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Research Article

Comparison of Different Ketofol Procedural Sedation and Analgesic Doses during Orthopedic Procedures in Patients Referred to the Emergency Department: A Double-Blind Randomized Clinical Trial

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Abstract

Background: Orthopedic procedures are one of the most common medical procedures in the emergency department (ED) and are also among the most painful procedures performed on the conscious patient. This study aimed to compare different doses of ketofol in procedural sedation and analgesia (PSA) in patients referred to the EDs.

Methods: In this double-blinded clinical trial, 296 patients aged 18 years or over who presented with the need for orthopedic procedures in the three academic EDs in 2020 were studied. After completing the written consent, the patients were randomly assigned to four treatment groups. Demographic information, underlying diseases, patients' physical condition, type of orthopedic injuries requiring intervention, and patients' vital signs were recorded in a checklist for each patient.

Results: In this study, the mean age, gender, level of education, addiction, patients' physical condition, type of procedures performed, apnea, hypoventilation, bradycardia, hypotension, and agitation in all four treatment groups were not statistically different, but hallucination and hypoxia in group C (propofol 1 mg/kg plus ketamine 0.33 mg/kg) were much less than other groups; thus, oxygen administration was more common in other groups.

Conclusion: By testing different doses of ketamine, we concluded that doses of 1 mg and 0.5 mg were associated with more side effects. A dose of 0.33 mg of ketamine has fewer side effects while causing analgesia and sedation as in the above doses. A dose of 0.25 mg of ketamine increases the likelihood of requiring subsequent doses. Therefore, it seems that 0.33 mg of ketamine is the best dose of choice.

Keywords: Orthopedic Procedures; Ketamine; Propofol; Analgesia; Pain Intensity

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Background

The International Pain Association defines pain as a sensory experience and unpleasant emotion accompanied by acute or potential tissue degeneration or damage. Uncontrolled acute pain causes the development of negative physiological responses, including increased metabolism, oxygen uptake, coagulability, and altered immune system function. Thus, adequate pain control is essential for emergency procedures (1). Unfortunately, despite scientific advances in pain pathophysiology, pharmacology of analgesics, and the development of practical techniques for pain treatment, patients hospitalized in the emergency department (ED), especially those who undergo orthopedic procedures, still experience displeasing pains (2, 3). Considering the dire need for emergency interventions in the EDs, use of sedative and analgesic drugs in emergency procedures is progressively increasing. However, many studies suggest that the extent of pain management is not adequate in the EDs (3-5). One of the reasons for failure in pain control in the ED is the ED personnel's unawareness or negligence on pain level and suitable methods for developing analgesia to perform therapeutic processes (6, 7). Presently, in most cases, to build sedation and analgesia, combinations of benzodiazepines and opioid drugs are used.

Benzodiazepines have anesthetic, anxiolytic, and sedative effects. Opioids, on the other hand, have potent analgesic effects and can enhance the drowsiness and forgetfulness effects of benzodiazepines. New combination drugs, including propofol with ketamine, are used to replace the previous regimen (1, 2, 4). Propofol is the most common intravenous (IV) anesthetic drug, whose onset of action and elimination rate are fast (1, 8). At therapeutic doses, it has a moderate respiratory depression effect, and its resulting apnea depends on the dose and rate of injection and the accompanying drug (8, 9). Among the positive effects of propofol are its bronchodilating effects, reduction of the extent of vasoconstriction of pulmonary vessels resulting from hypoxia (10), and 30-50 percent reduction in intracranial pressure (ICP). Moreover, one of its unique effects is anti-emetic effects, which develop at concentrations below its sedating dose (2). Some unwanted complications of propofol are pain at injection site, myoclonus, apnea, hypotension, and thrombophlebitis. Known or possible

sensitivity to soybean or egg is an absolute contraindication to propofol injection (1, 9).

Ketamine is a phencyclidine derivative that is unique from other hypnotic medications. Ketamine causes the development of hypnosis and dissociative analgesia. This medication is used for induction and maintenance of anesthesia (1, 2). Among the advantages of using ketamine is its minor effect on respiration, keeping the autonomous reflexes, and developing analgesia at blood levels lower than the dose required for anesthesia (2, 11, 12). The extent of sedative and analgesic effects of the combination of ketamine and propofol (ketofol) was first examined in 1993 on animals (13).

