age 16-65y)

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