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Ketamine

- Is a phenylcyclidine derivative introduced in the early 1960s as an I.V anesthetic agent.
- Pharmacologically, ketamine is classified as an NMDA(***N-Methyl-D-aspartate***) receptor antagonist.
- Ketamine acts as a noncompetitive antagonist of the ionotropic glutamate *N*-methyl-d-aspartate (NMDA) receptor.

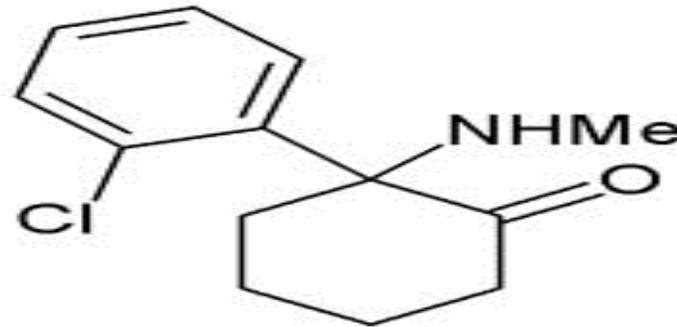




- Ketamine is a drug used in human & veterinary medicine developed by Parke-Davis in 1962.
- 1st used clinically on American Soldiers during the Vietnam War in 1970, & b'se of these combined effects it was thought that it might be the perfect i.v anaesthetic agent.
- Its hydrochloride salt is sold as Ketanest, Ketaset, and Ketalar.



KETAMINE IN ANAESTHESIA



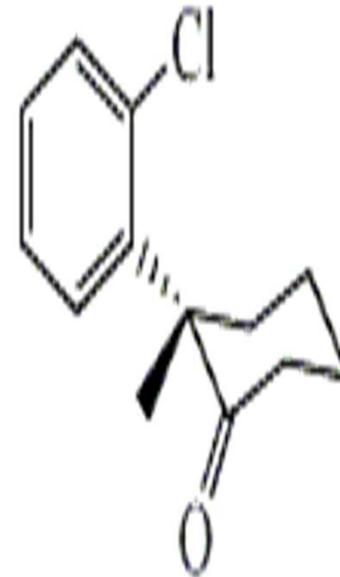
- Ketamine is the only anaesthetic available which has
 - Analgesic (pain relieving),
 - Hypnotic (sleep producing)
 - Amnesic (short term memory loss) effects.



Structure of Ketamine



- “Ketamine’s dual anesthetic/hallucinogenic nature comes from it being a chiral compound, with its two enantiomers having different effects.
- S-Ketamine produces anesthetic effects while its enantiomer R-Ketamine produces the hallucinogenic effects.



(S)-Ketamin
an anesthetic drug



(R)-Ketamin
a halucinogen



NEUROPHARMACOLOGY



- Ketamine, 1^o a non-competitive glutamate NMDA receptor antagonist.
- At low doses, the analgesia effects of Ketamine are mediated by antagonism on the NMDA receptors.
 - Evidence for this is reinforced by the fact that Naloxone, an opioid antagonist, doesn't reverse the analgesia.
- Studies also seem to indicate that ketamine is 'use dependent' meaning it only initiates its blocking action once a glutamate binds to the NMDA receptor.



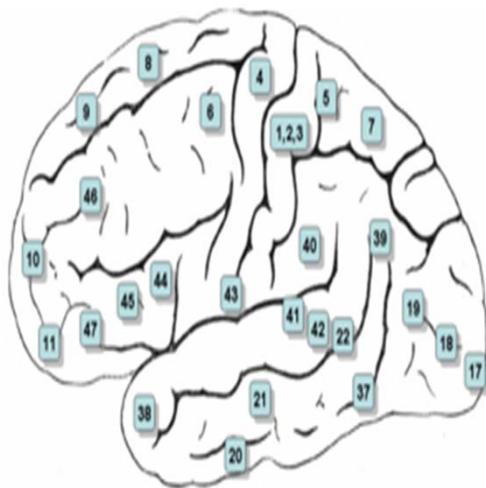
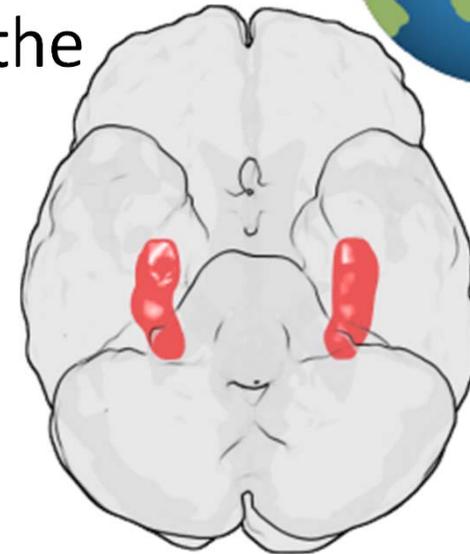