Tomoda et al. showed that a low ketamine dose could cause further sensitivity of the thalamus, causing arousal leading to interference with the sedative effect of propofol. This is due to the opposing effect of ketamine and the net inhibitory effect of propofol (13). Goh et al. indicated that ketofol better preserved hemodynamic conditions and reduced the risk of apnea (14). Akin et al. concluded that adding low-dose ketamine to propofol better kept the average arterial pressure and reduced the risk of respiratory complications and the need for medical interventions (15, 16).

Willman and Andolfatto examined 114 patients undergoing primary orthopedic procedures and receiving different ketofol doses (0.75 mg/kg ketamine and 0.75 mg/kg propofol on average with dose ranges of 0.20-2.05 mg/kg). They concluded that ketofol developed potent sedation, analgesia, and amnesia together with a short duration of action. It also provided patients with stable hemodynamics and favorable respiratory conditions (17). Andolfatto and Willman found that ketofol was very effective in operations requiring sedation and analgesia in children. Short recovery time and very few untoward effects were other results of this study (18).

Andolfatto et al. compared the analgesia in 284 patients in the ED undergoing painful procedures in the ketofol and propofol groups. Based on that, respiratory complications had no significant difference, but the depth of sedation was greater in the ketofol group. In Andolfatto et al.'s study, no significant difference was observed in the induction time, effectiveness, and sedation time across the two groups (19). In the survey conducted by Miner et al., 271 patients undergoing emergency procedures were compared across three groups, including propofol, ketofol 1:1, and ketofol 4:1, and no significant difference was observed in the incidence of respiratory complications among these three groups. However, the extent of agitation at recovery was significantly higher in the 1:1 group than in the other groups (20). In the study by Coulter et al., different ketofol doses (1:1 and 1:10 ratios) were compared. Ketamine to propofol ratio of 1:3 was proposed as the best bolus dose for short-term (5-20 minutes) procedures, while ratios above 1:3 were suggested for more prolonged procedures (21). Previous studies on ketofol (ketamine + propofol) have mostly been descriptive, and few comparative studies have been done. Further, similar studies have been less performed in Iran. Thus, this study was designed to compare the effect of analgesia and the complications resulting from prescribing different ketofol doses in emergency orthopedic procedures.

Methods

This research was a double-blind random clinical trial of applied type conducted in 2020. The present research studied 296 patients above 18 years of age requiring orthopedic procedures in the EDs of hospitals. Patients were randomely allocated to one of four treatment groups (64 patients for each group), with centralized randomization allocation concealment employed to ensure that neither the researchers nor the patients were aware of the treatment assignment prior to allocation. Both the patients and the healthcare providers administering the treatments were unaware of which treatment each patient received. The research plan was then explained to all the patients, and a written consent form was obtained from them before entering the study. Furthermore, the patients had the discretion to join the study or leave it anytime. The studied variables here included drug dose (the ketofol ratio used for analgesia), the intensity of pain, duration of the procedure, recovery time, extent of patient's satisfaction, physician's satisfaction, side effects of sedation, need to perform interventions, blood pressure [systolic blood pressure (SBP) and diastolic blood pressure (DBP)], heartbeats (per minute), and number of respirations (per minute). In this research, the patients requiring emergency orthopedic procedures according to diagnosis and order established by the physician, aged over 18 years, with consciousness and sound mental status to complete the consent form and respond to the questions related to the intensity of pain and complications, American Society of Anesthesiologists (ASA) class I and II physical status, and a stable hemodynamic state entered the study.

On the other hand, pregnant women, patients with multiple trauma, patients with sensitivity to ketamine, propofol, midazolam, fentanyl, and egg, patients with ICP, patients with memory and cognitive disorders, patients who had consumed a sedative, narcotic, alcohol, psychedelic, or psychoactive drugs, patients with a history of psychological disease, patients with heart failure, coronary artery disease, weight of less than 50 kg, and chronic obstructive pulmonary disease (COPD) were excluded from the study. Further, the demographic information (age, gender, weight, occupation, and level of education), underlying diseases, history of smoking, ASA class, physical status, and type of orthopedic injury requiring intervention were recorded in the checklist for each patient. After that, with the help of a random number table, the patients were assigned to four therapeutic groups. For patients in the first, second, third, and fourth groups, ketofol was prescribed with ratios of 1:1, 1:2, 1:3, and 1:4, respectively.

