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Clinical Notes

Ketamine for prehospital use: new look at an old drug

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Abstract

Introduction: Ketamine has been used extensively for analgesia and anesthesia in many situations, including disaster surgery where extra personnel and advanced monitoring are not available. There are many features of ketamine that seem to make it an ideal drug for prehospital use. The reported use of ketamine in the prehospital environment is limited, however. The purpose of this study is to review the experience in the use of ketamine in a regional air ambulance service and suggest indications for its use in the prehospital setting.

Methods: This was a retrospective study of all patients transported by a regional aeromedical program. Patients were included in this study if the crew had used ketamine at any time during the flight. Data regarding the transport collected included patient age, type of transport, indications for ketamine use, and adverse reactions.

Results: During the period studied, ketamine was used in 40 patients. The age range was 2 months to 75 years. The indications and situations requiring use were varied and included both trauma and medical patients. Hypotension with need for analgesia, agitation or combativeness and intact airway, or pain unresponsive to narcotic medications were the most common indications for use. Ketamine was used both intravenous and intramuscular, even without intravenous access. There were no adverse reactions.

Conclusions: Ketamine is an ideal drug for use in many prehospital situations. Our experience suggests that it is safe, effective, and may be more appropriate than drugs currently used by prehospital providers.

1. Introduction

Ketamine has been used extensively for analgesia and anesthesia in many situations, including disaster surgery where extra personnel and advanced monitoring are not available [1-3]. There are many features of ketamine that seem to make it an ideal drug for prehospital use [4]. It provides effective analgesia and provides amnesia to pain and events. Airway responses are protected; there are minimal cardiovascular effects. Furthermore, it has a rapid onset, short duration, and is titrateable. The reported use of ketamine in the prehospital environment is limited, however [5,6]. The purpose of this study is to review the experience in the use of ketamine in a regional air ambulance service and suggest indications for its use in the prehospital setting.

2. Methods

This was a retrospective study of all patients transported by a regional aeromedical program over the period January 1, 2003 to June 30, 2006. Patients were included in this

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study if the crew had used ketamine at any time during the flight. The program is a regional aeromedical critical care transport service. This program has 1 helicopter in service 24 h/d and a second helicopter availability 12 h/d. The medical crew consists of an attending flight physician and a flight nurse. Data regarding the transport were collected included patient age, type of transport, indications for ketamine use, and adverse reactions.

3. Results

During the period studied, ketamine was used in 40 patients. The age range was 2 months to 75 years. Twenty-three were trauma patients, 4 had burns, 4 were cardiac patients, and 9 were for other medical issues, mostly respiratory. Most patients received only 1 dose of ketamine, but 12 patients needed repeated doses to maintain analgesia during flight. Doses of ketamine ranged from 1 mg/kg IV to 5 mg/kg IM if intravenous (IV) access had not been established. Intramuscular (IM) doses were used for pain control and relief of agitation before extrication in 1 patient because of combativeness and inability to establish IV access in another 3. There were no adverse effects from ketamine use in these patients.

For the burn patients, ketamine was used for pain control and sedation. All had already received large doses of narcotics without relief. For those who had already been intubated, lack of pain control was assessed by significant tachycardia and hypertension, which responded to ketamine analgesia. All had significant relief.

All of the cardiac patients were hypotensive and intubated requiring sedation. One was hypotensive on propofol, and this was stopped. Blood pressure was maintained after ketamine dosing in these patients.

For the other medical patients, most had asthma, and ketamine was used for sedation, if intubated, or as part of a rapid sequence protocol for intubation. In 2 patients, a difficult airway was anticipated, so ketamine was used to maintain the patient's own ventilatory response.

Finally, for the trauma patients, most received ketamine for sedation and analgesia. In 8 patients, ketamine was used for pain control. In 3 of them, ketamine was used for pain control before extrication with or without IV access, the others had significant pelvic or long bone injuries and had no relief of pain with narcotics. Four patients were already hypotensive and, so, ketamine was considered safer than repeated doses of narcotics. As with the cardiac patients, none of these had any drop in their blood pressure after ketamine doses. In 5 patients, ketamine was used as an aid to procedural sedation: 2 with chest tubes, 2 for reduction of fractures before transport, and 1 patient for a lateral canthotomy. Four patients were combative but had intact airways and so ketamine was used for sedation during flight. All maintained airway responsiveness and oxygen saturations.

