Original Article

Efficacy of Tramadol Nebulizaton in Reducing Post-Operative Sore Throat

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ABSTRACT

Objective: To compare the efficacy of preoperative tramadol nebulization versus placebo in reducing postoperative sore throat.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Departments of Anesthesiology, Lahore General Hospital, Lahore and Arif Memorial Teaching affiliated with Rashid Latif Medical College Lahore from January 2018 to June 2018.

Materials and Methods: One hundred and sixty-four patients, aged 20-50 years undergoing general anesthesia. Group A was given pre-operative tramadol nebulization 1mg/kg in 3ml normal saline while Group B was given normal saline nebulization. Nalbuphine 0.1 mg per kg was used for intraoperative analgesia. After application of standard monitoring, induction was done with Propofol 2mg/kg and tracheal intubation with atracurium 0.5mg/kg. Maintenance of anesthesia was done with oxygen, nitrous and isoflurane 1.2% with IPPV. After extubation all patients were assessed after 12 hours for sore throat, hoarseness and pain (VRS score).

Results: The mean age of the patients was 38.65 ± 8.37 years in the tramadol group and 37.03±9.66 years in the placebo group (P-value = 0.311). 71.9% patients achieved efficacy of the drug in the tramadol group and 51.6% attained in the placebo group in terms of no or mild post-operative sore throat (p = 0.018).80.8% males in the tramadol group had no or mild sore throat as compared to65.8%) females.

Conclusion: Pre-operative tramadol nebulization can significantly reduce the incidence of POST as compared to placebo.

Key Words: Efficacy, Placebo, POST, Sore throat, Tramadol

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INTRODUCTION

Postoperative sore throat is an accepted phenomenon following general anesthesia with a reported incidence of 21-66%.[1-3] Postoperative sore throat (POST) is experienced by 30% to 65% of the patients after general anesthesia despite being perceived as a trivial problem.[4] POST is a major cause of patient annoyance and physical discomfort during the recovery phase and post hospital discharge and thus should be prevented.[2,5,6] Symptoms of sore throat manifests as dysphagia, dysphonia, hoarseness, continuous throat pain and pharyngealdryness.[3]

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It is attributed to various perioperative conditions, including local irritation and inflammation of airway, mucosal injury in the trachea, oropharyngeal suctioning, intra cuff pressure, use of throat pack, size of the endotracheal tube, duration of surgery and multiple attempts of intubation.[2] Female sex, pre-existing pulmonary disease, anesthesia time and staining of blood on tracheal tube on extubation are all related to the greatest risk of postoperative sore throat.[7] The peak of sore throat is in the initial period after surgery, 2 to 6 hours after extubation, but the incidence decreases quickly with time.[3]

Several techniques have been evaluated to reduce POST like drug-free interventions such as relatively small sized endotracheal tubes, reducing intracuff pressure to less than 18cm H^2O, lubrication of the endotracheal tube with water-soluble jelly, gentle airway handling, intubation with maximum muscle relaxation and extubation after full deflation of tracheal cuff.[8] Pharmacological measures such as clonidine, betamethasone gel, benzydamine hydrochloride, NSAIDs, local anaesthetics, ketamine gargles and chamomile extract spray have been used to reduce POST with variable responses.[1] Simple, safe, and inexpensive therapies to reduce or eliminate POST would be helpful and could improve patient satisfaction significantly.

Experimental studies have shown that NMDA (N-methyl-D-aspartate) receptor antagonists when intravenously administered have anodyne and anti-inflammatory effects and were effective in reducing POST.[2] Tramadol hydrochloride is a synthetic analogue of codeine, an opioid receptors agonist and a NMDA receptor antagonist. It hampers reabsorption of monoamines (noradrenaline and serotonin) and has some local anesthetic effect as well.[2] It acts on peripheral nerve endings in the pharyngeal mucosa and can reduce the incidence of sore throat.[8] The positive effects of tramadol on reducing sore throat have been seen in early research. In a study conducted by Lee CP et al, preoperative gargling with tramadol comforted pain in early POST.[9] Rashwan et al[10] in his study found the occurrence of postoperative sore throat to be remarkably low with preoperative tramadol gargles in comparison to placebo.