Ketofol was prepared by a trained nurse and provided for the physician prescribing the drug in dark syringes as coded. The groups were as follows:

Group A: One unit dose of propofol 1 mg was administered IV per kg of body weight plus ketamine 1 mg per kg of the body weight 3 minutes before the operation; if required, subsequent doses were injected with half of the first dose and other sedative drugs,

Group B: One unit dose of propofol 1 mg was administered IV per kg of the body weight plus ketamine 0.5 mg per kg of the body weight 3 minutes before the operation; if required, subsequent doses were injected with half of the first dose and other sedative drugs,

Group C: One unit dose of propofol 1 mg was administered IV per kg of the body weight plus ketamine 0.33 mg per kg of the body weight 3 minutes before the operation; if required, subsequent doses were injected with half of the first dose and other sedative drugs,

Group D: One unit dose of propofol 1 mg was

administered IV per kg of the body weight plus ketamine 0.25 mg per kg of the body weight3 minutes before the operation; if required, subsequent doses were injected with half of the first dose and other sedative drugs.

The patients' vital signs were measured using an automatic monitoring system before and during the procedure, recovery, and complete consciousness. They were then recorded in the checklist. Moreover, the duration of the course, recovery time (from the beginning of the first dose up to full consciousness), sedation duration, and hospitalization time in the ED (in the case of residence of over 120 minutes at the hospital due to sedation) were measured and recorded in the relevant checklist. After the intervention, the patients were asked about the extent of pain, remembering the procedure, pain during the procedure, and the extent of satisfaction. Additionally, during and after the procedure, the incidence of side effects such as intubation, central apnea, hypoventilation, laryngospasm, aspiration, increased salivation, intervention-required bradycardia, intervention-required hypotension, neurological side effects, hypoxia, nausea, vomiting, rash, and dysphonia was examined in the patients and recorded in the checklist. Further, the need to perform interventions such as oxygen therapy, airway opening devices, altered patient status, respiratory stimulants, Ambu bags, and masks for ventilation in patients was also registered. After the procedure, the physician was asked about the extent of satisfaction with the level of analgesia and conductance of the procedure by a pseudo-Likert scale (excellent, good, moderate, low, and poor).

To follow ethical rules in the research, the ethics committee approved the proposal (ethics code: 9211307022) and recorded it in the Clinical Trial Studies Registration Center (IRCT2015111825121N1). All the methods used to develop analgesia in the patients were among the routine pain mitigation methods, and there was no control group.

Descriptive results were presented by percentage and mean ± standard deviation (SD) (for categorical and numerical variables, respectively). Kolmogorov-Smirnov test was performed for the normality of the studied variables, which showed a statistically nonsignificant P-value. Analysis of variance (ANOVA) was used to compare the studied variables across the four therapy groups given the normality of the studied variables. To measure the extent of changes in vital signs before, during, and after the procedure and recovery, repeated measures ANOVA was utilized. To compare qualitative variables across the four treatment groups, a chi-square test was employed. For statistical analysis, SPSS software (version 22, IBM Corporation, Armonk, NY, USA) was used. P-values of 0.05 or less were considered statistically significant.

Results

In this study, 296 patients were assigned to 4 groups. Most of the studied individuals were men (84.1%), and most had no addiction to drugs and cigarettes (12.2%). The mean age of the patients in the four groups had no significant difference (P = 0.192). The summary of the participants' characteristics has been reported in table 1. It was observed that gender (P = 0.335), level of education (P = 0.420), addiction (P = 0.242), and smoking (P = 0.401) had no significant difference across the patients in the four treatment groups at the start of study (P > 0.05) (Table 1).

Table 1. Demographic characteristics and the comparison of the differences in four different treatment groups

Variable		Frequency in different treatment groups				%	P-value
		A	B	C	D		
Gender	Women	12	14	7	14	15.9	0.335
	Men	64	69	64	52	84.1	
Level of education	Illiterate	7	8	8	8	10.5	0.420
	High school	25	36	27	21	36.8	
	Diploma and post-diploma	42	31	27	31	44.2	
	Bachelor	1	7	8	6	7.4	
	Higher than bachelor	1	1	1	0	1.0	
Addiction	Negative	69	76	61	54	87.8	0.242
	Positive	7	7	10	12	12.2	
Smoking	Negative	51	61	43	45	67.6	0.401
	Positive	25	22	28	21	32.4	

