Original Article

Magnesium Gargle versus Ketamine Gargle in Postoperative Sore Throat Pain; A Randomized Placebo-Controlled Clinical Trial

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Abstract

Background: A wide range of approaches have been tested for the prevention and treatment of postoperative sore throat pain (POST pain). This study attempted to compare the effects of gargling with Ketamine or Magnesium Sulfate on POST pain.

Materials and Methods: In a randomized clinical trial, 60 patients scheduled for prone position laminectomy were randomly assigned into three groups: Ketamine (n=20), Magnesium (n=20), and Control (n=20). The Magnesium group received magnesium sulfate gargle (30 mg/kg in a total of 30 ml 5% Dextrose water), the Ketamine group received Ketamine gargle (0.5 mg/kg in a total of 30 ml 5% Dextrose water) and the control group received 30 ml 5% Dextrose water gargle; all these solutions were administered 10 min before anesthesia induction. Visual Analog Scale (VAS) for throat pain was recorded in the recovery room; immediately after arrival and then, at 2, 4, and 24 hours postoperatively in the ward. Would there be any VAS equal to or more than 3 of 10, rescue analgesics were administered immediately and their cumulative doses were recorded.

Results: The incidence of complaint-free patients in the Ketamine group was significantly higher than in the other two groups. The incidence of sore throat with VAS≥3, mandating rescue analgesia, was significantly lower than the other two groups. Patient satisfaction after surgery was significantly higher in the Ketamine group.

Conclusion: Patients experiencing POST pain treated with "Ketamine gargle" had better results compared with "Magnesium Sulfate" or "Placebo" gargle.

Keywords: Postoperative sore throat (POST), Ketamine, Magnesium Sulfate, Pre-emptive Analgesia, Prone Position, Laminectomy

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Introduction

Postoperative sore throat (POST) is known as a minor complication commonly occurring after general anesthesia (experienced by 30% to 65% of patients) (1, 2). It is especially seen in patients operated in the prone position (3). Factors that influence the occurrence of

POST include age, gender, cuff pressure, intraoperative endotracheal tube displacement, endotracheal tube size, intubation technique, and cigarette smoking (4). In most patients, a sore throat will heal on its own even if left untreated; however, in patients experiencing moderate to severe pain, treatment, and topical medication are recommended (5). Non-pharmacological preventive interventions and medications such as steroids, magnesium, and ketamine can be used to prevent sore throat after intubation (6).

Magnesium sulfate by blocking NMDA receptors inhibits calcium ions enter cells; leading to antinociceptive effects; also, this effect is related to the central sensitization prevention caused by peripheral tissue injury (7, 8). Magnesium sulfate has anti-nociceptive and anti-inflammatory effects and causes expression inhibition of inflammatory mediators (histamine, serotonin, and cytokines) in peripheral tissues (9, 10) and as an antagonist of the N-methyl-D-aspartate receptor affects both CNS(central nervous system) and peripheral nervous system (PNS) (11, 12). Magnesium significantly attenuates pain in acute and chronic pain states (13); however, various randomized controlled trials (effect of magnesium on POST) have demonstrated controversial results (6, 14-17).

Ketamine is also an NMDAR antagonist and has NMDAR inhibitory effect. Several reports showed ketamine affinity to many other receptors and ion channels, including cholinergic receptors, serotonin, dopamine, sigma, and opioid as well as hyperpolarization-activated cyclic nucleotide-gated (HCN) channels. According to laboratory judgments, Ketamine typically has a lower affinity (higher inhibitory constant—Ki—values) for these receptors and channels compared with NMDARs (18-21). Ketamine can be effective in preventing sore throat through the anti-inflammatory and anti-nociceptive effects in gargle or mouthwash or intravenous administration (22).

Methods

Patient selection and randomization: This randomized clinical trial was conducted at the Shahid Beheshti University of Medical Science and implemented at Shohada-e-Tajrish Hospital. The participants who registered for the study were candidates for Laminectomy surgery and in the age group between 30 -70 years. They were divided into three groups by random number table; ketamine (n=20), magnesium (n=20), and control (n=20). Exclusion criteria for the study were as follows: (A) difficult intubation (B) complaint of throat pain before the operation (C) allergies to ketamine and magnesium (D) several attempts for laryngoscopy (E) perioperative complications and (F) length of operation exceeding 3 hours.

