



A RANDOMIZED CONTROLLED STUDY OF REDUCTION IN SEVERITY OF POSTOPERATIVE SORETHROAT USING PREOPERATIVE KETAMINE NEBULIZATION.

Anesthesiology

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ABSTRACT

Endotracheal intubation is the prominent cause of airway mucosal injury which results in postoperative sore throat (POST). This study was conducted to evaluate the efficacy of nebulized ketamine in decreasing POST. 96 patients of the ASA grade 1–2, age 18–60 years, of either sex undergoing general anesthesia (GA) with tracheal intubation were randomized into two groups; Group 1 received ketamine 50 mg (1.0 ml) with 4.0 ml of saline nebulization, while Group 2 received saline nebulization 5.0 ml for 15 min before administering GA. On reaching postanesthesia care unit, POST monitoring was done at 0, 2, 4, 6, 12, and 24 h after extubation and graded on a four-point scale (0–3).

RESULTS: There was statistically significant reduction in severity of sore throat in ketamine group at 4 h ($P = 0.030^*$) and 6 h ($P = 0.016^*$) postextubation as compared to saline group.

CONCLUSION: Preoperative ketamine nebulization effectively reduced the incidence and severity of POST, with no adverse effects.

KEYWORDS

General anesthesia; intubation; ketamine; nebulization; sorethroat

INTRODUCTION

Postoperative sore throat (POST) is a usual complaint after endotracheal intubation, resulting in agony and disappointment to the patient with the quality of recovery from anesthesia. Various nonpharmacological and pharmacological methods had been studied extensively for decreasing POST with varying results.^[1,2,4,5] It is noted that N-methyl-D-aspartate (NMDA) has a role in nociception and inflammation.^[3] Ketamine, an NMDA receptor antagonist, has been used for decreasing POST because of its anti-nociceptive and anti-inflammatory action, as gargle as well as in nebulized form.^[4,5] However, nebulized ketamine is better tolerated in patients due to many reasons such as: It saves the patient from the bitter taste of ketamine, also much lesser volume is needed as against larger volumes required for gargle.^[5] This study was undertaken to evaluate the effectiveness of nebulized ketamine in alleviating POST in our population.

METHOD

After obtaining approval from hospital ethics committee and informed written consent, 96 patients, in the age group of 18–60 years, with American Society of Anesthesiologists (ASA) grade 1–2, who were scheduled to undergo elective surgical procedures in supine position under general anesthesia (GA) with endotracheal intubation, were enrolled in this prospective, double-blind, randomized, placebo-controlled study. Exclusion included history of preoperative sore throat, upper respiratory tract infection, chronic obstructive pulmonary disease, known allergy to study drug, pregnancy, Mallampati Grade >2, undergoing oral, nasal, head-and-neck surgeries, those required more than one attempt at intubation.

Patients recruited for the study were kept fasted for 6 h preceding surgery. On arrival at the operating room, patients were monitored by electrocardiogram, noninvasive blood pressure and pulse oximetry (SpO₂). Enlisted 96 patients were randomly allocated into two groups of 48 each: Group 1 received ketamine 50 mg (1 ml) with saline (4 ml) nebulisation and Group 2 received saline nebulization (5 ml), given through nebulization mask connected to wall-mounted oxygen driven source (8 L, 50 psi) for 15 min (min). GA was induced 15 min after completing nebulization, with intravenous (IV) fentanyl 2 mcg/kg and IV propofol 2 mg/kg. Three minutes after administering IV atracurium besylate 0.5 mg/kg, brisk and gentle laryngoscopy lasting <15 s, was done by an experienced anesthesiologist using a Macintosh laryngoscope blade (size 3 or 4). Trachea was then intubated with a sterile single-lumen cuffed polyvinyl chloride tracheal tube with an internal diameter of 7–7.5 mm for women and 8–8.5 mm for men. Tracheal tube cuff was inflated with a volume of room air until no air leakage was audible.

GA was maintained with oxygen 33% in nitrous oxide and isoflurane.

Analgesia during surgery was supplemented with paracetamol 1 g IV, thereafter 6th hourly in the postoperative period. IV ondansetron 4 mg was administered 30 min before the end of surgery and then 8th hourly in the postoperative period. At the end of surgery, the oropharynx was suctioned, using a soft disposable suction catheter and neuromuscular block was reversed with IV neostigmine 50 mcg/kg and glycopyrrolate 10 mcg/kg. The endotracheal tube was removed when the patient regained complete consciousness. After shifting the patient to postanesthesia care unit (PACU), sorethroat was assessed by the staff nurse in PACU, who was unaware of the group allocation of the patient, at 0, 2, 4, 6, 12, and 24 h postoperatively, from the time of extubation. POST was graded on a four point scale (0–3): 0 = no sore throat; 1 = mild sore throat (complains of sore throat only on asking); 2 = moderate sore throat (complains of sore throat on his/her own); and 3 = severe sore throat (change of voice or hoarseness, associated with throat pain). Even after 24 h, if patients still had moderate or severe sore throat, lukewarm saline gargle and decongestants were prescribed. If the symptoms still persisted, they were referred for oto-rhino-laryngology consultation. Side effects if any were noted 8th hourly during the first 24 h after extubation. The primary outcome of our study was to assess how effective ketamine nebulization was, in alleviating POST in adult patients undergoing GA. Secondary outcome being evaluation of side effects such as postoperative nausea and vomiting, cough, dry mouth, hallucinations, respiratory depression, and hemodynamic instability in both the groups.

