Single Dose versus Weight Based Dose Intra Nasal Ketamine for ED Management of Acute Musculoskeletal Pain

Sara Payami1, Mohammad Taghi Talebian2, Ali Ardalan3, Reza Shariat Moharari4, Fateme Hojati5 and Amir Nejati2

1Emergency Department, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
2Emergency Department & Hospital and Pre-Hospital Emergencies Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
3Department of Disaster and Emergency Health, National Institute of Health Research, and Department of Disaster Public Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
4Anesthesiology Department, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
5Physical Medicine and Rehabilitation Department, Shohada Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Background: Ketamine has been used widely in emergency departments for different procedures, prescribed only as a single dose or dose per weight. We compared single dose of ketamine with dose per weight ketamine for procedures done in cases with acute musculoskeletal pain.

Methods: This randomized double blind clinical trial, was conducted in the emergency department of Imam Khomeini Hospital during March and June 2012. Patients with traumatic or non-traumatic musculoskeletal pain with numeric rating scale (NRS) ≥ 4 were enrolled. Patients were divided to Weight groups and for each group 4 syringes with the same shape were considered. BP, PR, RR, O2 sat, level of consciousness and all complications were checked for the patients in minutes 20 and 30. First group received 50 mg and second group received 0.75 mg/kg intranasal ketamine.

Results: Out of 136 patients enrolled in this study, 27 cases were excluded. Patients were divided to two groups of 60 (dose per kg) and 59 (single dose) persons. The most type of injuries were fractures (37.8%) followed by lacerations (26%). O 2 sat, HR, systolic and diastolic BP and Mean NRSs before and after procedures were not significantly different in the two groups. Mean NRS reduction was not significant between two groups (comparing NRS at baseline with NRS at minutes 30, 40 and 60).

Discussion: Our study showed that 50 mg single dose of ketamine is the same as the 0.75 mg/kg dose per weight for reducing pain in cases with traumatic and non-traumatic musculoskeletal injuries.

Keywords: Ketamine; Intranasal; Acute pain; Emergency medicine; Dosage

Introduction

Pain is the most common complaint of patients referred to emergency departments (ED) [1], but there is no defined protocol for pain management in most EDs. Previous studies showed that near 70% of cases with acute pain who were referred to EDs were under treated with pain reducing medications [2-4]. Several causes include: inappropriate report, poor communication between patients and healthcare providers, inadequate education of providers and lack of proper protocols [1]. Acute pain is characterized by recent onset and limited duration and has a relationship with injury or disease.

Most patients referred to ED with acute pain are patients with musculoskeletal problems. The majority of fractures and dislocations are reduced in EDs and different medications are used for pain management in such cases [5]. Ketamine is N-methyl-D-aspartate (NMDA) receptor antagonist which has sedative, analgesic, and amnestic effects [6,7]. Due to its ability to pass across the blood-brain barrier ketamine can block pain perception and peripheral pain signaling [8]. In recent years, ketamine has been used widely in emergency departments for different procedures done in EDs [7,9-11].

In most previous studies, ketamine was prescribed only as a single dose or dose per weight, and there is no study comparing single versus dose per weight simultaneously. Administration of single dose ketamine is easier and faster and needs no information regarding weight. So, in this study we compared 50 mg intranasal ketamine with 0.75 mg/kg for procedures performed in cases with acute musculoskeletal pain.
Informed consent was obtained from all enrolled patients. The study had been approved by local ethics committee also known as Iranian Registry of Clinical Trials (IRCT). Randomization was performed by an expert technician. The assignment was conducted by means of block randomization (aabb). Patients who referred to ED in the shifts of responsible resident were enrolled. Weight was measured for each case. Weight groups considered as weight intervals of 5 (45-100 kg, while considering weight less than 45 as 45 and weight more than 100 as 100). For each group 4 syringes (two containing 50 mg and 2 containing 0.75 mg/kg) of ketamine were considered. All syringes were the same in shape, color and volume. A blinded technician assigned cases in each weight group into two groups, first group received 50 mg ketamine intranasal and second group received 0.75 mg/kg intranasal ketamine. Before administration of the content of the syringes, an expert nurse assessed blood pressure, heart rate, O₂ saturation (by means of pulse oximetry), NRS and patient’s weight and recorded them. Then the resident who was blind (to the content of syringes) picked up one syringe ad dropped the content into one of the patient's nasal cavity.