The Vice-Chancellor Affair, Shahid Beheshti University of Medical Science approved the ethical aspects of the study; coded (IR.SBMU.RETECH.REC.1398.599). besides, the study was registered at the Iranian Clinical Trial Registry Database; Coded IRCT20190131042569N2. Informed written consent was filled for all the patients by the Principal Investigator before their enrolment in the study. The Magnesium group received magnesium sulfate (30 mg/kg in a total of 30 ml 5%Dextrose water), the Ketamine group received Ketamine (0.5 mg/kg in a total of 30 ml 5% Dextrose water) and the Control group received 30 ml 5% Dextrose water that was administered 10 min before the induction of anesthesia; all as gargle solutions.

Perioperative management: Anesthesia was induced by an anesthesiologist with a minimum of 10 years of experience blinded to the group allocation. Standard monitoring and devices were applied. Premedication was: 0.03 mg/kg midazolam, 2 µg/kg Fentanyl and 1 mg/kg Lidocaine 2% and general anesthesia induced by: Propofol 1-1.5 mg/Kg and Atracurium 0.5 mg/Kg for neuromuscular blockade. Endotracheal intubation was done for all the patients by the same person and using the same devices (including No. 8 endotracheal tubes for men and No. 7.5 for women). The cuff pressure was maintained between 20-25 cmH2O being checked every 15 minutes until extubation using a non-invasive manometer.

Anesthesia was maintained with 1-1.5% isoflurane plus 50%-50% air-oxygen mixture 6 liters/hour. TOF stimulation of the ulnar nerve for neuromuscular blockade measurement was applied. The depth of anesthesia was monitored and was kept

Table 1: Demographic features in the three study groups

		Ketamine	Magnesium	Control
Age (y, Mean ± SD)		51.60±8.42	50.80±9.05	52.01±8.37
Gender	Female	6	9	7
	Male	14	11	13
Heart Rate		69.8±8.13	71.2±6.61	70.2±7.64
Systolic Blood Pressure (mmHg, Mean ± SD)		119.0±14.71	126.0±10.22	120.0±12.18
Diastolic Blood Pressure (mmHg, Mean ± SD)		78.0±6.91	81.0±5.20	79.0±6.29

between 40 to 60 (BISpectral Index). At the end of the surgery tracheal tube was removed after the patient had become fully awake (TOF>0.7 and BIS>80). Visual analog scale (VAS) for throat pain was recorded in the recovery room at arrival and after 2 hours, 4 hours, and 24 hours of admission by questionnaire. At any time, VAS was equal to or greater than four analgesics were administered.

Statistical analysis: The data entered into Microsoft Excel analyzed using student t-test, Chi-square tests, and ANOVA. A p-value of < 0.05 was considered statistically significant.

Results

The first follow up was made in the recovery room. The severity of throat pain was not significantly different between the groups. After 2 hours, and in the second follow up, the throat pain score (VAS) was significantly lower in the ketamine group compared to the Magnesium group (P=0.001) and control group (P=0.000), however, no significant differences were seen between the Magnesium group and Control group, nor after 4 hours and 24 hours post-operation.

Table 1 shows the demographic features in each of the three groups that there is no significant difference between mean age and values of vital signs, including mean heart rate, mean systolic and diastolic blood pressure in the Ketamine, Magnesium, and Control group.

Mean VAS in three groups over time

- *Arrival at recovery*: no significant difference between Ketamine, Magnesium and Control group.
- *Two hours after admission in the ward*: Ketamine group patients experienced significantly less pain and discomfort compared to the Magnesium (P-value<0.001) and Control (P-value<0.01) groups; no significant difference was seen between Magnesium and Control groups.
- *Four hours after admission in the ward*: Ketamine group patients experienced significantly less pain and discomfort compared to the Magnesium (P-value<0.003) and Control (P-value<0.001) groups; no significant difference was seen between Magnesium and Control groups.
- *24 hours after admission in the ward:* Ketamine group patients experienced significantly less pain and discomfort compared to the Magnesium (P-value<0.001) and Control (P-value<0.001) groups; no significant difference was seen between Magnesium and Control groups.

