Original Article

Dexmedetomidine is as Effective as Ketamine in Post-Operative Sore Throat: a Randomized Double Blind Study

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Abstract

Background: sore throat as one of the common postoperative challenges, with a prevalence of 65%, mandates more attention. Many therapeutic approaches have been tested; including ketamine gargle. This study compares the effect dexmedetomidine versus ketamine, both used as preoperative gargle, on the incidence and severity of postoperative sore throat in emergency surgical procedures.

Materials and Methods: All patients undergoing emergency surgical procedures who referred to Shohadaye-Tajrish Hospital and needed anesthesia using succinylcholine for rapid sequence induction were considered as the target population and patients with ASA class 1-2, who aged 18-64 years, were enrolled. Inside the operating theatre, patients' vital signs recorded and they were divided into ketamine and dexmedetomidine groups, each including 20 patients, receiving 0.5 mg/kg ketamine or 0.25µg/kg dexmedetomidine in 100cc water to gargle before induction of anesthesia. Standard similar anesthesia protocols were applied for all patients. In PACU sore throat was assessed using a visual analog scale (VAS) scoring.

Results: in the ketamine group, 8 cases and in the dexmedetomidine group, 12 had dry throat (p= 0.150). The mean severity of the postoperative sore throat was 2.10± (minimum score of one and a maximum of 3) without significant difference between the two groups (p=0.344). mean diastolic pressure and SpO2 were significantly lower in the dexmedetomidine group compared with the ketamine group (p=0.047 and 0.001).

Conclusion: both dexmedetomidine and ketamine gargle could be equally useful and effective in reducing postoperative sore throat.

Keywords: Ketamine, dexmedetomidine, Gargle, Postoperative sore throat

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Introduction

Endotracheal tube could be a potential source of discomfort and pain. Irritation by tube cuff pressure increases airway secretions and exacerbates cough and produces more discomfort (1). Endotheracheal intubation related sore thorat after operation is found to be second most common anesthesia related complication after nausea and

vomiting (2). Different methods have been used to attenuate this response, including extubation when patents are in deep anesthesia, administration of intravenous short-acting opioids, intravenous lidocaine, topical lidocaine, and intracuff application of lidocaine. Each of these methods has its limitations (3).

Ketamine is the most widely used N-methyl-D-aspartate receptor antagonist that found in peripheral nerves in addition to the central nervous system, which contributes to anti-inflammatory effects; some studies have proposed that ketamine leads to "Subunit-dependent inhibition" in nicotinic acetylcholine receptors of the human neurons; while others have proposed the role of ketamine as a synaptic transmission depressant molecule in hippocampus medial prefrontal cortex using D1 receptors mediated dopaminergic inflection leading to GABAA receptor augmentation. However, if the NMDA receptor is activated, mu-opioid receptors responsiveness would be diminished (4, 5).

A few studies have demonstrated the anti-inflammatory and topical analgesic effects of ketamine may prevent postoperative sore throat, especially after tracheal intubation (6). In addition, low ketamine doses have been demonstrated to reduce sore throat after pediatric tonsillectomy and decrease morphine intake (7).

Dexmedetomidine, a selective alpha-2 receptor agonist, is also administered for short-term sedation (8) with a specificity and an affinity are up to eight times higher than clonidine; however, needs more investigation (9-11).

This double-blind clinical trial was designed and performed to assess the effectivness of dexmedetomidine gargle before tracheal intubation; in order to assess its analgesic effetcs on prevention of postoperative throat pain and compare them with ketamine gargle.

Methods

A double blinded randomized clinical trial on patients undergoing general anesthesia for emergency abdominal surgeries using rapid sequence induction in Shohada Tajrish Hospital, Tehran, Iran in 2019 was done. This study was approved by Shahid Beheshti University of medical sciences Ethics Committee, (ethical code: IR. SBMU.UETCH.REC. 1398.169) and was registered on Iranian clinical trial registry under the number IRCT20181126041760N2.

