Mashhad University of Medical Sciences (MUMS)

Reviews in Clinical Medicine

Clinical Research Development Center Ghaem Hospital

Comparison between intravenous and intramuscular administration of ketamine in children sedation referred to emergency department

Behnaz Boroumand Rezazadeh(MD)[1], Mohammad Gharavifard(MD)[2], Hamid Zamani Moghadam (MD)[1*], Behrang Rezvani(MD)[1]

[1]*Department of Emergency Medicine, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[2]*Department of Anesthesiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

ARTICLE INFO

Article type
Review article

Article history
Received: 23 Apr 2014
Revised: 1 May 2014
Accepted: 3 May 2014

Keywords
Intramuscular
Intravenous
Ketamine
Pediatric sedation
Procedural sedation

ABSTRACT

Ketamine, among wide variety of sedative drugs, has shown beneficial effects when using during the procedural sedation, specifically in pediatrics. Various parameters should be considered in order to perform a safe and effective procedural sedation including optimum dosage of the sedative, administration methods of sedation, and need for applying any adjuvant drug. In this study, we aimed to review the studies, which have compared the efficacy of the different ways of the injection of ketamine such as intravenous or intramuscular ketamine application. Based on data obtained from the related articles, efficacy and safety of these two methods of ketamine usage in the pediatric procedural sedation were widely similar, but the intravenously administration of the ketamine can be proposed as the preferable mode.

Please cite this paper as:
Boroumand Rezazadeh B, Gharavifard M, Zamani Moghadam H, Rezvani B.Comparison between intravenous and intramuscular administration of ketamine in children sedation referred to emergency department. Rev Clin Med. 2015;2(1):1-4.

Introduction

Ketamine is one of the prominent members of the arylcyclohexylamines class of the anesthetic drugs, which acts through a broad range of chemical mechanisms. For over 50 years, ketamine has been applied in different kinds of therapeutic techniques conducted on either human or animals as a chemical agent. In human, it is mostly used as a sedative and analgesic chronic agent especially for emergency procedural sedation in children. The application of the ketamine for procedural sedation results in cognitive impairment and sensory deprivation. Ketamine puts its effects by severing the connections between thalamo-neocortical and limbic systems (1).

In addition to its major role as an anesthetic drug, its low doses would result in acute antidepressant effects in patients with treatment-resistant depression and can be administrated intravenously or intramuscularly (2).

Various adverse effects have been reported by using chronic and higher doses of ketamine or its administration in therapeutic targets including dysphoria, hallucinations, disorientation, nightmares, urological symptoms, and bladder damage (3).

Intravenous (IV) and intramuscular (IM) injection of ketamine are two methods of ketamine administration in pediatric procedural sedation and analgesia with significant acceptance in emer-

***Corresponding author:** Hamid Zamani Moghadam.
Department of Emergency Medicine, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
***E-mail:** zamanimh@mums.ac.ir*
***Tel:** 09155811238*

gency departments. Intravenous injection is the most favorable application method. Due to various adverse effects of ketamine, it is necessary to evaluate the safety and efficacy of the IV or IM application routes of the ketamine to identify the best way of its administration. In this study, we briefly reviewed various randomized clinical trials to evaluate different aspects of delivering ketamine, intravenously or intramuscularly, in pediatrics. We searched Medline for the related randomized control trials regarding the efficacy of ketamine administration (IV or IM) in procedural sedation in pediatrics.

Literature review

Based on our search results, although there were different kinds of articles regarding the application of the ketamine in procedural sedation, only six randomized control trials could be used for comparing two desired methods of the ketamine administration including intravenous (IV) or intramuscular (IM) (4-9). Among these six articles related to our review, only one article specifically compared IV and IM ketamine in pediatric procedural sedation (4).

According to the results of the mentioned study, there was substantial difference regarding the vomiting during and after the recovery time, which was more prevalent in IM group. In addition, they reported lower rate of observed distress and pain during the emergency process, and longer sedation duration in patients under the IM ketamine. They concluded that regardless of the method of the ketamine injection and its administrated dosage, emesis would occur during the recovery time or after that. The effect of the different doses of ketamine on the obtained results was not considered in the mentioned article (4). The shorter recovery time observed in pediatric with intravenous ketamine sedation in the mentioned article, has been confirmed in other studies such as the one performed by Ramaswamy et al. which was almost 42 minutes longer during pediatric intramuscular ketamine administration (10).

