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Clinical Efficacy of Dexmedetomidine versus Ketamine in Shoulder Dislocation Reduction: A Randomized Clinical Trial Study

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Abstract

Background: Shoulder joint dislocation and displacement is a common clinical condition. The present research aims to compare the clinical efficacy of ketamine versus dexmedetomidine during shoulder joint reduction.

Methods: In this randomized clinical double-blind trial method, patients aged 18 to 65 years with shoulder dislocation referred to the Emergency Hospital of Imam Khomeini Hospital in Ahvaz, Iran, were enrolled. Patients were separated into two groups, patients in group A received 1mg/kg nebu-lized ketamine and patients in group B received 1 µg/kg nebulized dexmedetomidine. Pain score was recorded at 5 different time points: Zero (before intervention), 10 minutes, 20 minutes, 30 minutes, and 60 minutes after intervention., The pain score was evaluated using the visual analog scale (VAS) test. A linear regression test was carried out to compare the slopes. Also, ANOVA repeated measures test variables differences between groups. Then Tukey's multiple comparisons as post-hock were applied to compare the pains at different time points. Using IBM SPSS version 19.0 software, all analyzes were accomplished.

Results: The pain score in both groups significantly decreased during different time points. The pain reduction slope in the group that received dexmedetomidine is meaningfully upper than that of ketamine (-0.08 vs. -0.06, p=0.012). The ketamine action onset time was 20 minutes after the in-tervention. In comparison, the effect of dexmedetomidine has an onset of 10 minutes after the in-tervention.

Conclusion: Overall, the results of current research demonstrated that although nebulized dexme-detomidine and nebulized ketamine produce a significant decrease in pain score, dexmedetomidine provides a faster effect. Therefore, nebulized dexmedetomidine seems to be used as an appropriate choice to induce sedation during shoulder joint reduction in emergency departments.

Keywords: Dexmedetomidine, Ketamine, Nebulized, Shoulder Dislocation, Trial, Reduction

Conflicts of Interest: *None declared*
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Introduction

Shoulder joint dislocation and displacement is a common clinical condition. The shoulder movement can be forward, downward, or backward, which in 85% of cases, the head of the humerus is displaced forward. Shoulder displacement is accounted for 45-50% of joint dislocations. Somewhere it forms t he joints of the body (1-3). The pain is a common complication during shoulder joint reduction that stimulates the autonomic nervous system and subsequently releases the catecholamines (4). If the pain is not controlled, a wide range of complications would be occurred including; increasing oxygen usage in the heart and consequently increasing myocardial

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↑What is "already known" in this topic:
Shoulder joint dislocation and displacement is a common clinical condition. The shoulder movement can be forward, downward, or backward, which in 85% of cases the head of the humerus is displaced forward.

→What this article adds:
Nebulized dexmedetomidine and nebulized ketamine produce a significant decrease in pain score. The dexmedetomidine provides a faster effect.

ischemic risk, immunosuppression, hyperglycemia, reducing the rate of wound healing, increased risk of atelectasis, drowsiness, nausea, abdominal pain, kidney problems, increased bleeding disorders and arrhythmias (5).

Ketamine, a derivative of phencyclidine, has been widely used for sedation since 1970 (6). It has low and predictable complications due to deep analgesic effects and minimal respiratory depression (7). The main routes of administration included intravenous and intramuscular. The superiority of these administration routes has not been described well (8). Patients with cerebral mass, abnormal brain, hydrocephalus, and head injury were contraindicated for ketamine injection (9). The Ketamine related complications are restlessness, transient apnea (0.8%), laryngospasm (0.3%), nausea and vomiting (8.4%), nightmares (2%), intraocular pressure, and increased brain pressure (6, 10). Another drug that has recently been introduced as an analgesic drug is dexmedetomidine, a highly selective alpha-2 adrenoceptor agonist (11). This drug as an adjuvant in general anesthesia, with sympatholytic effects, helps to hemodynamic stability and making strong anesthetic and analgesic effects (12), which reduces opioids needing, the response of stress and improving recovery quality (13, 14). The anesthetic effects of dexmedetomidine are unique and cause mild cognitive impairment that facilitates easy communication between the medical team and patients in the intensive care unit (ICU) (15).

Although several types of research have demonstrated the ketamine analgesic effect and dexmedetomidine as adjuvant therapy in controlling postoperative pain, there have not been enough studies on the efficacy of ketamine and dexmedetomidine in relieving acute pain and sedation in emergency settings. The present research aims to compare the ketamine clinical efficacy versus dexmedetomidine during shoulder joint reduction.

Methods

This study was conducted according to the Consolidated Standards of Reporting Trials (CONSORT) (16).

