Ketamine Administration - The good, the bad and the ugly……

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- NMDA receptors in the spinal cord are involved in the development of windup and central sensitisation
- Used in inflammatory, post op, neuropathic ischaemic and cancer pain
- NMDA may block and even reverse opioid tolerance and dependence
- Work in synergy with opioids
Ketamine was first synthesized in 1962
Used on American soldiers during the Vietnam War
Potential to cause emergence phenomena restricts its use in clinical practice.
Commonly used in Vet practice and remote retrieval
Full name: ketamine hydrochloride (Ketalar)
Anaesthetic agent for human and veterinary surgical procedures
Blocks nerve paths without depressing respiratory function
Anaesthetic in remote trauma settings
Potent analgesia in sub anaesthetic doses
Legal classification: S8 Drug
Pharmacology

*Ketamine is a rapid acting general anaesthetic producing

* Profound analgesia
* Normal pharyngeal/ laryngeal reflexes
* Normal or slightly enhanced skeletal muscle tone
* The anaesthetic state produced by ketamine has been termed `dissociative anaesthesia'
**Pharmacokinetics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Description</th>
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<tbody>
<tr>
<td>Onset of action</td>
<td>IV – seconds&lt;br&gt;IM/SC – 4 min</td>
</tr>
<tr>
<td>Duration</td>
<td>15-30 min</td>
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<tr>
<td>Excretion</td>
<td>renally excreted after liver metabolism</td>
</tr>
<tr>
<td>Half life</td>
<td>2-3 hrs</td>
</tr>
<tr>
<td>Dosage Anaesthetic</td>
<td>1-5mg/kg</td>
</tr>
<tr>
<td>Analgesia</td>
<td>0.01- 0.5mg/kg/hr</td>
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Indications for ketamine use are to be considered in all painful conditions and as a rescue drug in complex pain situations such as

* Poor opioid-response to pain
* Opioid tolerance including methadone
* Neuropathic pain
* Ischaemic pain
* Preventive (pre-emptive) analgesia
* Palliative care
* Ketamine has an opioid sparing effect in post operative pain (Level 1)

* Concurrent reduction in opioid related side effects (Level 1)

* Ketamine shows preventative analgesic effects (Level 1)

* Ketamine improves analgesia in patients with severe pain that is poorly controlled by opioids (Level 1)

Acute Pain Management: Scientific Evidence ANZCA. 2010
Perioperative ketamine reduces postoperative morphine requirements and reduces PONV.

Perioperative doses of ketamine reduced rescue analgesic requirements or pain intensity, or both.

Ketamine may provide for an earlier recovery of cognitive function.
- Ketamine/propofol (kefol) reduced RD commonly produced by using sedative-opioid combinations

- Ketamine produced positive mood effects after surgery

- Ketamine, peri operatively has had significant opioid-sparing effects without increasing the incidence of side effects

- A small doses of ketamine after surgery was alleged to improve analgesia in the presence of opioid-resistant pain
Side effects – the bad

- Interferes with sensory perception as well as perception of pain
- Hallucinations
- Dreaming – pleasant and unpleasant
- Dizziness and floating feelings
- Cardiovascular - hypertension
- Side effects may be reduced by reducing the dose or administering small doses of haloperidol/diazepam/midazolam concurrently
Cardiovascular system:
* Direct myocardial depressant
* Increase in systemic arterial pressure
* Increase in heart rate
* Increase in cardiac output

Pulmonary system:
* Bronchial smooth muscle relaxant
* Increase in pulmonary arterial pressure
* Increases salivary & tracheo bronchial secretion

* Can be as effective as inhalational agents in preventing bronchospasm!
At high doses or rapid intravenous administration, ketamine has also been found to bind to opioid mu and sigma receptors which causes the loss of consciousness.
Strong pain stimuli activate NMDA receptors and produce hyperexcitability of dorsal root neurons. This induces central sensitization, wind-up phenomenon, and pain memory.
Ketamine can block the initiation of central sensitisation (pain threshold changes, responses to pain magnified) caused by stimulation of the pain pathways.
Other Uses