NRS recorded for all cases 10, 20, 30, 40 and 60 minutes after application of the content of syringes. If NRS was more than 4 and the patient needed analgesic, 0.04 mg/kg morphine was intravenously injected.

BP, PR, RR, O2SAT, level of consciousness and all complications were checked for the patients in minutes 20 and 30.

All patients were under observation for one hour and complications were recorded. SPSS version 18 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Data was shown in mean ± SD. Independent sample t test and paired sample t test applied for continuous, as well as the Pearson X² test and the Chi-square test for categorical variables. P-value < 0.05 was considered statistically significant (Table 1).

Results

One hundred and thirty six patients were enrolled in this study. Twenty seven cases were excluded due to exclusion criteria (12 due to opioid consumption, 5 due to head trauma, 4 because of poor HTN control, 3 unstable hemo-dynamically, 1 due to recent nasopharyngeal surgery, and 2 due to language barrier). At the end, 119 cases were enrolled. Sixty patients evaluated in group 1 (dose per kg) and 59 evaluated in group 2 (single dose). Mean age and weight were not significantly different in two groups (Table 2).

The most type of injuries were fractures (37.8%) followed by lacerations (26%). Upper extremity (60%) was the most common site of injury in both groups of patients. O₂ saturation, heart rate, systolic and diastolic blood pressures before and after procedures were not significantly different in the two groups (Tables 2-4).

Mean NRSs were nor significantly different during evaluation time (Table 3 and 5).

Repeated measure ANOVA showed that mean NRS was significantly different in different times in both groups (p value <0.001). Mean NRS reduction was not significant between two groups (comparing NRS at baseline with NRS at minutes 30, 40 and 60). Mean NRS in different time in different weight groups were not significantly different. The most complication reported in each group was nausea (Table 6).

Discussion

| Weight | Dose of ketamine | Weight | Dose of ketamine |
|--------|------------------|--------|------------------|
| Less than 45kg | 31 | 75 kg | 56 |
| 45 kg | 34 | 80 kg | 60 |
| 50 kg | 38 | 85 kg | 64 |
| 55 kg | 41 | 90 kg | 68 |
| 60 kg | 45 | 95 kg | 71 |
| 65kg | 49 | 100 kg | 75 |
| 70 kg | 53 | More than 100 kg | 75 |

Table 1: Dose of ketamine in each weight group.

| Group 1 | Group2 | P value |
|---------|--------|---------|
| Age     | 35.8 ± 15.7 | 38.7 ± 17.2 | 0.3 |
| Weight  | 73.8 ± 14.1 | 75.8 ± 15 | 0.4 |
| Sex     | 46 | 54 | 0.02 |

Table 2: Demographic characteristics of patients in each group.

| Group 1 | Group2 | P value |
|---------|--------|---------|
| O₂ saturation before procedure | 97.7 ± 1.3 | 97.7 ± 1.2 | 0.9 |
| Systolic blood pressure before procedure | 130 ± 14.7 | 134 ± 13.7 | 0.1 |
| Diastolic blood pressure before procedure | 76.1 ± 9.7 | 78.7 ± 10.3 | 0.1 |
| Heart rate | 78.7 ± 9.9 | 80.4 ± 8.7 | 0.3 |

Table 3: O₂ saturation, heart rate, systolic and diastolic blood pressures before nasal ketamine application.

| Group 1 | Group2 | P value |
|---------|--------|---------|
| O₂ saturation after 20 minutes | 97.7 ± 1.3 | 97.7 ± 1.2 | 0.9 |
| Systolic blood pressure after 20 minutes | 129.6 ± 14.1 | 133.3 ± 12.8 | 0.1 |
| Diastolic blood pressure after 20 minutes | 75.2 ± 8.9 | 76.7 ± 9.7 | 0.3 |
| Heart rate | 77 ± 8.2 | 77.1 ± 7.3 | 0.9 |
| O₂ saturation after 30 minutes | 97.7 ± 1.3 | 97.7 ± 1.3 | 1 |
| Systolic blood pressure after 30 minutes | 127.1 ± 12.1 | 130.6 ± 12.4 | 0.1 |
| Diastolic blood pressure after 30 minutes | 74.1 ± 8.1 | 76.1 ± 9.4 | 0.2 |
| Heart rate | 74 ± 7 | 72.8 ± 10.8 | 0.4 |

Table 4: O₂ saturation, heart rate, systolic and diastolic blood pressures after nasal ketamine application.
Ketamine is useful for neuropathic pain control [17,18]. Nowadays it has peripheral pain. Lynch et al. and Gammaitoni et al. discovered that peripheral receptors of glutamate and acts as analgesic for controlling which has sedative, analgesic, and amnestic effects [6,7]. It also blocks ketamine could be considered as a safe drug for pain reduction.