In the present study, out of the 296 patients, 93.9% were in ASA class I, and 6.1% were present in ASA class II. The shoulder reduction procedure was performed more than other procedures on the patients (37.8%). In almost 85% of the patients studied, there was no need to reinject the medication. Further, apnea and hypoventilation were developed in 2.4% and 7.4% of the patients, respectively. Among the complications resulting from sedation in the studied patients, the major ones were hypoxia (29.7%) and hallucination (11.5%). Among the interventions performed on the patients, the need for oxygen was observed in 30.1% of them, while the need to conduct maneuvers during procedural sedation and analgesia (PSA) was seen in 27.7%. The extent of satisfaction with the procedure by the patients and physicians was 66.2% and 57.8%, respectively, which was evaluated as excellent. Of the 296 patients studied, 51.4% (152 patients) experienced no complications, but the rest had at least one complication (Table 2). Based on the chi-square results, it was observed that the percentage and frequencies of the procedures conducted, need for drug reinjection, development of apnea, development of hypoventilation, bradycardia, hypotension, agitation, need for oral airway placement, need to conduct maneuver during PSA, need for stimulation during PSA, need for bag-mask ventilation (BMV) during PSA, hallucination, the extent of patient's satisfaction, and the extent of physician satisfaction showed no statistically significant difference among the patients in the four treatment groups. Furthermore, the extent of physician's and patient's satisfaction was at a desirable level across the four treatment groups. Among the percentage and frequencies, hallucination, hypoxia, and need for oxygen significantly differed among the four treatment groups. The extent of complications among the four studied groups was significantly different, such that in groups A, B, and D, complications were significantly higher as compared to group C (P < 0.001) (Table 2).

The average pain intensity, based on the visual analogue scale (VAS), before the procedure and during the procedure showed no significant difference in the four treatment groups (P = 0.379 and P = 0550, respectively). The average pain intensity of the patient diminished significantly after the procedure (P < 0.001). The average pain mitigation was almost the same across the four studied groups (Table 3). The average patients' pain intensity during the procedure (after drug prescription) significantly diminished compared to the pre-procedure period (before drug prescription) in all groups (P < 0.001). Sedation time was significantly longer in group A than in other groups, though the other groups showed no significant difference.

Table 2. Frequency and percentage of disease severity and procedural sedation and analgesia (PSA) adverse effects in studied patients

Variable		Frequency in different treatment groups				%	P-value
		A	B	C	D		
Physical status (based on ASA) Procedure	Class I	73	78	69	58	93.9	0.105
	Class II	3	5	2	8	6.1	
	Shoulder reduction	27	30	29	26	37.8	0.668
	Distal radial reduction	29	31	24	23	36.1	
	Both bone of forearm reduction	3	3	1	1	2.7	
	Tibia reduction	4	10	5	2	7.1	
	Pelvis reduction	3	1	2	0	2.0	
	Femur fracture	2	4	3	2	3.7	
	Humorous fracture	1	1	3	4	3.0	
	Knee dislocation	0	2	0	0	0.7	
	Elbow dislocation	4	0	2	4	3.4	
	Finger dislocation	1	0	0	1	0.7	
	Ulnar fracture	0	0	0	1	0.3	
	Ankle dislocation	1	0	1	1	1.0	
	Others	1	1	1	1	1.4	
Subsequent doses (reinjection)	Negative	68	70	63	51	85.1	0.163
	Positive	8	13	8	15	14.9	
Apnea	Negative	75	80	71	63	97.6	0.261
	Positive	1	3	0	3	2.4	
Hypoventilation	Negative	66	79	66	63	92.6	0.154
	Positive	10	4	5	3	7.4	
Bradycardia	Negative	76	83	71	65	99.7	0.321
	Positive	0	0	0	1	0.3	
Hypotension	Negative	76	82	71	65	99.3	0.564
	Positive	0	1	0	1	0.7	
Agitation	Negative	71	76	69	66	95.3	0.073
	Positive	5	7	2	0	4.7	
Hallucination	Negative	63	72	69	58	88.5	0.048
	Positive	13	11	2	8	11.5	
Hypoxia	Negative	45	54	62	47	70.3	0.001
	Positive	31	29	9	19	29.7	
Oxygen therapy	Negative	49	54	61	43	69.9	0.010
	Positive	27	29	10	23	30.1	
Oral airway	Negative	74	80	70	63	97.0	0.733
	Positive	2	3	1	3	3.0	
Maneuver during PSA	Negative	49	59	59	47	72.3	0.087
	Positive	27	24	12	19	27.7	
Stimulation during PSA	Negative	70	80	70	64	95.9	0.223
	Positive	6	3	1	2	4.1	
BMV during PSA	Negative	72	78	71	62	95.6	0.225
	Positive	4	5	0	4	4.4	
Patient satisfaction	Low	0	2	0	1	1.0	0.745
	Moderate	3	3	4	3	4.4	
	Good	26	20	18	20	28.4	
	Excellent	47	58	49	42	66.2	
Physician satisfaction	Weak	1	1	0	2	1.4	0.386
	Low	0	1	0	0	0.3	
	Moderate	7	9	3	5	8.1	
	Good	32	24	20	20	32.4	
	Excellent	36	48	48	39	57.8	
Complications	Negative	30	33	54	35	51.4	< 0.001
	Positive	46	50	17	31	48.6	

