REVIEW

Ketamine in prehospital analgesia and anaesthesia

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SUMMARY

Ketamine is becoming more popular among doctors working in prehospital medicine, for both analgesia and anaesthesia. There have been longstanding concerns regarding the possibility of it producing rises in intracranial pressure, and hence worsening outcome in head injured patients. There is some evidence, however, that it may help improve outcome in brain injured animals. We present a review of the use of ketamine, and the evidence for its use in practice. We conclude that there is little or no evidence of harm in trauma patients. We also advocate larger scale studies, to assess whether or not it may be of benefit.

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1. Introduction

Ketamine has been routine part of the prehospital doctor’s toolkit for some years, principally used as an analgesic agent to allow procedures to facilitate safe extrication.1 Ketamine is a versatile drug, which can be used, in different doses, for analgesia, sedation and induction of general anaesthesia. It is favoured for its haemodynamic stability, and for allowing the preservation of upper airway reflexes in sedative doses.2 In extremis, this has allowed even field amputation to take place.1 It can also been used for the induction of general anaesthesia, as part of a modified rapid sequence induction (RSI).3 It has been popular within the military for some years now,4,5 and has long been favoured in resource poor healthcare systems.6,7 It has also been employed in the Emergency Department, for both procedural sedation and general anaesthesia.8

Despite its increased use, many standard textbooks express caution about using ketamine, citing concerns over raising intracranial pressure (ICP) as a contraindication to its use in head injured patients.2,9 The authors present a review of this topic, covering the utility of ketamine in prehospital medicine, and considering some of the concerns about its adverse effects.

2. Pharmacology

Ketamine is a phencyclidine derivative, and is available at 10, 50 or 100 mg/ml concentrations.10 It acts by blocking N-methyl-D-aspartate (NMDA) receptors. Doses of 1–2 mg/kg iv will induce anaesthesia, however smaller doses are used for analgesia or sedation, at 0.2–0.5 mg/kg. Ketamine can also be administered intramuscularly or via the intraosseous route, where iv access proves difficult. In practice, adults can be given doses of 10–20 mg iv, titrated to effect when effective analgesia or sedation is required. Its pharmacokinetics are a combination of lipid redistribution and hepatic metabolism to inactive metabolites, which are then excreted in urine. Its duration of action is dose related, and 2 mg/kg provides around 10–15 min of anaesthesia.2

In the cardiovascular system, it produces sympathetic activation, resulting in raised heart rate and blood pressure. Doses of over 1.5 mg/kg reduce myocardial activity.9 It must be used with care in patients with ischaemic heart disease, as increased heart rate will reduce diastole time, potentially reducing coronary blood flow.11

Respiratory effects include increased respiratory rate and bronchodilation, along with preservation of the upper airway reflexes. There is a small risk of laryngospasm, which may require intubation in a very small number (0.017%) of cases.12 In the central nervous system, ketamine produces a sense of dissociation and intense analgesia, taking about 90 s for maximum effect. In the gut, it causes increased motility, and consequently may reduce the risk of aspiration.2

3. Procedural sedation and analgesia

Ketamine can be used in analgesic doses to allow brief, painful procedures to be performed. Due to the dissociative state it produces, patients can tolerate procedures that would otherwise be impossible. As its onset is quick and duration of action is short, the patient is less likely to be oversedated after the painful stimulus is removed. Its advantage over entonox is that it does not require the patient to be compliant. The short duration of action, however, requires another analgesic agent, such as morphine, in order that the pain does not return during transfer to hospital.

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It is principally compared with midazolam, however, there are no trials directly comparing the two in prehospital, or indeed hospital, patients. We would advocate the use of ketamine in preference for procedural sedation, however. Our reason is that midazolam has an elimination half life of 1–2 h, which can be too long for a short procedure, in comparison with 10–15 min for ketamine. Ketamine also has the advantage of preserving upper airway reflexes better than midazolam, making it a safer choice in austere environments.

4. Induction of anaesthesia in head injured patients

In head injured patients, with reduced Glasgow Coma Score (GCS) and loss of airway reflexes, the use of prehospital RSI allows protection of the airway, and controlled ventilation, to prevent secondary brain injury as a result of hypercapnoea and hypoxia. A major concern in this patient group is hypotension, a common side effect of sedative drugs, such as thiopentone and propofol. It has been shown that even a single episode of hypotension worsens outcome in head injury, especially if they have multiple injuries. Ketamine has the advantage here of producing sympathetic activation, and hence a rise in pulse and blood pressure. This in turn would suggest that, in appropriate doses, ketamine is less likely to produce hypotension than thiopentone or propofol. This may result in better overall cerebral perfusion, and a reduction in secondary brain injury.

5. Intracranial pressure

The principle concern about the use of ketamine, especially for induction of anaesthesia in head injured patients, is the belief that ketamine raises ICP. Some studies suggested that ketamine caused a rise in ICP, which could lead to a reduction in cerebral perfusion in a head injured patient. These papers were based on small studies or case reports, and referred to patients with known intracranial pathology undergoing neurosurgery. Most of patients who showed increased pressure had abnormal CSF dynamics. Gibbs compared the effects of ketamine in patients undergoing discectomy, and those with an intracranial lesion. It reported that in the group with no space occupying lesion, no change in cerebrospinal (CSF) pressure was observed with ketamine administration. Some authors advise, however, that ketamine is relatively contraindicated in head injured patients.