4. Discussion

Our experience and those of others, suggest that ketamine is a safe and effective drug to be used in the prehospital environment [5,6]. Although ketamine was used infrequently during the study period, our increasing experience and drug safety profile suggest that there are many more cases where it might have been used. The aeromedical crew consists of a physician and nurse, but ketamine can be used safely by nonphysician personnel [6]. There are a variety of situations and conditions for which ketamine may be more appropriate than the current more common field medications, such as narcotics and benzodiazepines.

Ketamine has both analgesic and dissociative properties. Analgesia is dose-related, but the window before the dissociative state is small [7,8]. It has been used perioperatively as an analgesic and "narcotic-sparing" agent, but it is unclear whether the doses used are less than dissociative doses [9-11]. Doses for analgesia are 0.5 to 1.0 mg/kg IM or 0.2 to 0.5 mg/kg IV [4]. In somewhat higher doses, ketamine disconnects the thalamoneocortical and limbic systems, essentially dissociating it from outside stimuli. Thus, painful procedures or tolerance of extreme pain may be superior to that achieved even with large doses of benzodiazepines and opioids. Dissociative states can be induced with 1.0 to 2.0 mg/kg IV or 4 to 5 mg/kg IM. In our experience, we used ketamine in dissociative doses for sedation in the aeromedical setting. In several patients, extreme pain not responsive to large doses of opioids was controlled, or fracture reduction and stabilization were able to be performed. For example, a patient with bilateral displaced femur fractures had these quickly reduced and splinted in the field with one dose of ketamine, rather than repeated and titrating doses of opioids.

One advantage of ketamine is that dissociation is not dose-related [12]. It is either present or absent. This dissociative state has no progressive depth nor level, and additional doses do not enhance or deepen sedation. Thus, adequate sedation can be reliably and safely achieved with one dose or without IV access [12]. There are no reported cases in which IV access averted or would have averted an adverse outcome. IM use has been reported to control of combative patients and in prolonged extrication [13,14]. We used it for sedation in patients with extremely painful long bone injuries before extrication and IV access and for use with combative injured patients.

Ketamine induces the analgesic and dissociative state within 60 seconds after a single IV dose and within 3 to 5 minutes for an IM dose. This sedation lasts approximately 10 to 15 minutes for IV doses and 20 to 30 minutes for IM doses [15]. These kinetics have both advantages and disadvantages for prehospital care. First, the duration of analgesia and anesthesia are long enough for many transports, and so, the patient is not overly sedated or dissociated on arrival in the emergency department and can be

adequately examined by the staff. On the other hand, the duration is short enough that repeated doses may be necessary. It is often difficult to monitor these effects in the intubated patient. Thus, repeated doses or even a continuous infusion in order to avoid undersedation for long transports may be necessary. We rarely required more than 1 dose of ketamine for our transports and achieved adequate analgesia for the entire flight.

Ketamine has been shown to alleviate bronchospastic activity and reduce airway resistance in patients with pulmonary disease [16]. Case reports and series have suggested a beneficial effect of ketamine in airway dynamics of intubated asthmatic patients or in avoiding mechanical ventilation in those with severe asthma, although not all studies show a positive effect [16-18]. Given the safety profile of ketamine and its known effects on bronchospasm, it would seem to be a reasonable alternative for use in sedation of asthmatic patients, if needed. We used ketamine in several patients with asthma during transport. One potential use is for those requiring advanced airway support in which a difficult airway is anticipated. Thus, in these critical ventilatory situations, patients' airway drive and responses are maintained.

There have been concerns about the use of ketamine in the trauma setting or in patients with altered level of consciousness because of the potential for raising intracranial pressure [19-21]. However, subsequent studies have reported that ketamine may have a direct neuroprotective role and may, in patients being ventilated, have superior effects in cerebral circulation [22-24]. It has been suggested that ketamine may indeed be suitable for use in patients with head injury for induction of anesthesia [25]. Because both hypotension and hypoxia contribute to poor outcomes in patients with head injury, and since ketamine has mild sympathomimetic effects on blood pressure and maintains ventilatory drive, use for those with head injuries may be advantageous [26,27]. Our limited experience suggests that ketamine is safe for those with head injuries in the prehospital setting.