- At high doses, Ketamine has also been found to bind to opioid mu receptors & sigma receptors.
- This indicates that loss of consciousness @ high doses may be partially due to binding @opioid mu & sigma receptors.





- The effects seem to occur mainly in the hippocampal formation & in the prefrontal cortex.



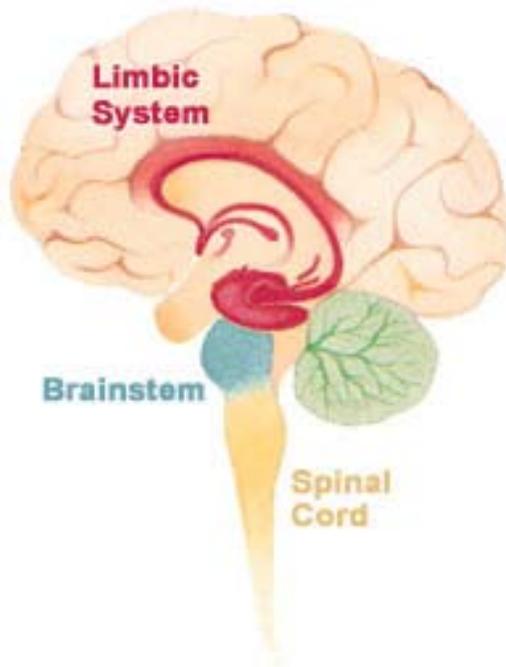
- This evidence along with the NMDA receptor's connection with the memory formation process explains ketamine's profound effects on memory and thought.





Pharmacodynamics

- Ketamine is effective both I.V, I.M & orally
- It produces a state of dissociative anaesthesia
- There is dissociation b/n the thalamic & limbic systems.



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"NOW, I KNOW I
CAME IN HERE
FOR SOMETHING!"



search ID: rmg121

- Ketamine is devoid of hypnotic properties, but causes amnesia & analgesia.
- Consciousness doesn't appear to be lost, but there is complete amnesia.
- Muscle tone is not ↓ed, but usually ↑ed & involuntary movements may occur which are unrelated to surgical stimulus, the eyes tend to be open.





- Vocalization may also occur
- The occurrence of vivid & sometimes unpleasant dreams is frequent after Ketamine anesthesia, although the incidence is less in children.
- It is conventional to avoid any stimulation of patients recovering from ketamine anaesthesia in order to ↓ the incidence of these emergence reactions, which can also be achieved with any sedative medication.



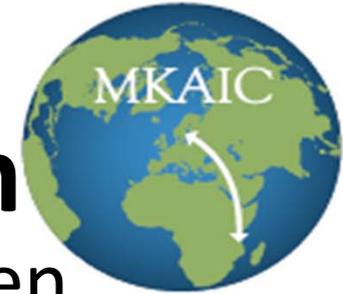


- Ketamine is available in three different concentrations 10mg/ml, 50mg/ml & 100mg/ml.



- 50mg/ml is most commonly stocked since it can be used for i.m. administration or diluted for i.v. use.





Routes of Administration



- Ketamine may be given
 - I.V (induction 1-2mg/kg, maintenance 0.5mg/kg) or
 - I.M (induction 5-10mg/kg, maintenance 3-5mg/kg) for anaesthesiaor
 - Orally (15mg/kg for a child to a max. of 500mg for an adult) for sedation.



CVS



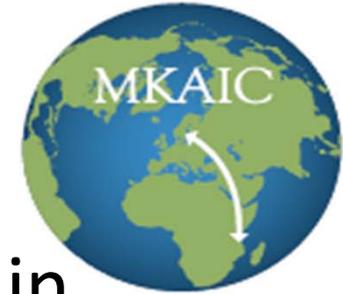
- Ketamine causes mild stimulation of the CVS.
- The B.P rises by about 25% (on average the systolic pressure rises by 20-30 mmHg) & H.R ↑ed by about 20%.
- The overall effect is 0°0 to ↑ the workload of the heart.
- This is b'se of central sympathetic stimulation.
- It causes pulmonary vasoconstriction & undesirable strain on the right heart in some cases of valvular heart disease.





