Unfamiliar drugs and how to use them

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Disclosures

• Chair of the WFSA/ICRC liaison committee

• Advisor to LabonaPhone, a Hong Kong based start-up
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History

- Designed as “monoanaesthetic” agent

- Developed as less potent derivative of phencyclidide (PCP)

- Keto derivative of an amine (ket-amine)

- Synthesised by Stephens in 1962

- First clinical use in early 1970’s
Physical Properties

- Water soluble, clear in solution
- Benzethonium Chloride preservative
- Different concentration: 1%, 5% and 10%
- Compatible (in syringe) with fentanyl, lignocaine, muscle relaxants, midazolam, propofol
Pharmacology

- NMDA receptor antagonist

- Accounts for most of analgesic, amnesic, psychotomimetic, and neuroprotective effects

- Predictable pharmacokinetics

- Hepatic metabolism Cytochrome P450

- Racemic mixture

- Single enantiomer mixture S(+) available

- Preservative free available
Clinical effects

The classic ketamine anaesthetic is best described as a dose-dependent CNS depression leading to a so called **dissociative state**, characterized by profound analgesia and amnesia but not necessarily loss of consciousness.
CVS & RS

- ↑ SBP/HR
- Direct myocardial depressant effect
- Minimal respiratory depression
- Airway reflexes relatively intact
- Bronchodilator
Other

• Uterine tone preserved
• Crosses the placenta easily
• Analgesia
• ↑ ICP
• ↑ IOP
• Nystagmus
Associated Problems

• Excess secretions

• Preserved muscle tone & spontaneous muscle movement

• Difficulty in assessing depth of anaesthesia

• Vocalisation

• Prolonged recovery time

• Emergence delirium
Why Ketamine?

- Versatile (IV, IM, PO, PR, central neuraxial use?)
- Cheap
- Good safety profile
- Ease of storage
- Only option in extreme resource limited environments
- And it is available *

(Hodges et al. Anaesthesia 2007)
Show your support...
Clinical use
• **Sole anaesthetic agent**
  
  • Short superficial procedures
  
  • Long procedures when resources very limited
  
  • Casualty extraction/road side anaesthesia
• Induction agent
  • In shocked patients
  • If no other agent available
  • IM induction especially in children
• **Analgesia**
  
  • During anaesthesia when no opioid available
  
  • Positioning of patient for neuraxial block
  
  • Emergency department; #, trauma, burns
  
  • Burns dressings
  
  • Post-operative pain
• Sedation
  • Premedication
  • ICU
  • Other
Thai Cave Rescue
Dr Richard Harris
(lead anaesthetist)

Medical Plan:
Each boy sedated & watertight whole-face mask used to deliver oxygen

Each boy administered:
Oral alprazolam premed 0.5mg
IM Ketamine 5mg/kg
IM Atropine
(re-dosed by divers 2-4 times using half dose)

To reduce salivation
Dose
• **IV**
  - Induction 1 – 2 mg/kg
  - Analgesia 0.2 – 1 mg/kg

• **IM**
  - Induction 6 – 10 mg/kg
  - Sedation/Analgesia 2 – 5 mg/kg

• **Oral**
  - Sedation/Analgesia 5 – 15 mg/kg

• **Caudal/Epidural**
  - 0.25 – 1 mg/kg
• 3mg/kg/hr  SV  (one drop/kg/min)
• 1-2mg/kg/hr IPPV
Ketofol

The Frankston way

200mg/100mg (propofol/ketamine) in 20 ml

Titrate to effect

Frail/elderly: 1 – 2 ml for femoral nerve block
1 – 2 ml for positioning
5 – 15 ml/hr infusion

The Fiji way

50mg each of ketamine and propofol dilute up to 10ml

5mg/ml and titrate to effect
Contraindications
Contraindications

- Few, mostly relative
- Ischaemic heart disease
- Severe hypertension
- ↑ ICP/IOP
- Psychiatric history

- Needs to be seen in context of available alternatives and resources
What about head injuries?
‘I think it is now quite safe to say that ketamine can be used both as an anaesthetic and for sedation/analgesia in the ICU, even for patients with damage to the CNS’
Current practice of avoiding ketamine use in RSI and intubation of HI patients not evidence based

Multiple trauma/ CV instability – avoidance secondary Brain injury - Ketamine
• In the Real World usually not a great worry

• Often no other/better alternative

• Induce and control ventilation if possible
Adjuvant drugs
• Atropine: 10 – 20 mcg/kg. Not routinely needed. Can be given IV in case of excessive salivation.

• Benzodiazepine:
  • Minimises movement
  • Minimises the emergence delirium

• Opioid:
  • Minimises the emergence delirium

• Clonidine:
  • Enhances the analgesic effect of Ketamine
  • Minimises the emergence delirium
Conclusion

• Ketamine certainly is a life saver in many situations

• Although all the side effects are real, they often do not pose a problem:
  • Without it, anaesthesia may not be available
  • Must be seen in the context of poor resources
  • For war or disaster anaesthesia very little needs to be carried
• Invaluable role in Real World anaesthesia

• Safe in trained hands

• Expanding role in and outside operating theatres
• Halogenated hydrocarbon

• Introduced into clinical practice in the UK in 1956

• All you have heard about Halothane is true

• But does it matter?