Ketamine exerts sympathomimetic effects producing mild increases in blood pressure, heart rate, cardiac output, and myocardial oxygen consumption. Concern has been raised that these increases may not be accompanied by parallel increases in coronary perfusion so that ketamine may provoke ischemia in patients with coronary artery disease [27]. In limited studies, patients undergoing cardiac surgery had hemodyamic stability with ketamine [28]. Ketamine has been safely used for adult procedural sedation even in those with systolic blood pressures as high as 218 mm Hg [29]. We used ketamine in patients with known cardiac disease with relative hypotension. In addition, we found that ketamine had beneficial hemodynamic effects in hypertensive patients in the need for sedation. Although advanced age (and the potential for unknown coronary disease), known cardiac disease, or hypertension may be relative contraindications for the use of ketamine, we would suggest that even in these patients, cardiac instability or the beneficial hemodynamic effects of needed sedation may outweigh these risks.

Ketamine can induce dreaming and hallucinations during recovery, and these effects have traditionally limited its use in adults. However, the number and incidence of these reactions may be lower and less intense than what has been traditionally reported [30]. Furthermore, ketamine appears to have a wide margin of safety. Adverse outcomes have not been reported even with inadvertent overdoses of 5 to 100 times the intended dose [31]. We had no adverse events in our patients regardless of age. Although this is a small sample, this again mirrors the known safety profile of ketamine in a number of settings.

Because of its wide margin of safety, ketamine is used regularly for surgery in the developing world. Ketamine has been used effectively in surgery in disaster and war situations. Patients maintain spontaneous ventilation, and surgeries can be performed with minimal additional personnel and no monitoring equipment [1-3]. In addition, the simplicity and efficacy of its administration make it effective in battlefield and disaster situations where general anesthesia is not available. We suggest that these same effects make it ideal for prehospital use both in the developed and undeveloped world.

4.1. Potential for airway deterioration and need for airway skills

The most common respiratory side effect of ketamine is laryngeal spasm. This is transitory, and patients can be bagged throughout. Patients also have excessive salivation. Vomiting occurs in about 10% of patients [32]. This can be ameliorated with the addition of midazolam. Many of our patients had ketamine and rapids sequence intubation. Short of failed airway, the respiratory complications in this situation are no different than those of failed airways with other situations. Airway responses are maintained, rather, than may be the case in those excessive sedated with narcotics and benzodiazepines.

5. Conclusions

Ketamine is an ideal drug for use in many prehospital situations. Our experience suggests that it is safe, effective, and may be more appropriate than drugs currently used by prehospital providers.

References

[1] Read D, Ashford B. Surgical aspects of operation Bali assist: initial wound surgery on the tarmac and in flight. ANZ J Surg 2004;74:986-91.
[2] Bonanno FG. Ketamine in war/tropical surgery (a final tribute to the racemic mixture). Injury 2002;33:323-7.
[3] Ketcham DW. Where there is no anaesthesiologist: the many uses of ketamine. Trop Doctor 1990;20:163-6.