- In majority of pts the B.P rises steadily over 3-5 mins & then returns to N 10-20 mins after inj.
- There is wide individual variation in cardiovascular responses.
- There is no evidence to suggest that patients with a high preoperative B.P are @ greater risk of developing a rise in B.P following Ketamine administration when compared with normotensive patients.





- Premedication with diazepam ↓ this rise in B.P.
- If the B.P rises excessively after induction, a further small I.V dose of diazepam (2mg to the average 60-70 kg adult) may help to ↓ the pressure.
- Myocardial O₂ consumption is ↑ed by ketamine & it is contraindicated in patients with ischaemic heart disease.





- This ↑ed workload for the heart means that ketamine should be avoided, if possible, in those patients with ischaemic heart d'se.
- Patients with diabetes should have an ECG, if available, to R/o “silent” ischaemia (ischaemia without chest pain), since this is a common feature of poorly controlled diabetes.





Respiratory System

- After a slow I.V induction, breathing is well maintained & may even \uparrow slightly.
- Self maintenance of the airway is a usual feature of Ketamine anaesthesia.





R.S

- With ketamine the airway is usually well maintained it also preserves the laryngeal & pharyngeal reflexes to some degree.
- This is not always guaranteed however, standard techniques, where required, for Px of aspiration & maintenance of a patent airway must be used.
- When ketamine is given slowly respiration is usually well maintained, after rapid I.V injection the breathing may stop for a short while but usually restarts within a minute.
- For this reason ketamine is a very useful anaesthetic agent in areas where there is no oxygen or only limited oxygen available.
- Ketamine is an effective bronchodilator ,making it a useful anaesthetic drug for patients with asthma.



GIT



- Salivation is ↑ed, → to airway problems due to laryngeal spasm or obstruction.
- May also make the taping of E.T.T more difficult.
- To ↓ this salivation
 - Atropine is usually given either as a premed (20mcg/kg i.m.) 30 minutes preoperatively,
 - or @ time of induction iv (10-20mcg/kg).





Skeletal muscle

- Spontaneous movements may occur during anaesthesia but reflex response to surgery is uncommon if the patient is adequately anaesthetised.
- Ketamine ↑es skeletal muscle tone.
- This is most prominent after the initial iv bolus & gradually ↓es.
- It is improved by administration of benzodiazepines.
- It is rarely a problem intraoperatively.





Uterus & Placenta

- Crosses the placenta easily & conc. in the fetus are \approx ly the same as those in the mother.

Placenta

Crosses the placenta & if used during a C/S the neonate, which may be affected, should receive the appropriate care & monitoring.





The Eyes

- I.O.P ↑ for a short time following administration.
- Eye movements may continue throughout surgery.
- It is **not suitable** for use in patients with a perforated eye injury or for ophthalmic surgery where a still eye is required
- It is also common for the eyes to move during ketamine anaesthesia (nystagmus).
- This makes it an unsuitable agent for use in ophthalmic surgery.





Nervous System

- It ↑es cerebral O₂ consumption, CBF & I.C.P.
- Produces Dissociative anaesthesia (detached from surroundings).
- This means that unlike with other anaesthetic agents the pts may have their eyes open & make reflex movements during the operation.
- It has a slower onset after an I.V bolus (1-5 minutes).
- The duration of action depends on the route of administration (20-30 min. for i.m. & 10-15 minutes for iv).





N.S

- Ketamine provides very good analgesia & may be used without any other analgesics intraoperatively.
- Consideration does then have to be given however to postoperative pain relief.
- Co-administration of opiates or Tramadol intraoperatively can ↓ amount of Ketamine required for maintenance of anaesthesia & ↓ the incidence & duration of postoperative hallucinations.
- This does however ↑ the risk of Apnoea during the operation



N.S



- In recovery the patient may be agitated : as hallucinations are associated with Ketamine anaesthesia.
- These hallucinations can be:
 - ↓ed by Premedication with Benzodiazepines (usually diazepam 0.15mg/kg orally 1Hr preoperatively /0.1mg/kg I.V) & recovering the pt in a quiet area.