Another randomized control trial resulted longer recovery time by IV administration of ketamine/midazolam compared with IV propofol/fentanyl. Similar results were obtained regarding the application of combination of sedatives on decreasing the patient pain and distress during the emergency procedure and using IV ketamine plus midazolam facilitated performing painless minor procedures in pediatrics in comparison with applying intranasal midazolam (6). Similar results were indicated through comparing the sedation efficacy of pediatric IV ketamine injection with adding midazolam, which was performed by Wathen et al. (7). The combination of the ketamine and midazolam in pediatrics resulted in greater sedation efficacy, lower pain, and observed distress compared to using the combination of fentanyl and midazolam (9).

Based on the clinical randomized trials we studied in this review, emesis accounted for the highest rate of the observed adverse effects mostly through IM ketamine sedation. Vomiting was the only post-operative side effect of the pediatric IM ketamine sedation and no other adverse effect was identified in the study of Holloway et al. (11).

According to the meta-analysis of Green et al. administrating high IV doses of the ketamine (initial dose≥2.5mg/kg and a total dose 5mg/kg), the IM method of ketamine injection and the increasing age can be proposed as the predictors of the emesis. The peak age is 12 years old. It was also concluded in their study that a low level of IM ketamine and high doses of the IV ketamine might result in patients' recovery agitation (12).

Different adverse effects can occur by combining ketamine with other drugs, for example, the occurrence of oxygen desaturation more frequent when midazolam was added to IV ketamine than applying ketamine alone (7). It has been proposed that adjunctive midazolam did not have any beneficial effects on diminishing the side effects of the pediatric ketamine sedation (8). Detailed data of these trials are summarized in Table 1.

There was different articles regarding the efficacy of ketamine administration in pediatric procedural sedation, which were mainly about orthopedic procedures. Based on the mentioned articles in this review, several parameters should be considered while comparing IV vs. IM ketamine such as different adverse effects, patient age, severity of the required procedures, the administrated sedative dosage, application of the adjuvant drug for reducing the risk of adverse effects and various influential parameters. There was only one randomized control trial, which directly compared the pediatric IV ketamine sedation with IM ketamine that was conducted by Roback et al. in 2006 (4). The optimum and adequate dosage (the minimum required dose) of the ketamine in each injection method (IV and IM) was proposed as following: 4-5 mg/kg for IM (13), 1.5 mg/kg as the loading dose in IV (8,14).

Midazolam was used in some randomized control trials as an adjuvant drug to reduce the possible adverse effects of the ketamine alone and resulted in longer recovery time (5,6,9).

Conclusion

Ketamine is a safe, effective, and well-tolerated

Table 1. Detailed information about the randomized clinical trials regarding the intravenous (IV) or intramuscular (IM) ketamine

Author Year Reference	Intervention	Recovery time	Complication	Result
Roback 2006 (4)	Children 7 years median -IV*(116 patients):1 mg/kg -IM** (106 patients):4 mg/kg Glycopyrrolate for both groups:5 mg/kg	IM:129 minutes IV:80 minutes	Emesis:Odds ratio (OR) 2.6 95% CI:1.2–5.9 Desaturation:OR 0.47	The 4 mg/kg IM ketamine was more effective in pediatrics sedation than 1 mg/kg IV ketamine
Godambe 2003 (5)	Children 3.1 years median -IV (54 patients):Ketamine (1–2 mg/kg)+midazolam (0.05mg/kg)	Median 54 minutes	Emesis 4% Desaturation 7% Dysphoric reaction 3/54 (5%)	Midazolam resulted in reducing the adverse effects of the ketamine
Acworth 2001 (6)	Children 4.6 years median -IV (26 patients):Ketamine (1mg/kg)+midazolam (0.5-1 mg/kg)	Mean 97.9 minutes	Emesis 15% Desaturation 3.8% Excessive Salivation 3.8%	Midazolam resulted in reducing the adverse effects of the ketamine
Wathen 2000 (7)	Children 6.8 years median -IV (137 patients): Ketamine (1mg/kg)+midazolam (1mg/kg) -IV (129 patients): ketamine(1mg/kg)	-Ketamine+midazolam:75 minutes -Ketamin:78 minutes	Emesis: Ketamin:19.4% Ketamine+Midazolam:9.6% Desaturation: 1.6% in ketamine 7.3% in ketamine+midazolam	Oxygen desaturation was more frequent in the group of ketamine plus midazolam
Sherwin 2000 (8)	Children 6 years old -IV(104 patients):ketamine (1 mg/kg)+midazolam (0.05-2mg/kg) -IV(53 patients):Ketamine1mg/kg+midazolam (0.05-2mg/kg) IV(51 patients):Ketamin(1mg/kg)+placebo	Ketamine 64 minutes -Ketamine+Midazolam:61 minutes	Emesis: Ketamin:12%, Ketamine+midazolam:2%	No considerable benefit in recovery agitation of midazolam added to ketamine
Kennedy 1989 (9)	-IV(130 patients):Ketamine (1.76 mg/kg)+midazolam (0.07mg/kg)	127.6 minutes	Emesis 9% during recovery, 12% home Hypoxia 6%	Lower pain and distress in ketamine+midazolam group

