

KETAMINE

a new look at an old drug



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Ketamine



- ❖ General anaesthesia in children, adults and fragile patients (hypovolemia, cardiac ischaemia and cerebral injury)
 - ❖ An potent analgesic drug
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Ketamine

- ❖ A phencyclidine derivative developed in the 1960s
- ❖ The main molecular target is the N-methyl-D-aspartate (NMDA) glutamate receptor
- ❖ Inhibit the formation of nerve growth factor in the preparation of human smooth muscle cells: mechanism for the proposed pre-emptive analgesic effect, local anaesthetics in periphery (Durieux *et al*)
- ❖ Local anaesthetic effect is weak with high concentrations of ketamine (Koppert *et al*)

Cerebral and anaesthetic effects



- ❖ **Sakai *et al***: different doses of ketamine + propofol infusion (3mg/kg/h) looking for effects of the combination on sleep, reaction to noxious stimuli, and BIS (electroencephalography bispectral index)
- ❖ **Additive**

Cerebral and anaesthetic effects

- ❖ Hans *et al*: thiopentone 5mg/kg with ketamine 2.5mg/kg + rocuronium 0.6mg/kg 1 min intubation.
- ❖ The degree of neuromuscular block was similar
- ❖ The vocal cord relaxation and the diaphragmatic response to intubation were significantly more favourable after ketamine (analgesic effect)

Cerebral and anaesthetic effects

- ▶ Ketamine may increase intracranial pressure. Recent studies: advantageous to the patient with cerebral damage.
- ▶ Sakai *et al*: ketamine did not alter the middle cerebral artery blood flow or cerebrovascular carbon dioxide response
- ▶ Denz *et al*: increased arterial pressure and cerebral perfusion pressure (S-ketamine). No increase in brain oedema in pigs
- ▶ Ketamine anesthesia: cerebralvascular autoregulation seems to be preserved
- ▶ Inhalational anesthesia may impair and slow down the vasoregulatory response

Cardiovascular effects

- ▶ Ketamine acts as a myocardial depressant on isolated heart muscle preparation
- ▶ In vivo: sympathomimetic effect: positive inotropy, chronotropy.
- ▶ Kienbaum *et al*: sympathetic activity in peroneal nerves and muscles in healthy volunteers.
- ▶ Systemic blood pressure increased: a decreased sympathetic output
- ▶ Blood pressure stable (nitroprusside): the sympathetic nerve outflow normal
- ▶ The plasma concentrations of both adrenaline, noradrenaline increased. Ketamine: decrease catecholamine reuptake

Respiratory effects

- ❖ Minor, with some reduction in airway reflexes with increasing dose



Sedation

- ❖ Frey *et al*: propofol + ketamine with propofol alone for sedation of elderly patients → a faster onset and better quality of sedation, without side effects (hallucinations or any need for assistance of ventilation)
- ❖ Ketamine 100-200ng/ml + alfentanil
50ng/ml: in volunteers produced subjective effects of abnormal perception in almost all subjects.
- ❖ 1 volunteer: anxiety, agitation (200ng/ml)
- ❖ 50ng/ml: no result in such effects

Sedation

- ▶ Gruber and Morley: amnesia in 133/134 patients, 14 patients transient oxygen desaturation, 1 patient bad dreams
- ▶ Friedberg: 2059 officebased plastic surgery with 2mg midazolam+propofol infusion until sleep, + 50mg ketamine before application of local anesthesia: 99% had oxygen saturation greater than 90% while breathing room air, only 2% needed anti-emetic medication
- ▶ →use of ketamine for emergency patients by nonanaesthesiologists

General anaesthesia



- ❖ Bergman, Granry *et al*: sedation, general anaesthesia, pain control in children. In a case report of severe status asthmaticus in an 8-month-old infant.
- ❖ Nehama : excellent results with an infusion of ketamine. A comprehensive review of the use of ketamine in children.

An analgesic

- ❖ Schmid *et al*: the use of low-dose ketamine in the management of acute postoperative pain from 1966 to 1998.
- ❖ < 1mg/kg IV or epidural
- ❖ < 20mcg/kg/min infusion
- ❖ < 2mg/kg IM
- ❖ → a valuable adjunct to other drugs for postoperative pain control



An analgesic

- ❖ Outpatient surgery: reduced opioid requirements of 40% with ketamine 75mcg/kg IV
- ❖ Increased drowsiness with 100mcg/kg
- ❖ 150mcg/kg/h infusion + PCA morphine 48h postoperative: reduced morphine requirements 50%, the overall incidence of nausea

Pre-emptive analgesia

- ❖ Blocking pain mediators before pain is initiated may reduce the subsequent need for analgesics due to reduction of wind-up mechanisms in the spinal cord. The NMDA receptors in the spinal cord: to be responsible for such wind-up.



