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

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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, O_2 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 health care 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.

Material and Methods

This randomized double blinded clinical trial was conducted in the emergency department of Imam Khomeini Hospital between March and June 2012. Imam hospital complex is a referral hospital in Tehran (capital of Iran) consisting of a cancer institute, Valiasr hospital and Imam Hospital. It is a large teaching hospital of Iran which has helicopter landing place for transferring traumatic cases. The emergency department of this complex has 46 beds in wards I and II and 24 in ward III. Twelve professors and 69 residents work in these three wards. Traumatized patients constitute near 25% of all referred cases. Patients who were referred to the hospital due to traumatic or non-traumatic musculoskeletal pain with numeric pain rating scale (NRS) ≥ 4 were enrolled. Exclusion criteria were: age less than 15, unable to express their pain (Altered Mental State, language Barrier), un-controlled HTN (SBP>180, DBP>110), decompensated or severe symptomatic heart failure, acute coronary syndrome, pregnant women, opioid consumption in the last 24 hours, allergy to ketamine, abnormal airway anatomy, head trauma, recent nasopharyngeal surgery, nose deformity or fracture, head, cervical, thoracic or abdominal pain, increased intra

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cranial or intra orbital pressure.

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, O_2 saturation (by means of pulse oxymetry), 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 with Fisher's exact test used for assessment of 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 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. O_2 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.

	Group1	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 Male female	 46 14	 54 5	 0.02

Table 2: Demographic characteristics of patients in each group.

	Group 1	Group2	P value
O_2 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: O_2 saturation, heart rate, systolic and diastolic blood pressures before nasal ketamine application.

	Group 1	Group2	P value
O_2 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
O_2 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 Systolic blood pressure after 30 minutes	74 ± 7	72.8 ± 10.8	0.4

Table 4: O_2 saturation, heart rate, systolic and diastolic blood pressures after nasal ketamine application

The result of the current study showed that single dose of ketamine is the same as the dose per weight for reducing pain in cases with traumatic or non-traumatic musculoskeletal injuries. The result showed that mean NRS scores were not significantly different between two groups during evaluation. We also found that the need for morphine consumption was not significantly different between two groups. In previous studies, single dose of ketamine or dose per weight was only evaluated separately and we could not find any study evaluating single dose or dose per weight simultaneously. In our previous study, cases who were candidate for nasogastric tube insertion randomly received 50 mg intranasal ketamine or placebo.

The result showed that mean VAS score was significantly higher

	Group 1	Group2	P value
NRS before procedure	7.8 ± 1.5	7.5 ± 1.5	0.2
NRS 10 minutes after procedure	6.7 ± 1.8	6.2 ± 2	0.2
NRS 20 minutes after procedure	5.2 ± 1.2	4.7 ± 1.9	0.1
NRS 30 minutes after procedure	4.6 ± 1.8	4.4 ± 1.9	0.4
NRS 40 minutes after procedure	4.7 ± 1.8	4.4 ± 1.9	0.3
NRS 60 minutes after procedure	5 ± 2	4.4 ± 2	0.1

Table 5: Mean NRS in each group in different times.

	Group 1	Group2	P value
Nausea	4	4	0.6
Cough	2	1	
Vertigo	1	2	

Table 6: Complications of the drug in each group.

in placebo group than the other group [10]. Andolfatto et al used 0.5-0.75 mg/kg intranasal ketamine for patients with orthopedic injuries and investigated that pain score reduced significantly (13 mm) in 88% [12]. Eghbal et al. randomly assigned children who were candidates for tonsillectomy to receive 0.25 mg/kg ketamine or placebo. They investigated that pain score, agitation rate and paracetamol use was significantly lower in the ketamine group than the control group [13].

These findings could show that as brain weight is nearly similar in all patients, single dose of analgesic drugs could be as effective as dose per weight in patients while single dose regimen does not need weighting. The amount of analgesic needed was similar in the current study which could mean that single dose of ketamine is similar as dose per weight for pain control in cases with orthopedic injuries. This is different from Eghbal et al., Borner et al. and Erhan et al. findings who found that analgesic need is significantly lower in the ketamine group than the control group [6,13,14]. As our study lack control group, we were unable to compare results with the control group.

Blood pressure, O_2 saturation and heart rate were similar in both groups after ketamine use which is compatible with our previous findings [10]. We evaluated single versus dose per weight of ketamine and found that these two routs of ketamine are the same. We also found that the most pain reduction was in 30 and 40 minutes after drug application but it seems that pain control was more constant in single dose group. We also investigated that nausea followed by vertigo were the most common complications of ketamine use in both groups. In our previous experience nausea and vomiting were the most complications of intranasal ketamine [10]. Newton and Fitton applied 0.5-1 mg/kg intravenous ketamine in emergency department and reported recovery agitation as the most common adverse effect [15]. Mccarty et al. randomly assigned 114 children who referred to ED for reduction to receive 2 or 4 mg/kg ketamine before procedure. Their result demonstrated nausea and emesis as the most prevalent complications [16]. As the adverse effects of ketamine are transient and self-limited, ketamine could be considered as a safe drug for pain reduction.

Ketamine is N-methyl-D-aspartate (NMDA) receptor antagonist which has sedative, analgesic, and amnestic effects [6,7]. It also blocks peripheral receptors of glutamate and acts as analgesic for controlling peripheral pain. Lynch et al. and Gammaitoni et al. discovered that ketamine is useful for neuropathic pain control [17,18]. Nowadays it has become routine in ED but is not widely used. More studies with large sample sizes for different groups of patients are recommended. Our study was a single center study and only patients with musculoskeletal injuries were evaluated. Multi centric studies with larger sample sizes are recommended.

Limitations

According to exclusion criteria, the total number of patients enrolled in this study was 109 patients with 60 indivisuals in dose per weight group and 59 in single dose group. So we had a small control group as one of the limitations in this study.

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.

Conclusion

Single dose ketamine (50 mg) is as effective as 0.75 mg/kg ketamine for pain control in patients with musculoskeletal pain who referred to emergency department.

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