More recent work has been done on critical care patients, and has shown, in general, that ketamine has small or no impact on ICP. Bourgoin et al conducted two studies in head injured patients, comparing ketamine with the opioid sufentanil. They found that ketamine did not affect intracranial pressure, and concluded that it was safe to administer it to head injured patients. Albanese administered ketamine in conjunction with propofol to head injured patients, and recorded a significant fall in intracranial pressure. One study on children with traumatic brain injury, and found it reduced ICP by up to 30%, and improved cerebral perfusion. Several recent reviews of the evidence suggested that the evidence for rises in intracranial pressure was limited, and likely to be overstated.

There has been some work looking at the effects of ketamine on cerebral metabolism. Längsjö et al found that it increased cerebral blood flow, probably as a result of increased arterial pressure, but that it did not affect cerebral oxygen demand. A study conducted on children undergoing lumbar puncture for suspected aseptic meningitis, however, did find that ketamine increased CSF pressure, although it made no difference to outcome. Whether or not this can be generalised to trauma patients is uncertain. We would suggest that the evidence suggests that concerns about raised intracranial pressure are not sufficient to prevent the use of ketamine as an induction agent in head injured patients.

6. The emergence phenomenon

At offset, patients occasionally have vivid hallucinations (The “emergence phenomenon”), which can lead to agitation. A case series of 504 children sedated within the emergency department with ketamine showed that moderate or severe agitation occurred in around 3.8% of cases. In adults, quoted rates vary from 5 to 30%. It is common practice to administer small doses of midazolam to prevent this. A randomised trial showed that this significantly reduced agitation in adults, but one in children found it did not. Midazolam, however, also increase the risk of hypoxia. This is, of course, not a consideration when ketamine is used for induction of anaesthesia, but may be problematic in sedation, and close monitoring of patients is advisable.

7. Comparison with etomidate

Some advocate the use of etomidate in the prehospital modified RSI, and there are some services in which its use is routine. It is reported to be more cardiovascularly stable than thiopentone or propofol, and hence more suitable for induction of anaesthesia in hypovolemic trauma patients. It can also be transported as a ready made solution, rather than requiring reconstitution.

There have been longstanding concerns with the use of etomidate as a sedative in critically ill patients. This is due to adrenal suppression, and has led to ending of use of infusions in intensive care patients. There is evidence that a single dose at induction does worsen outcome in trauma patients, possibly as a result of its effects on the inflammatory response. The CORTICUS study, designed to investigate the use of steroids in critically ill septic patients, reported increased mortality in patients who received etomidate as an induction drug. It may be, however, that the study simply observed that more seriously ill patients are likely to receive etomidate, and so have higher mortality. The KETASED trial compared ketamine directly with etomidate, and showed no difference in efficacy, but a significantly increased rate of adrenocortical suppression in the etomidate group. The study, however, lacked sufficient power to detect differences in mortality or ICU stay length, and did not differentiate between medical patients and trauma patients.

A retrospective study conducted in emergency department patients in the UK found that mortality appeared higher in patients admitted to ICU following administration of etomidate. They noted, however, that etomidate tended to be given to older and sicker patients. When controlled for age and physiological status, etomidate did not appear to be independently associated with mortality.

Although evidence is conflicting, there appears to be evidence that etomidate, even in a single dose, may worsen outcome. There is no such similar evidence for ketamine, although it is much less studied. This would therefore favour greater use of ketamine in clinical practice, and larger studies investigating its use in trauma patients.

8. Neuroprotection

This is a topic which has caused considerable recent debate. Early studies in animal models suggested that ketamine may have a direct neuroprotective role. This was thought to be due to the role of the NMDA pathways in neuronal death. There is also some evidence that ketamine has a role in reducing spreading
depolarisation waves, which are thought to injure the ischaemic brain. The overall hypothesis is that by preventing intrinsic excitation, ketamine may act to reduce secondary brain injury in trauma. All the studies have been conducted using infusions in animals, and so the effectiveness of a single prehospital induction dose is difficult to quantify from them. There has been some preliminary work on the use of NMDA antagonists in brain injured humans, and this has suggested that there may be a beneficial effect. This trial used a number of bolus doses of gacyclidine, a similar NMDA antagonist, over a period of time, and so is not directly comparable. The work does, however, suggest the possibility of benefit, and further studies may shed more light on the mechanisms involved.

9. Conclusion

Ketamine is a versatile drug, which finds several applications in prehospital medicine. It does lack evidence of safety when used for prehospital anaesthesia, however, there is little evidence for the use of any agent in this setting. The widely cited fears about increasing ICP appear to be without solid evidence, and may in fact be the opposite of the truth. We would advocate wider use of ketamine as a prehospital induction agent. We would also advocate larger scale studies, both to confirm its safety, and to assess whether or not administration of ketamine improves outcome in head injured patients.

Conflict of interest statement

The authors are unaware of any actual or potential conflict of interest contained in this paper.

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