Effects of ketamine added to ropivacaine in pediatric caudal block

- ❖ Authors: Odes R, Erhan OL, Demirci M
- ❖ Source: the journal of the Turkish society of Algology. 2010 april
- ❖ 45 patients (1-4 years), scheduled to undergo inguinal hernia repair with caudal anesthesia
 - * Group R: 2mg/kg ropivacaine 0.2%
 - * Group K: 0.5mg/kg ketamine
 - * Group R+K: 2mg/kg ropivacaine 0.2%+ 0.5mg/kg ketamine

Effects of ketamine added to ropivacaine in pediatric caudal block



Results: at the postoperative 45th , 60th mins, the CHEOP score was significantly higher in Gr R compared to Gr K and Gr R+K , 60th min ($p < 0.05$)

- ▶ The effective analgesic period is higher in Gr K and Gr R+K than in GrR. The analgesic requirement in the first 24h postoperation was lower in Gr R+K than the other group.
- ▶ Sedation scores were below 2 in all groups.No differences adverse effects

Conclusion: ketamine combined with ropivacaine lengthened the duration of analgesia while lowering analgesic requirements





Comparison of caudal epidural bupivacaine with bupivacaine plus tramadol and bupivacaine plus ketamine for postoperative analgesia in children

- ❖ **Author:** Choudhuri AH, et al. Departement of Anaesthesiology, Aruna Asaf Ali Government Hospital, Delhi, India
 - ❖ **Source:** Anaesthesia and intensive care. 2008 Mar
 - ❖ 75 children 3-9age, scheduled for elective unilateral inguinal hernia repair
 - ❖ 3 groups: 0.5ml/kg bupi 0.25%, bupi+ketamine 0.5mg/kg, bupi+ tramadol 1mg/kg.
 - ❖ **Results:** caudally administered bupi plus ketamine or tramadol provided significantly longer duration of analgesia without an increase in the adverse effects when compared to bupi alone.
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Comparison of propofol versus propofol-ketamine combination for sedation during spinal anesthesia in children



- ❖ Source: Paediatric anaesthesia. 2010 May
 - ❖ Author: Singh R, Batra YK, Bharti N
 - ❖ 40 patients (aged 3-8), spinal anesthesia for lower abdominal surgeries.
 - ❖ Conclusion: Propofol-ketamine better quality of sedation with lesser complications than propofol alone and thus can be option for sedation during spinal anesthesia in children
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Comparison of ketamine and fentanyl for postoperative pain relief in children following adenotonsillectomy



- ❖ Source: Pakistan journal of biological sciences. 2010 May
 - ❖ Authors: Taheri R et al
 - ❖ 60 patients (3-12 years):
 - * Group 1 ketamine 0.5mg/kg IV
 - * Group 2 fentanyl 1 mcg/kg IV
 - ❖ Conclusion: extended time to first analgesic in children. Fentanyl and Ketamine did not differ in post-operative vomiting
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Efficacy and adverse effects of ketamine as an additive for paediatric caudal anaesthesia

- ▶ **Author:** A. Schnabell, et al. Department of Anesthesiology and Intensive Care, university hospital of Munster, Germany.
 - ▶ Accepted May, 2011.
 - ▶ The efficacy and adverse effects of ketamine added to caudal local anaesthetics in comparison with local anaesthetics alone in children undergoing urological, lower abdominal, lower limb surgery.
 - ▶ 13 RCTs(1991-2008), 584 patients
 - ▶ **Conclusion:** caudally administered ketamine provides prolonged postoperative analgesia with few adverse effects .
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Intramuscular ketamine for prevention of postanaesthesia shivering in children



- ▶ **Authors:** Zahra FA et al. Source: Saudi medical journal. September 2008.
- ▶ **Objective:** to compare the effects of intramuscular ketamine with pethidine and placebo on postoperative shivering in children undergoing tonsillectomy
- ▶ **120 patients, ASA 1, 5-12 age**
- ▶ **Results:** the use of a prophylactic low dose ketamine was found to be effective in preventing post anesthesia shivering in children. Ketamine may have at least theoretical advantages over pethidine as regared respiratory depression, nausea, vomiting.

Conclusions

- ❖ Ketamine in subanaesthetic dose is effective in reducing morphine requirements in the first 24 h after surgery. Adverse effects are mild or absent. Ketamine reduces postoperative nausea and vomiting
- ❖ There is a clear benefit of caudal ketamine, but the uncertainties about neurotoxicity relating to the dose of ketamine, single vs repeated doses and the child of age, still need to be clarified for use in clinical practice.

Perioperative ketamine for acute postoperative pain



Conclusion:

- ❖ Ketamine in subanaesthetic dose is effective in reducing morphine requirements in the first 24 hours after surgery.
- ❖ Reduces postoperative nausea and vomiting
- ❖ Adverse effects are mild or absent