[4] Wedmore IS, Johnson T, Czarnik J, Hendrix S. Pain management in the wilderness and operational setting. Emerg Med Clin North Am 2005;23:585-601.
[5] Gofrit ON, Leibovici D, Shemer J, Henig A, Shapira SC. Ketamine in the field: the use of ketamine for induction of anaesthesia before intubation in injured patients in the field. Injury 1997;28:41-3.
[6] Porter K. Ketamine in prehospital care. Emerg Med J 2004;21:351-4.
[7] Hocking G, Cousins MJ. Ketamine in chronic pain management: an evidence-based review. Anesth Analg 2003;97:1730-9.
[8] Sadove MS, Shulman M, Hatano S, Fevold N. Analgesic effects of ketamine administered in subdissociative doses. Anaesth Analg 1971; 50:452-7.
[9] Javery KB, Ussery TW, Steger HG, Colclough GW. Comparison of morphine and morphine with ketamine for postoperative analgesia. Can J Anaesth 1996;43:212-5.
[10] Bion JF. Infusion analgesia for acute war injuries: a comparison of pentazocine and ketamine. Anaesthesia 1982;39:560-4.
[11] Stehle R. Anesthesiological care in a field hospital in Thailand with special regard to ketamine. Anaesthesist 1983;32:130-2.
[12] Green SM, Krauss B. Clinical practice guidelines for emergency department ketamine dissociative sedation in children. Ann Emerg Med 2004;460-71.
[13] Roberts JR, Geeting GK. Intramuscular ketamine for the rapid tranquilization of the uncontrollable, violent, and dangerous adult patient. J Trauma 2001;51:1008-10.
[14] Cottingham R, Thomson K. Use of ketamine in prolonged entrapment. J Accid Emerg Med 1994;11:189-91.
[15] Guldner GT, Petinaux B, Clemens P, Foster S, Antoine S. ketamine for procedural sedation and analgesia by nonanesthesiologists in the field: a review for military health care providers. Mil Med 2006; 171:484-90.
[16] Lau TT, Zed PJ. Does ketamine have a role in managing severe exacerbation of asthma in adults. Pharmacotherapy 2001; 21:1100-6.
[17] Denmark TK, Crane HA, Brown L. Ketamine to avoid mechanical ventilation in severe pediatric asthma. J Emerg Med 2006;30:163-6.
[18] Allen JY, Macias CH. Efficacy of ketamine in pediatric emergency department patients who present with acute severe asthma. Ann Emerg Med 2005;46:43-50.
[19] Shapiro HM, Wyte SR, Harris AB. Ketamine anaesthesia in patients with intracranial pathology. Br J Anaesth 1972;44:1200-4.
[20] Schwedler M, Miletich DJ, Albrecht RF. Cerebral blood flow and metabolism following ketamine administration. Can Anaesth Soc J 1982;29:222-6.
[21] Pfenninger E, Grunert A, Bowdler I, Kilian J. The effects of ketamine on ICP during haemorrhage shock under conditions of both spontaneous breathing and controlled ventilation. Acta Neurochir 1985;78:113-8.
[22] Marcoux FX, Goodrich JE, Dominick MA. Ketamine prevents ischaemic neuronal injury. Brain Res 1988;452:329-55.
[23] Albanese J, Arnaud S, Rey M, Thomachot L, Alliez B, Martin C. Ketamine decreases intracranial pressure and electroencephalographic activity in traumatic brain injury patients during propofol sedation. Anesthesiology 1997;87:1328-34.
[24] Hijazi Y, Bodonian C, Bolon M, Salord F, Boulieu R. Pharmacokinetics and haemodynamics of ketamine in intensive care patients with brain or spinal cord injury. Br J Anaesth 2003;90:155-60.
[25] Sehdev RS, Symmons ADA, Kindl K. Ketamine for rapid sequence induction in patients with head injury in the emergency department. Emerg Med Australas 2006;18:37-44.
[26] Chestnut RM, Marshall LF, Klauber MR, Blunt RA, Baldwiin N, Eisenberg HM, et al. The role of secondary brain injury in determining outcome from severe head injury. J Trauma 1993;34:216-22.
[27] Green SM, Li J. Ketamine in adults: what emergency physicians need to know about patient selection and emergence reactions. Acad Emerg Med 2000;7:278-81.
[28] Jackson APF, Dhadphale PR, Callaghan ML, Alseri S. Haemodynamic studies during the induction of anaesthesia for open-heart surgery using diazepam and ketamine. Br J Anaesth 1978;50:375-7.
[29] Chudnofsky CR, Weber JE, Stoyanoff PJ, Colone PD, Wilkerson MD, Hallinen DL, et al. A combination of midazolam and ketamine for procedural sedation and analgesia in adult emergency department patients. Acad Emerg Med 2000;7:228-35.
[30] Green SM, Sherwin TS. Incidence and severity of recovery agitation after ketamine sedation in young adults. Am J Emerg Med 2005;23:142-4.
[31] Green SM, Clark R, Hostetler MA, Cohen M, Carlson D, Rothrock SG. Inadvertent ketamine overdose in children: clinical manifestations and outcome. Ann Emerg Med 1999;34:492-7.
[32] Roback MG, Wathen JE, Bajaj L, Bothner JP. Adverse events associated with procedural sedation and analgesia in a pediatric emergency department: a comparison of common parenteral drugs. Acad Emerg Med 2005;12:508-13.