As demonstrated in Table 3, the prevalence of sore throat with VAS≥3 was significantly lower in the Ketamine group after 2, 4, and 24 hours of ward admission. The incidence of patients without complaint in the Ketamine group after 2, 4, and 24

hours of ward admission was 80%, 84%, and 80%, respectively; which was significantly higher than in the other groups. The incidence of sore throat with VAS≥3 requiring rescue analgesics medication in the Ketamine group (2, 4, and 24 hours after admission to ward) was 4%, 8%, and 4%, respectively; being significantly lower than the other groups.

Discussion

Post-operative sore throat is a common complication experienced after especially those operated in a prone position perform tracheal intubation. This complication may significantly affect patient satisfaction and as one of the major complaints of patients in recovery, it needs to be prevented and treated. According to the study conducted by Lehmann et al on a pool of 12, 276 patients, POST was found to be the second-highest cause for complaint (23). In another study conducted by Jin Young Lee et al on a group of 207 patients, the prevalence of POST was determined to be 57.5% (4). Considering the high prevalence rate of POST and the effect it has on patient satisfaction, several studies have been undertaken to

Table 2: Mean VAS in three study groups over time.

Time		VAS(Mean)	Magnesium	Control
Recovery	Ketamine	1.04	P = 0.461	P = 0.402
	Magnesium	0.82		P = 0.190
	Control	1.59		
2 hours after surgery	Ketamine	0.32	P = 0.001	P = 0.01
	Magnesium	2.18		P = 0.794
	Control	1.91		
4 hours after surgery	Ketamine	0.4	P = 0.003	P = 0.001
	Magnesium	1.55		P = 0.919
	Control	1.68		
24 hours after surgery	Ketamine	0.4	P = 0.001	P = 0.001
	Magnesium	1.29		P = 0.204
	Control	1.38		

- At recovery arrival illustrating, there is no significant difference between Ketamine, Magnesium and Control group.
- After 2 hours of ward admission the patients in the Ketamine group experienced significantly less pain and discomfort compared to the Magnesium (P-value<0.001) and Control (P-value<0.01) groups and that there exists no significant difference between the Magnesium and Control groups.
- After 4 hours of ward admission the patients of the Ketamine group experienced significantly less pain and discomfort compared to the Magnesium (P-value<0.003) and Control (P-value<0.001) groups and that there exists no significant difference between the Magnesium and Control groups.
- After 24 hours of ward admission the patients in the ketamine group experienced significantly less pain and discomfort compared to the Magnesium (P-value<0.001) and Control (P-value<0.001) groups and that there exists no significant difference between the Magnesium and Control groups.

prevent and treat sore throat and several procedures have been suggested.

In various studies, the use of different medications such as Dexamethasone, Ketamine, Magnesium Sulfate, and Lidocaine via different methods such as topical, intravenous, and gargling were compared and recommended.

In a study by Mansoor Aqil et al, the incidence and severity of POST pain after the performance of intubation was compared with the Macintosh Laryngoscope and Glide scope technique and found that the incidence and severity of POST pain are reduced using the Glide scope technique (2).

In this study, we compared the effects of magnesium sulfate and ketamine in preventing post-operative sore throat and found that the patients in the Ketamine group experienced significantly less POST than did the patients in the Magnesium Sulfate group. Several studies similar to ours have already been conducted. In a study by Jin Ha Park et al, the incidences of POST in patients placed in magnesium and dexamethasone groups were compared (50.7% versus 49.3%) and It was found that the gargle of magnesium sulfate was similar to Dexamethasone for the treatment of postoperative sore throat (24).