Study Design

All procedures after obtaining permission from the ethics committee of Jundishapur University of Medical Sciences, Ahvaz, as well as receiving the clinical trial code (IRCT20180530039917N1), http://www.irct.ir and performed by the ethical standards laid down in the 1964 Declaration of Helsinki. In this clinical trial with a double-blind method, patients aged 18 to 65 years with shoulder dislocation referred to the Emergency Hospital of Imam Khomeini Hospital in Ahvaz, Iran, were enrolled.

Participants

Patients with decreased consciousness, trauma with damage to other organs, cardiovascular diseases, respiratory problems, metabolic disease, pregnancy, inability to speak for any reason, impaired vital signs such as blood pressure less than 90mmHg and respiratory rate less than 10-12, analgesic intake before entering the emergency room, any history of drug-related anaphylaxis and who decline to participate in the study were excluded. An informed consent letter for each patient was obtained.

Therapeutic intervention

By the block randomization method, patients were separated into two groups randomly, and the researchers were not involved in assigning individuals to groups. The patient and the nurse did not know the type of prescription. Patients in group A received 1mg/kg nebulized ketamine and patients in group B received 1 µg/kg nebulized dexmedetomidine. Pain score was recorded at 5 different time points: Zero (before intervention), 10 minutes, 20 minutes, 30 minutes, and 60 minutes after intervention.

Outcome

The visual analog scale (VAS) test was used to assess the pain score. It is a one-dimensional measuring instrument used to measure the severity of pain in adults. The test has 11 points and is diagnosed based on the intensity of the patient's pain. The patient is asked to rate the intensity of pain on a scale of 0 to 10. The interpretation of various scores is 0 (no pain), 13 (mild pain), 46 (moderate pain), 710 (severe pain). If both groups of patients did not respond adequately to the intervention, other treatments were used and the patient was excluded from the study. The drug administration and the completion of the questionnaire were carried out by a trained doctor who did not know the type of drug. The patient was also not informed of the type of medication.

Randomization

Use the Randomization Software 2.0 to set the randomization. Participants are randomly assigned to two groups using a block randomization program, and matching objects in each block are made through a computer-generated block randomization list.

Statistical analysis

Considering the 90% power, to identify a correlation as small as 0.25, values bigger than 0.25 are named a strong relationship for the Cramer's V (17). With a type I error of 0.05, at least 46 samples are required. Data were first analyzed for descriptive indexes such as mean and S.D. Then, the Mann-Whitney test and independent samples t-test were applied to compare the quantitative data between the two groups based on the normality of the data. A linear regression test was carried out to compare the slopes. Also, using the ANOVA repeated measures test, differences between the groups were analyzed. Tukey's multiple comparisons and post-hock were applied to compare the pains at different time points. Using IBM SPSS version 19.0 software, all analyzes were accomplished (18). The level of significance was less than 0.05.

Results

Fifty-eight patients were studied, and 12 patients were excluded for different reasons (Fig. 1). Finally, 46 patients