Ketamine ↑es I.C.P & for this reason should be avoided wherever possible in those patients with recent head injuries





Pharmacokinetics

- Ketamine is rapidly & extensively distributed throughout the body.
- Undergoes extensive & complicated Metabolism in the liver & only about 4% appears unchanged in the urine.





Indications

1. May be used as induction agent of anaesthesia. It is an effective agent in poor risk patients & those with a tendency to hypotension.
2. As a sole agent for minor operations.
3. When airway control is difficult, such as burns or trauma





4. When maintenance B.P is important e.g. in state of shock in poor risk patients & in the elderly.
5. For dressing of burns
6. Sub anaesthetic doses have been used to produce analgesia.
7. When intramuscularly injection is more convenient than intravenous.



Dosage and administration



- INDUCTION:
 - **I.V Injection** of 1-2mg/kg produces surgical anaesthesia within 30sec - 60sec
 - MAINTENANCE: 0.5mg/kg, Repeated doses may be given without significant cumulative effects.

- INDUCTION

- **Intramuscular injection** :5-10 mg/kg
- MAINTANENCE: 3-5mg/kg

I.M doses Produces surgical anaesthesia within 3 - 4 minutes, lasting 15 - 30 minutes, Repeated intramuscular injections result in a prolonged recovery time.

- Orally :15mg/kg for a child to a max of 500mg for an adult.





Adverse effect

- Rise in B.P & pulse-rate which may be disadvantageous in hypertensive
- Transient erythematous rashes have been reported.
- Vivid unpleasant dreams & occasionally true hallucination.





Precautions

- It should be avoided in patient with a Hx of C.V.A, M.I & HTN.
- It is C.I in patients with raised I.CP & penetrating eye injuries.
- Stimulation of the patient during emergency from anaesthesia should be avoided.





Case 1 Practicals

- A 22 yrs Old man has been admitted with a gun shot wound to the abdomen. He is shocked from major internal bleeding and requires a laparotomy . You have very small supply of inotropes and want to try not to use them. what will you do for induction and maintenance of anaesthesia



SOLUTIONS TO CASES:

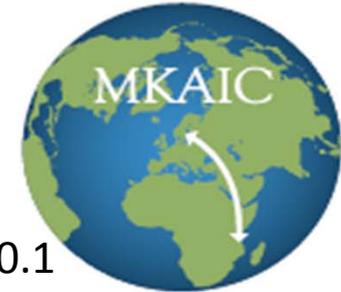


Case 1

- This gunshot victim is shocked & requires a laparotomy, you have a limited inotropes , KETAMINE would be an ideal anaesthetics agent in this case due to cardiovascular effects of \uparrow ing the B.P & H.R all other anaesthetic agents have a cardiac depressant effects.



Case 1 solu. ct



- Induction: i.v Ketamine(1-2mg/kg) ,atropine (10-20mcg/kg) & Diazepam (0.1 mg/kg). It is still possible to perform modified RSI with Ketamine despite its slower onset.
- Maintenance: (several options)
 - 1.intermittent boluses of I.V Ketamine (0.5mg/kg) given according to the patients reponses : pupil size, H.R, B.P & movements.
 - 2.Ketamine infusion:500mg →500mls of N/S or 5%Dextrose,run this @1-2mls/min(1-2mg/min),some patient may require more ,so titrating is important
 - Ketamine needs to be discontinued 20-30 min before the end of operation to avoid long waiting for the patient to wake up.
 - This technique of LAPARATOMY is best used without Non depolarising muscle relaxant(avoid Pancuronium) as combined with Ketamine will may have very high B.P↑.
 - It is however possible but difficult to perform laparatomy under ketamine alone



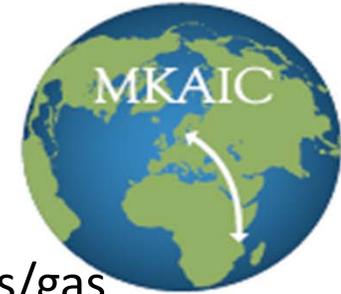


Case 2

- A 2 yr old boy needs repair of his hernia. He is extremely frightened of the hospital & its staff. You think obtaining an I.V access will be very difficult & that a gas induction will be difficult as well b'se of his agitation .How will you anaesthetise this child.