• Again it depends on the context and what else is available

• Be aware of possible side effects
Pharmacokinetic Properties

- Blood-Gas solubility coefficient = 2.3 (sevo 0.6)
- Oil-Gas solubility coefficient = 234 (sevo 53)
- MAC 0.75
- Degrades when exposed to light
- Thymol
- Significant hepatic metabolism
CVS

• Dose dependent decrease in cardiac contractility, heart rate and systemic vascular resistance

• It sensitises the myocardium to circulating catecholamines

• Arrhythmias especially with hypercarbia

• It does not cause coronary vasodilatation.
RS

- Dose dependent reduction in tidal and minute volume
- Respiratory rate stays the same or may increase
- Bronchodilator
- Reduces bronchial secretions
- Non-irritant
CNS

- Not analgesic
- It causes cerebral vasodilatation
- Increase intracranial pressure
- It is not epileptogenic
Other

- Reduces salivation
- Relaxes the uterus
- Halothane shakes
- Halothane hepatitis (1 : 35,000)
Slow induction and emergence

Blood/gas solubility 2.3

Oil/gas solubility 234
Clinical use

• Over pressure on induction +/- hyperventilation 2-3%

• Maintain with 0.5 – 2% -- SV vs IPPV

• Stop in time **but** if low on opioids they wake up quicker than you expect

• Easy on the opioids when spontaneous ventilation

• Control CO$_2$ if possible
Arrhythmias

- Bigemini and nodal most common
- If possible control CO$_2$
- Question is too deep or too light?
- Careful when infiltrating adrenaline
Liver toxicity

- Two forms:
  - Reversible – subclinical, increased transaminases
  - Fulminant hepatic necrosis (‘halothane hepatitis’) – 1:35,000 (less frequent in children)
    - Diagnosis by exclusion – exclude hepatitis, other hepatotoxic drugs, transfusion reaction, malaria
    - More common in multiple exposures, female, middle aged and obese
    - Mortality 50%

- Repeat anaesthesia?
Gas induction

- Two schools of thought:
  1. 0.5% increase every 3 breaths up to 4 – 5%
     - Takes time
  1. Start with 4 or 5%
     - Breath holding rare

- Once asleep decrease %
Emergence

- Slower than sevoflurane. Turn off halothane 10 minutes or so before the end of the case e.g. when closing the peritoneum in a laparotomy.

- Neonates (especially premature) are prone to periodic breathing when awakening (Michael Cooper)
  - only extubate when they are opening their eyes spontaneously and trying to cry
  - be patient.
If you can choose only one inhalational agent which one would you choose?
Quartermaster Ether for Anaesthesia

Contains about 2 1/4% Alcohol
Purified, analyzed and packaged specifically for anesthetic purposes

Poison

Mallinckrodt Chemical Works
Why ether?

• In Uganda in 2007 ether was the “most widely used volatile agent and always available to 68% of respondents” Hodges e.a.

• Possibly still used in Malawi, Nepal and missionary hospital in India
Pharmacokinetic Properties

- MAC* 1.92

- Blood/gas solubility co-efficient 12

- Oil/gas solubility co-efficient 65

- 85-90 % excreted unchanged.

- 6 % is metabolised in liver to produce acetaldehyde, alcohol, acetic acid and alcohol.
CVS

• Cardiac output, heart rate and blood pressure are maintained

• Direct negative inotrope

• It also activates the sympathetic nervous system

• It does not sensitise the myocardium to circulating catecholamines

• Arrhythmias are uncommon

• Dilatation of coronary arteries.
RS

- Initially a respiratory stimulant and increases RR
- At higher concentration a respiratory depressant
- Bronchodilatation
- A respiratory irritant causing coughing and breath holding
CNS

- Mild analgesic
- Cerebral vasodilatation and therefore increases intracranial pressure
- It can cause convulsions
Other

- Salivation (antisialogogue premedication)
- Post operative nausea and vomiting is very common
- Relaxes the pregnant uterus
Epstein Mackintosh Oxford (EMO)
Use

- Slow inhalational induction over 20 minutes up to 20%
- Co-induction with halothane
- IV induction and maintenance with ether 2 – 4% IPPV
- PONV ++++

**Beware:**
- Flammable in air
- Explosive in oxygen
IV Ether!

THE
ADMINISTRATION OF ETHER.
By
J. H. T. CHALLIS, D.A.
Anaesthetist, London Hospital.

POST-GRADUATE MEDICAL JOURNAL October, 1946
The intravenous injection of ether in saline and the rectal administration of it has become obsolete but the addition of 10 to 20 c.c. of ether to 450 c.c. of saline or glucose with 2 gms. of pentothal sodium certainly greatly adds to the smoothness and ease of administration of this type of intravenous anaesthesia.
Thank you