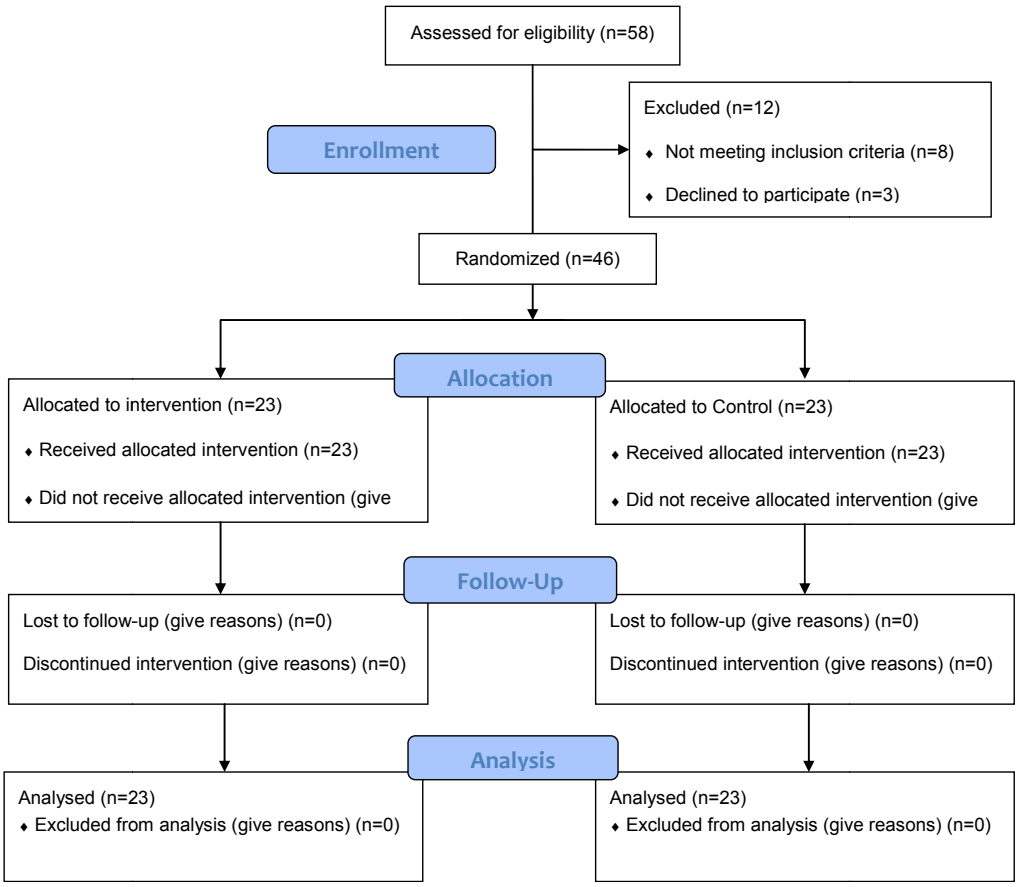

Fig. 1. Study design flowchart

were evaluated. The mean age of the patients was 29.74 ± 8.81. Most of the patients (43 patients included 93.55%) were male. More than 70% of patients had a history of shoulder dislocation. Also, half of the patients were smokers. The right shoulder involvement was about twice more common than the left shoulder (Table 1).

In Table 2, the baseline characteristics of patients were compared. Based on these evaluations, patients in both groups did not display meaningful differences in terms of mean age and weight, gender distribution, predisposing

Table 1. Patients' characteristics

Characteristics		(N = 46)
Age, Mean (range) ± SD		29.74 (19-59) ± 8.81
Gender, N (%)	Male	43 (93.51)
	Female	3 (6.50)
Weight, Mean (range) ± SD		77.7 (66-88) ± 5.67
Risk Factors, N (%)	Previous Dislocation	35 (76.15)
	Familial History	0
HTN, N (%)		2 (4.39)
Smoking, N (%)		23 (50)
CVD, N (%)		0
Dislocated Side, N (%)	Left	14 (30.41)
	Right	32 (69.61)

Table 2. Baseline characteristics comparison

Characteristics	Ketamine (N = 23)	Dexmedetomidine (N = 23)	P-value *
Age, Mean (range) ± SD	29.65 ± 9.54	29.83 ± 8.24	0.941 *
Weight, Mean (range) ± SD	77.96 ± 6.25	77.43 ± 5.15	0.758 *
Gender (Male), N (%)	21 (91.31)	22 (95.72)	0.536 *
Previous Dislocation, N (%)	17 (73.94)	18 (78.31)	0.738 *
HTN, N (%)	1 (4.30)	1 (4.33)	0.990 **
Smoking, N (%)	13 (56.53)	10 (43.57)	0.370 *
Dislocated Side (right), N (%)	18 (78.36)	14 (60.91)	0.201 *

*t-test
** Mann-Whitney

Table 3. Linear regression evaluation, slope comparison of pain changes at different time points (before intervention and 60 minutes after intervention)

Variables		Dexmedetomidine	Ketamine	Slop Comparison
Slope	Slope	-0.080 ± 0.004	-0.066 ± 0.003	
	Y-intercept when X=0.0	9.38 ± 0.13	9.45 ± 0.10	P=0.011
	X-intercept when Y=0.0	116.6	142.10	
	1/slope	-12.43	-15.02	
Is slope significantly non-zero?	DFn, DFd	1.00, 98.00	1.00, 113.00	
	P value	< 0.001	< 0.001	
	Deviation from zero?	Significant	Significant	

factors, and dislocated shoulder side.

Regarding the linear regression, pain scores in both groups significantly decreased during different time points. Also, the pain score trend line was compared in both groups, and it was found that the pain reduction slope in the dexmedetomidine receiving patients is significantly higher than that of ketamine (-0.08 vs. -0.06, p=0.012) (Table 3). Also, pain changes at different time points were evaluated in comparison to the zero minutes (before the intervention). The results of this evaluation demonstrated that the ketamine action onset time was 20 minutes after the intervention (Fig. 2). The effect of dexmedetomidine has an onset of 10 minutes after the intervention (Fig. 3).