According to another study by Narinder P Singh et al, the incidence of POST in patients allocated in a magnesium(topical) group was significantly lower than those in the control group (6). In another study, Aigbedia et al compared Ketamine Gargle and Lidocaine Jelly, finding that the incidence of POST in patients in the Ketamine group was significantly lower

Table 3: percentage of sore throat prevalence

Group	Recovery arrival	2hrs after surgery	4hrs after surgery	24hrs after surgery
Ketamine	48 %	80 %	84 %	80 %
	36 %	16 %	8 %	16 %
	16%	4 %	8 %	4 %
Magnesium sulfate	41 %	37 %	24 %	63 %
	39 %	41 %	62 %	18 %
	20 %	22 %	14 %	9 %
Control	30 %	21 %	18 %	31 %
	32 %	43 %	51 %	46 %
	38 %	36 %	31 %	23 %

VAS = 0

VAS = 1,2

VAS ≥3

This table shows the percentage of sore throat prevalence and its rate at specified times in the three study groups. Prevalence of sore throat with VAS≥3 is significantly lower in the ketamine group after 2, 4 and 24 hours of admission. The incidence of patients without complaint in the Ketamine group after 2, 4 and 24 hours of ward admission was 80%, 84% and 80 % which is significantly higher than in the other groups. The incidence of sore throat with VAS≥3 which required medication was 4%, 8%, and 4% in the Ketamine group after 2, 4 and 24 hours of ward admission which is significantly lower than in the other groups.

than in the Lidocaine group (22). Based on a study by Surajit Chattopadhyay et al, the incidence of POST in patients in the magnesium (gargle) group was significantly lower than in the Aspirin group (16).

Given the importance of the subject, we decided to conduct this study to improve patient satisfaction after surgery. As pre-emptive analgesia seems to be more effective than its treatment, in this study we used ketamine and magnesium as a gargle to prevent POST in patients undergoing laminectomy surgery in the prone position.

Our study was conducted on 60 patients scheduled for laminectomy surgery in the prone position, which was divided into three groups of 20 patients. The first group received ketamine, the second group received magnesium, and the control group received dextrose serum as a gargle before surgery. Visual analog scale (VAS) for throat pain was recorded in the recovery room at arrival and after 2 hours, 4 hours, and 24 hours of admission by questionnaire.

According to the information in the table-5, the incidence of patients experiencing POST without complaint in the Ketamine group after 2, 4, and 24 hours of ward admission are 80%, 84%, and 80%, and in the magnesium group are 37%, 24%, and 63% and in the control group are 21%, 18%, and 31%. The incidence of sore throat with VAS≥3 that requires medication is 4% in the ketamine group VS 22% in the Magnesium group VS 36% in the control group after 2 hours of ward admission. The incidence of POST with VAS≥3 after 4 hours of ward admission is 8% in the Ketamine group VS 14% in the Magnesium group VS 31% in the control group. The incidence of POST with VAS≥3 after 24 hours of ward admission is 4% in the Ketamine group VS 9% in the Magnesium group VS 23% in the control group. It seems that patients in the ketamine group are more satisfied and they need less medication for their POST.

As shown in Table 2, efficacy and at the first evaluation at recovery, there was no significant difference between the groups. This may be due to the residual effect of opiates and anesthetic agents. The data shows the difference between VAS in each of the 3 groups after 2 hours of ward admission illustrating that the patients in the ketamine group experienced significantly less pain and discomfort than those in the magnesium and control groups, however, there exists no significant difference between the magnesium and control groups. Additionally, the data show the difference between the VAS in each of the 3 groups after 4 hours and 24 hours of ward admission illustrating that the patients in the ketamine group experienced significantly less pain and discomfort than those in the magnesium and control group and that there exists no significant difference between the magnesium and control groups.

These results regarding the effectiveness of ketamine as pre-emptive analgesia on POST and lower incidence of medication needed in the ketamine group may be associated with its anti-inflammatory and antinociceptive effects and its impact on N-Methyl-D Aspartate receptors as an inhibitor in PNS and effect on ion channels and decreasing intracellular calcium levels (25-27). Moreover, this pain reduction may be due to the mechanism of the local analgesic effect of Ketamine which is the depression of sodium channel function (28).

Conclusion

According to the data obtained in this study, ketamine gargle with a dose of 0.5 mg/kg seems to have a significant pre-emptive analgesic effect on POST and it is recommended in high-risk patients for the POST. More studies on the efficacy of ketamine for the POST reduction (larger sample size and by combining ketamine with other medications) to minimize the possibility of occurrence of sore throat is also recommended.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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