*IV: Intravenous; **IM: Intramuscular

drug that can be used in pediatric procedural sedation. According to the studied literature both of the ketamine administration methods (IV and IM) have been effective in creation of the safe procedural sedation in children. Based on the conducted studies, IV can be proposed as the more preferred method for ketamine delivery due to lower recovery time and side effects. In situations facing difficulties and stress in inserting the IV access for children, it is preferred to apply IM method.

Acknowledgement

We would like to thank Clinical Research Development Center of Ghaem Hospital for their assistant in this manuscript. This study was supported by a grant from the Vice Chancellor for Research of the Mashhad University of Medical Sciences for the research project as a medical student thesis with approval number of 910384.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Badina L, Norbedo S, Barbi E. Procedural sedation and analgesia in children. Lancet. 2006;367:1900-1901.
2. Chilukuri H, Reddy NP, Pathapati RM, et al. Acute antidepressant effects of intramuscular versus intravenous ketamine. Indian J Psychol Med. 2014;36:71.
3. Godwin SA, Caro DA, Wolf SJ, et al. Clinical policy: procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2005;45:177-196.
4. Roback MG, Wathen JE, MacKenzie T, et al. A randomized, controlled trial of i.v. versus i.m. ketamine for sedation of pediatric patients receiving emergency department orthopedic procedures. Ann Emerg Med. 2006;48:605-612.
5. Godambe SA, Elliot V, Matheny D, et al. Comparison of propofol/fentanyl versus ketamine/midazolam for brief orthopedic procedural sedation in a pediatric emergency department. Pediatrics. 2003;112:116-123.
6. Acworth J, Purdie D, Clark R. Intravenous ketamine plus midazolam is superior to intranasal midazolam for emergency paediatric procedural sedation. Emerg Med J. 2001;18:39-45.

7. Wathen JE, Roback MG, Mackenzie T, et al. Does midazolam alter the clinical effects of intravenous ketamine sedation in children? A double-blind, randomized, controlled, emergency department trial. Ann Emerg Med. 2000;36:579-588.
8. Sherwin TS, Green SM, Khan A, et al. Does adjunctive midazolam reduce recovery agitation after ketamine sedation for pediatric procedures? A randomized, double-blind, placebo-controlled trial. Ann Emerg Med. 2000;35:229-238.
9. Kennedy RM, Porter FL, Miller JP, et al. Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies. Pediatrics. 1998;102:956-963.
10. Ramaswamy P, Babl FE, Deasy C, et al. Pediatric procedural sedation with ketamine: time to discharge after intramuscular versus intravenous administration. Acad Emerg Med. 2009;16:101-107.
11. Holloway VJ, Husain HM, Saetta JP, et al. Accident and emergency department led implementation of ketamine sedation in paediatric practice and parental response. J Accid Emerg Med. 2000;17:25-28.
12. Green SM, Roback MG, Krauss B, et al. Predictors of emesis and recovery agitation with emergency department ketamine sedation: an individual-patient data meta-analysis of 8,282 children. Ann Emerg Med. 2009;54:171-80.
13. Green SM, Hummel CB, Wittlake WA, et al. What is the optimal dose of intramuscular ketamine for pediatric sedation? Acad Emerg Med. 1999;6:21-26.
14. Dachs RJ, Innes GM. Intravenous ketamine sedation of pediatric patients in the emergency department. Ann Emerg Med. 1997;29:146-150.