CASE 2 SOLUTION



- This child is clearly going to be uncooperative and either i.v access/gas induction will be difficult. In these circumstances I.M Ketamine is very useful:

2 possible options:

- Induce anaesthesia with I.M Ketamine:
 - 1. Ketamine 5-10mg/kg + Atropine (20mcg/kg) + Diazepam(0.1mg/kg)- these may be mixed in the same syringe. Onset starts: 5min after injection.
 - Disadvantage : Requires relatively Large I.M injection, while in most text book quote 8-10 mcg/kg for induction but 5mg/kg sometimes are sufficient
 - 2.Sedate with I.M Ketamine (2mg /kg) + Atropine (20mcg/kg) + Diazepam (0.1mg/kg)
 - After 5min you will have a docile child who will cooperate with either cannulation or a gas induction.
- However option 2 is more preferred as can be done in mother's lap & less traumatic





Case 3

- A 37 year old girl is recovering from 45% burns. she needs dressing changes every 2 days which are very painful. She has very few sites for left for I.V access & you don't want to use them as she has further surgery to come. She is also very scared of needles .How will you manage?



Case 3 SOLUTION



- This woman require recurrent sedation for the burns dressing .
- I.V Ketamine is possible but in burn cases there are limited sites for the cannulation & are best saved trips for the theater.
- I.M Ketamine is an option but requires relatively large Painful I.M injections. Instead the intravenous preparation of ketamine can be used **ORALLY**
- ADULT: 500mg +Diazepam 5mg
- CHILD: 15 mg/kg + 0.2 mg/kg Diazepam(you can use I.V preparation but it tastes very bad & can be hidden in the juice).
- The dressing change can be started after 20 min but responses can be unpredictable and onset may be slower, however there **should be always be** equipped with Suction & face mask ventilation and pulse oximeter





Case 4

- Your Laparotomy patient (case1)is back in the ward. He has severe post operative pain but you have been unable to get any morphine this month. How can you manage this postoperative pain?





Case 4

- Ketamine for post operative analgesia.
- Is very good analgesic & can be a solution for severe pain when morphine is not available.
- Its use post operatively is limited by its occurrence of Hallucinations, however these are less of a problems when a relatively low doses are used .
- Adult :in severe pain loading dose – 0.5-1mg/kg I.M, this can be followed by infusion of 60-180mcg/kg/hr(4-12mg/hr for a 70 kg adult)
- A reasonable regime:500mg→500mls of N/S O 5% dextrose (0.1mg/ml ketamine)& run this @40-120nls/hr i.e over 4-12hrs for a adult of 70kg.
- This regime is safe even whole infusion is given by Accident the patient is unlikely to go to deep anaesthesed but the pts needs to be closely monitored.





Case 5

- A 25yrs old man has had his leg amputated after a motor bike accident . He is suffering from lots of problems with Phantom limb pain . You have tried giving him amitryptiline and carbamezapine but without effect. What could be your third line option?





Case 5

- Many patients with amputations /patients with spinal-cord injuries have problem with chronic pain.
- Nature of this pain is Neuropathic(originating from the nerve injury) & has unpleasant , burning sensation and shooting quality to it. when traditional 1line treatment for neuropathic such as Amitriptyline or Carbamazepine have failed Ketamine may also be added & has been shown to have successful
- Dosing :Adult 50mg orally (use I.V preparation) 3 times a day.
- Problems with Hallucinations& salivations are rare.
- Ketamine may be Discontinued after 3 weeks of good pain Control , reducing the dose gradually to see if any pain symptoms recurr.
- Same regime for Phantom limb pain (for 1 week)





Case 6

- An 18yrs old girl has been admitted with severe asthma. You have been asked to see her as she has not improved with subcutaneous injections of salbutamol or I.V aminophyline. She is getting tired and her oxygen saturation is falling. Can you do any thing to help?





Case 6

- Ketamine for treatment for Asthma.
- Effective Bronchodilator & can be used for the patient who is not responding to the conventional Bronchodilators such as Salbutamol & aminophylline.
- The Dose of Ketamine require are very low & problems with Hallucinations are rare.
- Loading Dose :0.2mg/kg I.V is given Initially followed by an infusion of 0.5mg/kg/hr for 3hr, this may be continued as necessary
- Close monitoring should be required and anaesthetist should be available if necessary



Ketamine



- Is Good drug
- And use per its Indication.
- Thanks .