All patients with American Society of Anesthesiologists physical status I–II, low to moderate-risk surgeries, 18-64 years old and Operation time 1 to 3 hours needed emergency surgery using succinylcholine were enrolled in the study. preoperative sore throat, upper respiratory tract infection, chronic smoking, any medical condition that limited endotracheal intubation, use of quinolone or tetracycline antibiotics, or history of allergy to Ketamine and Dexmedetomidine were exclusion criteria.

The patients participating in the study were divided into ketamine and dexmedetomidine groups.

Five minutes before anesthesia induction, patients gargled ketamine and dexmedetomidine (0.5 mg and 0.25 µg/kg body weight in 100 ml of water) for one minute. Standard fluid therapy and the same anesthesia induction method (7) were employed for both groups. The anesthesiologist with at least 10 years' experience chose the appropriate tracheal tube of suitable size for each patient and did the direct laryngoscopy.

If intubation was not successful in the first attempt, intubation was difficult, or the oxygen level dropped, the patient was excluded from the study.

Co-induction of anesthesia was administered with midazolam 0.02 mg/kg, fentanyl 2 µg/kg, lidocaine 1 mg/kg, propofol 2 mg/kg, succinylcholine 1.5 mg/kg and the ED 95 dose of atracurium in advance. In addition, isoflurane, neostigmine, atropine, and dexamethasone (4 mg) were used for maintenance and reversal of anesthesia, no opioids were prescribed during operation. If it was necessary to administer opioids during surgery and/or at recovery room, the prescribed values were recorded. Patients were monitored for vital signs, BIS and TOF during surgery.

All investigators, patients, and anesthesia staff were blinded to group allocation. Computer-generated Randomization was accomplished to allocation the patients to Ketamine or Dexmedetomidine group.

Data were analyzed using SPSS 21 software. Descriptive data were analyzed using indices of central tendency such as mean, median and mode and dispersion indices, including standard deviation and variance. Since the total number of samples was over thirty, t-test was used to compare the mean of variables between two groups and the chi-square test to compare qualitative variables. P-value less than 0.05 was considered as statically significant.

Results

Twenty patients in the ketamine group and 20 patients in the dexmedetomidine group were studied. Demographic features and results of pretreatment with Dexmedetomidine and Ketamine on sore throat are shown in Table 1.

As shown in table 1, comparing the mean values of vital signs, including mean BIS, heart rate, systolic blood pressure, and respiratory rate showed no significant difference between both groups ($p>0.05$). However, there was a significant difference in diastolic blood pressure between two groups, with the mean diastolic blood pressure as well as SpO2 in the dexmedetomidine group being lower than that of the ketamine group ($p=0.047$ and 0.001). In addition, there was no significant difference between sore throat severity and dryness between Dexmedetomidine and Ketamine groups ($p=0.34$ and 0.15).

Discussion

Results showed that gargling Dexmedetomidine and ketamine have no significant difference in reducing sore throat severity and incidence of the dry throat in patients after extubation. Results showed that 8 patients (40%) in the ketamine and 12 patients (60%) in the dexmedetomidine group suffered from dry throat (difference was not statistically significant). Even though there was 20% difference in clinical complains (12).

Dexmedetomidine (selective alpha-2 receptor agonist), is water-soluble; so, an injectable formulation is available. dexmedetomidine has hypnotic and analgesic effects and reduces inhaled and intravenous anesthesia demand when used together with other general anesthetics. Dexmedetomidine is also administered for short-term sedation (8).

Edomwonyi et al., found that 63% of patients with endotracheal tube had complications resulting from throat injury. The chief complaints were sore throat in 49%, cough in 36%, and dry throat in 15% of patients (13). In a study by Park et al., the prevalence of dry throat was 11.3% in the chlorhexidine group and 16.7% in the triamcinolone group (two groups were not significantly different in this respect) (14). In both studies, the incidence of dry throat reported was lower compared to our study. Using different interventions and differences in the type of surgery and intubation techniques could be the cause of differences between these studies. Another major cause of the difference in the prevalence of dry throat was the type of anesthetic used for anesthesia induction. In the study by SolatPour et al., 57.5% of participants in the succinylcholine group had sore throat (15), which is similar to the values obtained in our study. In the cis-atracurium group, the prevalence was 17.5%. It is concluded that one of the causes of the high prevalence of throat dryness in ours compared to other studies was the type of drug used to induce anesthesia and that succinylcholine could lead to increased prevalence of dry throat (14, 15).