MATERIALS AND METHODS

It is a randomized controlled trial conducted at the Departments of Anesthesiology, Lahore General Hospital, Lahore and Arif Memorial Teaching affiliated with Rashid Latif Medical College Lahore from 1st January 2018 to 30th June 2018. A total of 164 patients were enrolled. All patients undergoing elective general anesthesia with an age range of 20 to 50 years, including both genders belonging to ASAI and ASAII were included. Approval was seeked from hospital ethical committee and informed consent was obtained from each patient. Group A was given pre-operative tramadol nebulization 1mg/kg in 3ml normal saline (treatment group) while Group B was given normal saline nebulization (placebo group). No other preoperative sedative premedication was used. Nalbuphine 0.1 mg per kg was used for intraoperative analgesia. After application of standard monitoring, induction was done with Propofol 2mg/kg and tracheal intubation with atracurium 0.5mg/kg. Oxygen, nitrous and isoflurane 1.2% with IPPV were used for maintenance of anesthesia. At the end of surgery reversal was given and patient extubated. All patients were assessed after 12 hours for sore throat, hoarseness and pain (VRS score).

Data was analyzed by SPSS 20. Descriptive statistics were calculated for outcome variables. T-test for continuous and Chi-square test for categorical was applied to check the significance among groups. P-value ≤ 0.05 was considered as significant.

RESULTS

The mean age of the patients in tramadol group was 38.65 ± 8.37 years and 37.03±9.65 in the placebo group (Table 1). Baseline body mass index among patients of both groups was comparable and calculated to be (25.47±2.82 vs 25.71±3.10) kg/m^2 in tramadol versus placebo group respectively (Table2). The mean verbal rating scale score was calculated to be 2.64±1.66 in tramadol group versus 3.89±2.39 in the placebo group. Significant difference was detected for the VRS score among both groups with P-value = 0.001 (Table 3). In the tramadol group patients, the efficacy (in terms of no or mild post-operative sore throat) was observed in 46/64 (71.9%) and 33/64 (51.6%) in placebo group. Significant difference was seen in the occurrence of sore throat among the groups (p=0.018). The percentage of efficacy was better in the tramadol group (Table 4).

Table No.1: Comparison of age

Group	Mean±SD	P value
Group A (Tramadol)	38.65±8.37	0.311
Group B (Placebo)	37.03±9.66	

Table No.2: Comparison of body mass index (mg/m^2)

Group	Mean±SD	P value
Group A (Tramadol)	25.47±2.83	0.637
Group B (Placebo)	25.71±3.10	

Table No.3: Comparison of verbal rating scale

Group	Mean±SD	P value
Group A (Tramadol)	2.64±1.66	0.001
Group B (Placebo)	3.89±2.39	

Table No.4: Comparison of efficacy of treatment

Group	Efficacy		P value
	Yes	No	
Tramadol			
Count	64	18	0.018
% within Groups of the patients	71.9%	28.1%	
Placebo			
Count	33	31	
% within Groups of the patients	51.6	48.4	

Table No.5: Comparison of operative time according to efficacy of the drug

Operative time (min)	Efficacy of the drug	Tramadol	Placebo	P value
≤60	Yes	12 (75%)	10(62.4%)	0.446
	No	4 (25%)	6 (37.6%)	
>60 to ≤120	Yes	25(71.4%)	16(59.3%)	0.315
	No	10(28.6%)	11(40.7%)	
>120 to ≤180	Yes	9(69.2%)	7(33.3%)	0.042
	No	4(30.8%)	16(66.7%)	
Total	Yes	46(71.9%)	33(51.6%)	0.018
	No	18(28.1%)	31(48.4%)	

No significant difference was found among the groups with duration of surgery less than 120 minutes (p value=0.315). In surgical procedures lasting for more than 120 minutes, significant difference was seen among the groups. In tramadol group 69.2% (9/13)

patients versus 33.3% (7/21) in placebo group did not complain of sore throat (p value=0.042) (Table 5). When data was stratified with respect to gender it revealed that 21/26 (80.8%) males in the tramadol group had no or mild sore throat as compared to females 25/38 (65.8%) in the tramadol group which demonstrate that the highest efficacy was achieved in males with statistically significant difference between the groups [p = 0.015] (Table 6).