With 95% confidence level and power of study at 80%, the minimum sample size required was found to be 48 in each group. The statistical calculations were performed using the software Statistical Package for the Social Sciences (SPSS) for Windows version 15.0 (SPSS Inc., Chicago, IL, USA). Student *t*-test and Chi-square test were used. The level of significance was set at 0.05.

RESULTS

Ninety six patients were recruited and allocated into two groups of 48 each. Both groups were comparable in distribution of age, gender, body weight, ASA, and duration of surgery [Table 1]. In this study, the overall incidence of POST was 25%: Seven patients in Group 1 (ketamine) and 17 patients in Group 2 (saline) developed POST at some point of the study.

Table 1: Demographic & clinical characteristics

Characteristics	Group 1	Group 2	P
Age (years)	38.94 (14.58)	35.17 (13.41)	0.190
Weight (kg)	63.67 (8.45)	66.29 (7.93)	0.110
Duration of surgery (min)	87.29 (18.62)	92.88 (15.6)	0.108
Male/female	22/26	22/26	1.00
ASA (Grade 1/2)	29/19	31/17	0.673

Data expressed as mean (SD) SD: Standard deviation; ASA: American Society of Anesthesiologists

Table 2: Severity of postoperative sore throat in patients

Time period	Sore throat grade	Group 1	Group 2	P
0h	0	41	33	0.123
	1	7	14	
	2	0	1	
2h	0	42	32	0.051
	1	5	14	
	2	1	2	
4h	0	42	31	0.030*
	1	5	13	
	2	1	4	
6h	0	42	31	0.016*
	1	6	13	
	2	0	4	
12h	0	43	35	0.079
	1	5	11	
	2	0	2	
24h	0	44	37	0.124
	1	4	10	
	2	0	1	

None of the patients had severe sorethroat (Grade 3) in both groups. No adverse effects were noticed in both groups.

DISCUSSION

POST is a frequent complaint after endotracheal intubation, which results in significant patient discomfort. Several trials had been done recently with ketamine, an NMDA-receptor antagonist, in various routes such as gargle, nebulization as well as IV, in reducing POST.^[3,4,5] The present study was designed to determine the effectiveness of nebulized ketamine in attenuating POST, following GA with tracheal intubation. Several factors have been identified in earlier studies contributing to sore throat after surgery, including patient age, sex, cuff design, intracuff pressure, and tracheal tube size.^[6] In our study, both groups were comparable demographically and clinically, hence no correlation with sore throat was noted. POST is probably caused by injury to the pharyngeal mucosa during laryngoscopy, resulting in an aseptic inflammatory process or irritation to the tracheal mucosa produced by endotracheal tube cuff or it can also be due to injury to tissues during intubation and extubation.^[6] Chan *et al.*, in his study using ketamine gargle for reducing POST,^[7] measured intraoperative serum ketamine levels. They demonstrated low serum levels of ketamine and suggested a topical action of ketamine resulted in the attenuation of POST rather than a systemic effect. Hence, the significant reduction in the incidence and severity of postoperative sore throat in our study can be attributed to the topical effect of ketamine nebulization, by its NMDA-antagonistic and anti-inflammatory action, which relieved the local inflammation and produced peripheral analgesia.^[3,8]

In a study done by Ahuja *et al.*,^[5] they observed a decrease in the incidence of POST in ketamine group, which was statistically significant only at 2 h and 4 h postoperatively and concluded that ketamine nebulization when given preoperatively lessened the incidence and severity of POST, particularly during the initial hours of postoperative period. However, in the present study, we noticed that the incidence of POST in ketamine group showed a statistically significant decrease at 2, 4, 6, 12, and 24 h, postextubation. In an experimental animal study, ketamine nebulization was reported to have a shielding effect on airway inflammation.^[9] In another study, 3.0 ml (225 mg) of isotonic magnesium sulfate which is also a NMDA-receptor antagonist, when given preoperatively, revealed an attenuation in severity of POST at 0, 2, 4, and 24 h postoperatively.^[9] Hence, a prophylactic use of nebulized ketamine could prevent airway inflammation and cause peripheral analgesia, which might be responsible for the significant decline in the incidence and severity of sorethroat in this study, during the first postoperative day. We used nebulized form of ketamine in this study instead of its other forms such as oral, IV or gargle, mainly due to the fact that, it was safe and more easy to administer to the patient, especially at a time immediately before surgery. For this, we used a wall-mounted oxygen driven nebulization method. In this method, liquid is broken up into droplets by the compressed air. Largest droplets are filtered within the nebulizer, but larger particles (10–25 microns) mostly deposit in

mouth and throat and those of 5–10 microns diameter get deposited in a passage from mouth to airway.^[10] This settling of aerosol in mouth and upper airway might probably be the reason for the decreased incidence and severity of POST in ketamine group, due to its topical analgesic, anti-inflammatory, and NMDA-receptor antagonistic effect.

CONCLUSION

Preoperative administration of nebulized ketamine effectively attenuated the incidence and severity of POST in patients undergoing GA with endotracheal intubation, with no adverse effects.

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Conflicts of interest

There are no conflicts of interest.

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