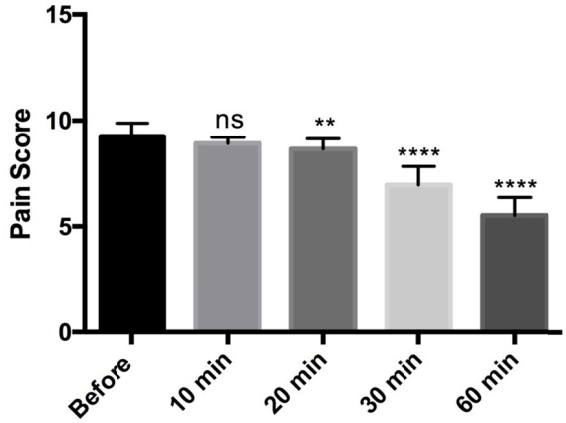

Fig. 2. Pain at different time points in the ketamine receiving group

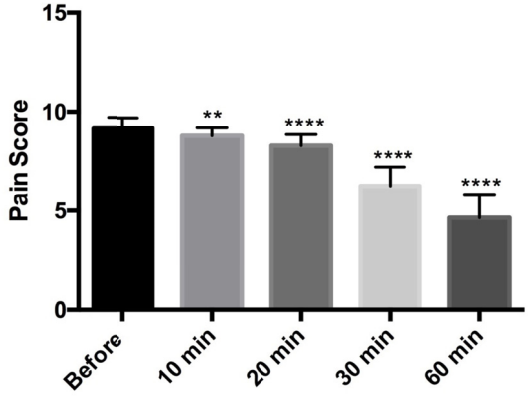

Fig. 3. Pain at different time points in the dexmedetomidine receiving group

Discussion

The human shoulder is the most mobile joint in the body. This joint can be rotated in many positions, but this feature makes it more vulnerable to dislocation. Shoulder joint dislocation is the most usual articular dislocation in humans (17 per 100,000). Its manifestations include severe pain and the inability of the patient to perform some shoulder movements. Dexmedetomidine is an agonist of the α2 receptor adrenergic, which directly affects the peripheral nervous system and causes dose-dependent Aα fibers and C-fiber inhibition. Receptors of Alpha 2 adrenergic affect the locus ceruleus region and cause inhibition of pain neurotransmission toward the posterior the spinal cord horn (19). Receptors of Alpha-2 adrenergic also affect the presynaptic membrane, which inhibits norepinephrine release, and subsequently inducts hyperpolarization and inhibit the pain signal transmission to the brain. Dexmedetomidine also induces acetylcholine release from spinal neurons, which consequently increases the synthesis and nitric oxide release, thereby participating in the analgesia regulation (20). Dexmedetomidine can be prescribed in several routes, the most common routes are intravenous, intramuscular, oral, buccal and intranasal (21-25). Buccal and intranasal administration of dexmedetomidine has provided the highest bioavailability (26). Due to the high mucosal absorption of dexmedetomidine in the current study, we used the nebulizing method for prescribing the drug.

Our findings suggest that although both ketamine and dexmedetomidine significantly reduce pain within 60 minutes of administration, dexmedetomidine provided a faster onset of action. On contrary, Rodney et al., in a study that assessed the effects of ketamine and dexmedetomidine, showed that plasma levels of both drugs had no significant difference, and both had similar absorption and distribution (27). However, the onset of the action differences between these two drugs may be related to the location and mechanism of their action. On the other hand, in line with our findings, Mostafa et al., in a research comparison the relief effect of intranasal doses of dexmedetomidine, ketamine, and midazolam, showed that Dexemodemidine produced the fastest relief, and its onset of action is 10 minutes after the administration (28). Also, many studies have reported similar findings when assessed the analgesic effects of dexmedetomidine in a variety of conditions. In a research by Ghodrati et al. the efficacy of intranasal dexmedetomidine to induct moderate sedation in patients undergoing biliary endotracheal endoscopy was evaluated and has been

shown that it could be used as an adjuvant to sedation of the patients under ERCP (29). Ola M. Zanaty et al. compared the effects of nebulized dexmedetomidine, nebulized ketamine, and their combination in the children referred for dental surgery. Their findings showed that the group receiving the combination of both drugs was more satisfied than those who receive dexmedetomidine, or ketamine alone (30). Masoumi et al. showed that dexmedetomidine causes a quicker and higher level of analgesia than midazolam-fentanyl (31).

Conclusion

Overall, the results of current research demonstrated that although nebulized dexmedetomidine and nebulized ketamine produce a significant decrease in pain score, the dexmedetomidine provides a faster effect. Therefore, nebulized dexmedetomidine seems to be used as an appropriate choice to induce sedation during shoulder joint reduction in the emergency departments.

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Conflict of Interests

The authors declare that they have no competing interests.

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