The second major complication studied in this research was a sore throat. The distribution of sore throat scores showed no significant difference between them. In a study conducted in Iran in 2015, authors investigated the effects of magnesium sulfate and ketamine gargle on sore throat. Results showed that over 40% of participants in both groups had a sore throat during recovery. The prevalence rate remained at about 40-45% in the ketamine group 2, 4, and 24 hours after the surgery, whereas 24 hours after surgery, the prevalence rate in the magnesium group gradually decreased to below 20%. In addition, pain intensity during recovery was about 2.8 in both groups,

Table 1: Preoperative and postoperative serum levels of the studied enzymes in both groups.

		Dexmedetomidine	Ketamine	P value
Age (years, Mean±SD)		28.60±8.525	28.60±9.052	0.1
Gender	**Male**	12	16	0.011
	Female	8	4	
BIS		50.6±7.3	52.0±4.7	0.48
Heart Rate		70.2±8.1	70.8±6.6	0.80
Systolic Blood Pressure (mmHg, Mean±SD)		127.0±14.7	125.0±10.2	0.62
Diastolic Blood Pressure (mmHg, Mean±SD)		78.0±6.9	82.0±5.2	0.047
Respiratory Rate		13.0±1.4	13.6±1.6	0.23
SpO2 (%)		98.4±1.3	99.6±0.5	0.001
Dry throat	Yes	4	8	0.15
	No	16	12	
Severity of Sore throat (12)	1	4	4	0.34
	2	12	8	
	3	4	8	

and it gradually decreased in magnesium and increased in ketamine group. Significant differences were seen between the two groups in postoperative sore throat pain intensity. Researchers concluded that low-dose magnesium sulfate gargle had a greater effect on postoperative sore throat pain intensity compared to ketamine. The prevalence of sore throat in the ketamine group in this study was similar to that in the ketamine group in our research. Moreover, in previous corresponding author's study sore throat pain intensity in the ketamine group during recovery was close to our new results, indicating a similar effect of ketamine on a postoperative sore throat. However, in our study, we did not record pain score in surgery ward.

In another study, researchers showed that the prescribed dose of 40 to 50 mg of ketamine for preoperative gargles before surgery significantly reduced postoperative sore throat at five different times (0, 2, 4, 8, and 24 hours after surgery). The study concluded that using ketamine for preoperative gargle was an excellent way to reduce sore throat pain and discomfort after surgery under general anesthesia (16). This is consistent with the results of our study. Another study compared sore throat pain intensity after surgery and its incidence between ketamine gargle, betamethasone gel applied to the endotracheal tube and a control group. For this purpose, 25 patients

in the ketamine group gargled 40 mg of ketamine in 30 ml saline for 60 seconds, and, for the other 25 patients, the endotracheal tubes were soaked with 0.05% betamethasone before application. In the third group, no action was taken. Sore throat incidence and sore throat pain intensity after surgery in the recovery room and 2, 4, and 24 hours after surgery were measured. The results showed that the incidence of sore throat and postoperative sore throat pain intensity, cough, and hoarseness at all studied times following surgery were less in ketamine compared to betamethasone and control groups. Researchers concluded postoperative incidence of sore throat and pain intensity effectively in ketamine group was reduced; their results were I favor of ours (17).

Gargling Dexmedetomidine could be considered as alternative in particular circumstances in which there is no intravenous access. Patton *et al.* showed that many drugs could prescribed by tracheal route due to lung's permeability to small molecules (18). Recent reports revealed that Dexmedetomidine could decrease the incidence of emergence agitation (19, 20). Our results showed that a single dose of gargled Dexmedetomidine (0.5 µg/kg) has the same effect as the intravenous administration, on reducing cough rate and postoperative pain score with no complications. or significant side effects.