- Palliative Care:
  - Burst ketamine - Reverses tolerance of opioids
  - Antidepressants – mental health
  - Alcohol and substance abuse clinics
  - Treatment of stroke victims
  - Alleviation of phantom pains
  - Management of Complex Regional Pain Syndrome.
Peri-operative

* Intraop small dose ketamine successfully used as an adjunct to opioids for postop analgesia.
* Reduces postop opioid needs
* Reduces PONV 2º to opioids
* Improves mobilisation 24 hours
* Post op PMP and infusion in complex pain patients
* Beneficial in emotionally labile patients
Low dose ketamine (0.5 mg/kg) administered 20 minutes before end of surgery under GA resulted in lower incidence of post-operative shivering.
Abdo Hyster in recovery post op

C/o pain crying dropping off to sleep waking stating pain 8/10 dropping off etc

Given 8mg ketamine in 2mg increments

Pain 2/10 patient easily roused

Commenced on PCA

Total usage 5mg 18hrs

Step down to oral analgesia
Case History - Opioid tolerant

- 60Yo Male with Left Diaphragmatic hernia
- Large amount of small bowel herniated into left thorax

Previous History
- Asthma COPD  PVD Chronic Lower Limb Ulcers Chronic Back Pain  Anaemia  Malnutrition x IVDU  Opioid Dependence

AIM
- Duty of care to provide adequate analgesia without increasing baseline opioid requirements.
- Non punitive
Drugs (analgesia only)

- Pregabalin 150mg PO TDS
- Panadol Osteo SR 1330mg PO TDS**
- Oxycontin CR 80mg PO BD (240 mg oral morphine)
- Oxycodone 10mg PO QID PRN(60mg oral morphine)
- (actually takes up to 40mg/dose)
- 300mg oral morphine/day +/-
All bloods normal

Surgery:
Lap reduction and R/O incarcerated diaphragmatic hernia + mini laparotomy and SB Resection

Anaesthetic:
GA, ketamine incrementally, TAP blocks at end of surgery
PMP morphine 10mg
- PCA Morphine 1mg basal and 2mg bolus
- Ketamine 10mg infusion
- No load necessary - Pt comfortable
- Paracetamol 1g TDS (malnourished)

Ketamine Protocol – 2mg/ml
- PMP Ketamine 2-4mg every 3-5 mins
- Care with bolus doses
Day 1:
* PCA morphine 146.5 mg
* Ketamine increased to 20mg/hour (Maximise)
* TAP’s 20mls ropivacaine tds
* Clear fluids

Day 2:
* PCA 202mg
* Ketamine 20mg/hour
* TAP’s TDS
* HPF -Commence Oxycontin nocte
Day 3:
* Cease basal continue PCA mode only (168mg)
* Oxycontin 80mg BD
* Ketamine 20mg/hour

Day 4:
* Cease PCA (69mg)
* Commence oxycodone 15-20mg 3/24
* Cease Ketamine after lunch

Day 5:
* Cease TAP’S Continue OxyContin and PRN oxycodone

**Patient home on same analgesia**
In the early 1990’s Ketamine became a popular drug of abuse among the **RAVE** and techno scene due to its hallucinogenic properties.

**Forms:**
- powder for snorting, liquid for injection or added to drinks
- No smell or taste, so it is difficult to detect.
- Date rape drug
- Detected in urine for 2-4 days

**Additives:**
- often mixed with MDMA (ecstasy), “Ice” (methaphetamine), benzodiazepines etc
- Hallucinogenic dose: 30mg
Street Names

- Kit kat
- Special "K"
- Vitamin K
- Super C

Signs and symptoms:
Altered perception, disorientation, drowsiness, N&V hallucinations, numbness, strange muscle movements, **Catatonic state** with a mask face, an open mouth, fixed staring with dilated pupils, and rigid posturing
In sub anaesthetic doses provides excellent analgesia
Acts on NMDA receptors
May be combined with opioid or infused separately
Administered IV, SC
200-500 mg /day
Half life of 2-3 hrs
Opioid sparing effect
Useful adjunct medication
Ketamine

So good,

the horses want it back