ASA: American Society of Anesthesiologists; PSA: Procedural sedation and analgesia; BMV: Bag-mask ventilation

Table 3. Evaluation of patient pain intensity and respiration, procedure, and recovery times in four treatment groups

Variables	Treatment groups (mean ± SD)			
	A	B	C	D
VAS score before	7.82 ± 1.57	7.42 ± 1.57	7.57 ± 1.44	7.51 ± 1.42
VAS score during	0.57 ± 1.24	0.57 ± 1.21	0.39 ± 1.21	0.69 ± 1.28
Sedation time	20.90 ± 1.10	16.80 ± 16.80	16.30 ± 16.30	15.90 ± 15.90
Procedure time	6.72 ± 6.72	6.33 ± 6.33	5.90 ± 5.90	5.80 ± 5.80
Recovery time	11.50 ± 11.50	7.66 ± 7.66	7.52 ± 7.52	7.74 ± 7.74

VAS: Visual analogue scale; SD: Standard deviation

Recovery time was significantly longer in group A, but other groups showed no significant difference and there was no significant difference within the groups regarding procedure time (P = 0.518) (Table 3).

Based on the results of repeated measures test, it was observed that the average SBP, average DBP, average pulse rate (PR), average respiratory rate (RR), and the average oxygen saturation level (SpO2) measured at four different times had a significant difference across the measured intervals in each treatment group (P < 0.001) (Table 4). It was found that during SBP and DBP procedures, they increased significantly across the four studied groups (P < 0.001). With a more detailed assessment, it was observed that during the SpO2 procedure, it decreased significantly, while during RR recovery, it increased significantly. Further, it was noticed that during the PR procedure, it increased significantly (P < 0.001).

Discussion

In the ED, the aim of controlling acute pain is first to develop patients' comfort and then prevent the development of physiological responses. Adequate pain control is essential for emergency procedures. Unfortunately, despite the scientific advances in pain pathophysiology, pain pharmacology, and the development of practical techniques for pain management, patients hospitalized in the ED still experience debilitating pain.

In this research, the age, gender, and level of education of the studied patients in the four treatment groups showed no significant difference. In a study conducted by Andolfatto et al. (19), Miner et al. (20), and Coulter et al. (21), no significant difference was observed either in terms of age or gender across the different groups.

Considering the percentage of addiction and smoking, again, no significant difference was observed among the different treatment groups. Regarding physical status, no significant difference was observed according to the ASA and the type of procedures conducted on the studied groups. In the research by Miner et al., there was also no significant difference in terms of the type of procedures conducted (20).

Table 4. Results of analysis of variance (ANOVA) with repeated measurements on the studied variables in four measured times

	Variables	Mean ± SD	95% CI		P-value
			Lower limit	Upper limit	
Mean SBP	Before the procedure	134.80 ± 1.03	132.80	136.86	< 0.001
	During the procedure	138.40 ± 1.14	136.19	140.69	
	After the procedure	136.10 ± 1.06	134.01	138.19	
	Recovery	134.10 ± 0.98	132.20	136.09	
Mean DBP	Before the procedure	83.10 ± 0.82	81.50	84.74	< 0.001
	During the procedure	87.10 ± 0.84	85.44	88.76	
	After the procedure	84.40 ± 0.74	83.00	85.93	
	Recovery	83.30 ± 0.76	81.86	84.86	
Mean PR	Before the procedure	89.30 ± 0.74	87.88	90.82	< 0.001
	During the procedure	96.40 ± 3.54	89.48	103.45	
	After the procedure	88.90 ± 0.71	87.50	90.30	
	Recovery	86.50 ± 0.67	85.19	87.83	
Mean O2 saturation	Before the procedure	96.90 ± 0.09	96.72	97.07	< 0.001
	During the procedure	92.80 ± 0.28	92.30	93.42	
	After the procedure	96.30 ± 0.14	96.04	96.60	
	Recovery	96.90 ± 0.09	96.72	97.09	