On the other hand our results revealed the reduction of sympathetic and laryngeal nerve sensitivity after extubation using Dexmedetomidine gargle in favor of other previous studies; dexmedetomidine can be absorbed rapidly through the lungs to exert its effect during intratracheal use (21, 22). Dexmedetomidine can reduce the hyperalgesia effect of remifentanil after pain stimulus, mainly through enhancing N-methyl-D-aspartate receptors (both their function and their quantity) which is mainly mediated by activation of protein kinase C and calcium/calmodulin-dependent protein kinase II (22-24). Previous reports showed the efficacy of intranasal Dexmedetomidine as sedative premedication and anxiolytic for decreasing agitation during recovery from general anesthesia (25, 26). Besides, intravenous pretreatment with a single dose of Dexmedetomidine, could attenuate airway reflexes during recovery period after general anesthesia, preventing throat and vocal cord damage and maintain hemodynamic stability (12). Dexmedetomidine (a selective agonist of alpha$_2$ adrenoceptor at locus ceruleus with hypnotic effect) has known adverse effects such as bradycardia, hypotension, and prolonged time of recovery; however, none of these adverse effects occurred in our study that might be related to use appropriate dose of Dexmedetomidine (0.5µg/kg); meanwhile, less frequent side effects of Dexmedetomidine may be related to small number of subjects (only 20 in each group) (27- 33).

The mean values of vital signs were compared in patients of two groups. There were no significant differences in mean BIS values, heart rate, systolic blood pressure, and respiratory rate ($p>0.05$). However, two groups showed significant difference in diastolic blood pressure and oxygen saturation level (SpO2): mean diastolic blood pressure and SpO2 levels had lower values in dexmedetomidine than ketamine group ($p=0.047$ and 0.001). Although these were not important, few clinical studies have investigated the effect of ketamine gargle on vital signs. Previous studies showed that ketamine has no considerable deleterious effect on oxygenation status including SpO2 especially in high risk patients (31-34). The result of this study was also different from those found in our research. However, these studies were conducted to determine the effect of systemic administration of ketamine, whereas ketamine gargle was prescribed in our study. In addition, although our study showed SpO2 values had statistically remarkable difference in two groups, SpO2 levels were clinically acceptable in both groups, i.e. 99.60% in the ketamine group and 98.40% in the dexmedetomidine on average. Moreover, mean diastolic blood pressure levels for the two groups were 82 and 78 mmHg, which indicated a significant statistical difference. However, this difference was not clinically significant. On the other hand, researchers have stated that the administration of ketamine and dexmedetomidine leads to vasoconstriction; therefore, assessment of SpO2 is not reliable when administering ketamine and dexmedetomidine (33-36). Though the above paragraphs consider the results of clinical studies, there are a number of potential explanations that should be sought through cellular and molecular

mechanisms of dexmedetomidine action. So, the last word in the mechanistic explanation for dexmedetomidine is to be said (4- 5, 31-34, 37-38).

This study has some limitations, which need to be considered. First, although we found that Dexmedetomidine gargle medication may have the same effect as ketamine in the reducing severity of sore throat and dry throat. Although our study showed the effectiveness of gargling dexmedetomidine, more studies is now required to accept routine clinical use of this method. multiple centers studies with more subjects might be needed to reach more acceptable results and to record all side effects of Dexmedetomidine gargle. This study tested a single dose of Dexmedetomidine (0.5µg/kg); therefore, effects of different doses of Dexmedetomidine gargle on airway reflexes can be investigate in next studies.

Conclusion

The current study offers perioperative use of Dexmedetomidine gargle at a dose of 0.5µg/kg that could be as effective as ketamine to smooth extubation and balanced anesthesia recovery. Dexmedetomidine gargle should be considered as an alternative to ketamine for attenuating sore throat caused by rapid sequence induction and intubation for general anesthesia.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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