As the adverse effects of ketamine are transient and self-limited, we recommend bigger studies with no significant difference in demographic parameters between study and control groups to be directed in future to recheck these results.

Another limitation in this study is the significant difference in gender spread between 2 groups of study. So we recommend bigger studies with no significant difference in demographic parameters between study and control groups to be directed in future to recheck these results.

References

1. Stalnikowicz R, Mahamid R, Kaspi S, Brezis M (2005) Undertreatment of acute pain in the emergency department: a challenge. Int J Qual Health Care 17:173-176.

2. Lewis LM, Lasater LC, Brooks CB (1994) Are emergency physicians too stingy with analgesics? South Med J 87:7-9.

3. Selbst SM, Clark M (1990) Analgesic use in the emergency department. Ann Emerg Med 19: 1010-1013.

4. Wendel TD (2001) Risk factors for opioid analgesia in US emergency departments. Academic Emergency Medicine 8:427.

5. Cevik E, Bilgic S, Klic E, Cinar O, Hasman H, et al. (2013) Comparison of ketamine-low-dose midozolam with midazolam-fentanyl for orthopedic emergencies: a double-blind randomized trial. Am J Emerg Med 31: 108-113.

6. Erhan OL, Gökksu H, Alpay C, BeA/YaA Y A (2007) Ketamine in post-tonsillectomy pain. Int J Pediatr Otorhinolaryngol 71: 735-739.

7. Nejati A, Moharari RS, Ashraf H, Labaf A, Golshani K (2011) Ketamine/Propofol Versus Midazolam/Fentanyl for Procedural Sedation and Analgesia in the Emergency Department: A Randomized, Prospective, Double-Blind Trial. Acad Emerg Med 18: 800-806.

8. Carlton SM (2001) Peripheral excitatory amino acids. Curr Opin Pharmacol 1: 52-56.

9. Nejati A, Golshani K, Moradi Lakeh M, Khashayar P, Moharari RS (2010) Ketamine improves nasogastric tube insertion. Emerg Med J 27: 582-586.

10. Jamal SM, Fathil SM, Nidzwani MM, Ismail AK, Yatim FM (2011) Intravenous ketamine is as effective as midazolam/fentanyl for procedural sedation and analgesia in the emergency department. Med J Malaysia 66: 231-233.

11. Luhmann JD, Schootman M, Luhmann SJ, Kennedy RM (2006) A randomized, prospective, double-blind trial. Acad Emerg Med 13: 600-606.

12. Andolfatto G, Willman E, Joo D, Miller P, Wong WB, et al. (2013) Intranasal ketamine for analgesia in the emergency department: a prospective observational series. Acad Emerg Med 20: 1050-1054.

13. Eghbal MH, Taregh S, Amin A, Sahmeddini M (2013) Ketamine improves postoperative pain and emergence agitation following adenotonsillectomy in children. Randomized clinical trial. Middle East J Anesthesiol 22: 155-160.

14. Borner M, Bürkle H, Trojan S, Horoshun G, Riewendt HD, et al. (2007) Intranasal ketamine after arthroscopic knee surgery. Optimisation of postoperative analgesia. Anaesthesia 56: 1120-1127.
16. McCarty EC, Mencio GA, Walker LA, Green NE (2000) Ketamine sedation for the reduction of children's fractures in the emergency department. J Bone Joint Surg Am 82-82A: 912-8.

17. Gammaitoni A, Gallagher RM, Welz-Bosna M (2000) Topical ketamine gel: possible role in treating neuropathic pain. Pain Med 1: 97-100.

18. Lynch ME, Clark AJ, Sawynok J, Sullivan MJ (2005) Topical amitriptyline and ketamine in neuropathic pain syndromes: an open-label study. J Pain 6: 644-649.