Table No.6: Comparison of gender according to groups

Gender	Tramadol	Placebo	Total
Male			
Count	26	32	58
% within Groups of the patients	40.6%	50%	45.3%
Female			
Count	38	32	70
% within Groups of the patients	59.4%	50%	54.7%

DISCUSSION

Postoperative sore throat has a complex etiology, and multiple factors contribute to POST include age, sex, type of surgery, mode of anesthesia, dimensions and cuff pressure of endotracheal tube, pharyngolaryngeal mucosal trauma from laryngoscopy, injury while insertion of airway, suctioning, and procedural handling of the airway and surrounding tissue.[1,3] It indicated that irritation of pharynx, larynx, or trachea leading to inflammation may be the causes for POST.[8] There are various pharmacological methods for prevention of POST and include steroid both in intravenous and topical preparation, topical benzydamine hydrochloride, topical magnesium, ketamine gargles and topical liquorice.[3] According to study by Subedi et al[11] dexamethasone lowered the incidence of POST. Ahuja et al[12] concluded that ketamine nebulization markedly reduced the prevalence and intensity of POST, especially in the immediate post-operative period with no harmful outcomes. Similar results were observed by Amingad and Jayaram[13] who found ketamine nebulization to be effective in attenuating POST. Although previous studies have been done with different drugs by nebulization but data is sparse with tramadol use for POST. Pneumatic nebulization generates large sized particles which deposit in the mouth and throat during nebulization rendering low frequency and severity of post-operative sorethroat.[1]

The current study showed that tramadol nebulization 1mg/kg in 3ml normal saline administered pre-operatively reduced POST, at 12 hours after surgery, post general anesthesia with laryngoscopy and or tracheal intubation. Tramadol nebulization showed no side effects in the treatment group. It is suggested that NMDA antagonists significantly reduced the frequency and severity of POST because of their pain relieving and anti-inflammatory effects.[14]

The efficacy in our study results was achieved in 71.9% of the patients in the tramadol group in comparison to 51.6% in the placebo group however the incidence of postoperative sore throat (regardless of its severity) was notably reduced in tramadol treated group compared to placebo group. Consistent with the results of our study, Yadav and Gopinath compared the effect of Ketamine, tramadol, 1.5% saline and normal saline gargles on postoperative sore throat and found decrease in incidence of sore throat with ketamine and tramadol after 2,4 and 24 hours ($p < 0.05$). They did not find any marked difference in incidence of sore throat in association with gender which was different from our study.[8]

Similar to the current study results, the work done by Kudva and Hegde found preoperative Tramadol gargle to be proportional with Ketamine gargle in reducing the incidence and severity of POST at 2,4 and 24 hours postoperatively.[2]

Lee et al[9] compared tramadol and benzydamine gargle in relieving POST after Proseal Laryngeal Mask Airway (PLMA) anesthesia. Similar to our study results they found significantly few patients complaining of sore throat with preoperative tramadol gargling at 30 minutes of removal of PLMA. In contrast to our observation POST was not affected by duration of surgery in their study which could be because of placement of PLMA and not ETT.

Comparable to our results, the frequency of postoperative sore throat (regardless of its severity) was significantly lower in tramadol treated group compared to placebo group at 2, 6, 12, and 24 h ($p<0.05$) in study by Rashwan et al.[10]

Farzam et al[15] studied the effects of tramadol and lidocaine gel on complications of or otrachea lintubation. Inconsistent with the results of our study they did not find significant effect on reduction of sore throat with 5% tramadol gel and 2% lignocaine gel. The difference in results could be due to use of gel in comparison to our study where we nebulized with tramadol.

The etiology of POST includes exasperation of the mucosa and cuff-induced pressure on the mucosa followed by an aseptic inflammatory process. Tramadol is NMDA receptor antagonist that acts on peripheral nerves of pharyngeal mucosa and thus reduces inflammation.[8, 14]

One limitation of our study was that we did not observe the haemodynamic changes and side effects that could have occurred with tramadol nebulization. Also serum levels of tramadol were not measured. Future studies can be done with different doses of tramadol and measuring the hemodynamic changes and serum levels.

CONCLUSION

Pre-operative tramadol nebulization can significantly reduce the incidence of post-operative sore throat as compared to placebo in patients undergoing elective surgeries utilizing general anesthesia. Thus we can make some practical recommendations in our routine practice guidelines to decrease post-operative sore throat in order to improve the patient's satisfaction and decrease the morbidity of patients.

Author's Contribution:

Concept & Design of Study:	Umar Iqbal
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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