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PR: Pulse rate; RR: Respiratory rate; CI: Confidence interval; SD: Standard deviation

Across the four studied groups, there was no significant difference in terms of apnea, hypoventilation, bradycardia, hypotension, and agitation. However, complications such as hallucination and hypoxia were significantly different among the groups. The mentioned complications were far less in group C when compared with the other groups. In the study of Miner et al., the extent of agitation was greater in the 1:1 (propofol/ketamine) group (the doses were similar to group A in our study), as compared to the other groups (20). Similarly, in the research conducted by Walravens et al., minimum complications were observed in the 1:3 (the doses were similar to group C in our study) group (23). In a study by Coulter et al., hallucination was also far more frequent in the 1:1 (the doses were similar to group A in our study) group, as compared to the other groups (21).

Considering the performed interventions such as placing oral airway, conducting maneuvers during PSA, stimulation during PSA, and using BMV, there was no significant difference across the four studied groups. On the other hand, prescription and use of oxygen was far less in group C, when compared with the other groups. In addition, in terms of the extent of physician's and patient's satisfaction, no significant difference was observed. Miner et al. showed no significant difference in terms of the extent of satisfaction, and a high level of satisfaction was reported (20). Nejati et al. observed that there was no significant difference in the extent of physician's satisfaction with analgesia and sedation of patients in the two treatment groups. However, in the ketofol group, the extent of perceived pain was significantly lower as compared to the other groups. Ketofol was mentioned as a risk-free and effective agent in emergency interventions (24).

In the study conducted by David and Shipp, no significant difference was observed in the extent of complications resulting from sedation by propofol or ketamine and without ketamine. On the other hand, the extent of emergency personnel's and patients' satisfaction with the resulting analgesia was significantly higher in the ketofol group, as compared to the propofol group (25).

In terms of VAS before and after the procedure, there was no significant difference among the studied groups. The level of SBP significantly increased during the procedure, but at other time intervals (before the procedure, after the procedure, and during recovery), there was no significant difference across the four studied groups. The level of DBP, as with SBP, increased significantly during the procedure. However, at other time intervals, there was no significant difference among the four studied groups.

The PR considerably increased during the procedure, but at other time intervals, the treatment groups had no significant difference. The average RR showed a significant increase during the recovery. However, at other time intervals, there was no significant difference across the groups. The average SPO2 decreased significantly during the procedure. However, at other time intervals, there was no significant difference across the groups. Generally, vital signs and hemodynamic status were stable in the four groups, and no considerable change was observed. In a study, also, the hemodynamic situation of patients receiving ketofol had no considerable change, and the hemodynamic status was stable (19-21, 26).

The extent of occurrence of complications was significantly lower in group C, as compared to the other groups. Moreover, in the study by Coulter et al., the extent of occurrence of complications was lower in the 1:3 group (the doses were similar to group C in our study) as compared to the other groups. The average reuse of medication was significantly higher in group D, as compared to the other groups. Furthermore, the average time of recovery, sedation time, was significantly longer in group A (21). In the other studies, the recovery time was also longer in group 1:1 (the doses were similar to group A in our study), as compared to the other groups (19-21).

Based on the findings obtained from this research and by testing different ketamine doses, it was observed that 1 and 0.5 mg doses resulted in more complications. The 0.33 mg dose of ketamine managed to develop analgesia and sedation as with the above doses while having fewer complications. Based on the investigation, 0.25 mg ketamine may increase the probability of the need to use a subsequent dose. Thus, 0.33 mg seems to be the best ketamine dose.

Like other studies, this research has some limitations. Among the limitations is the noninvolvement of patients due to bad general health status. This limitation was rectified by explaining to the patients that the best method of analgesia was used for them. The lack of cooperation of a number of specialists and colleagues was another limitation, which was again solved by explaining the proposal to them. The probability of failure in pain control in a number of patients was the third limitation, in which case, other analgesia development methods were used for them.

Conclusion

By testing different doses of ketamine, we concluded that doses of 1 mg and 0.5 mg were associated with more

side effects. A dose of 0.33 mg of ketamine has fewer side effects while causing analgesia and sedation as in the above doses. A dose of 0.25 mg ketamine increases the likelihood of requiring subsequent doses. Therefore, it seems that 0.33 mg of ketamine is the best dose of choice.

Conflict of Interest

The authors declare no conflict of interest in this study.

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