Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(4): 579-585
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5418.12

Comparison of the Effect of Ketamine, Tramadol, 1.5% Saline and Normal Saline Gargle on Post-Operative Sore Throat after Endotracheal Intubation

Monu Yadav[1], R. Gopinath[2]

[1]Associate Professor [2]Professor and Head, Department of Anaesthesiology and Critical Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana 500082, India.

Abstract

Postoperative sore throat (POST) is a frequent complaint following endotracheal intubation with incidence rates varying from 14.4% to 61%. Regardless of the incidence or duration, POST is rated as a patient's 8th most undesirable outcome in the postoperative period, and is certainly an opportunity to improve patient outcomes.

Background and Objectives: Various non-pharmacological and pharmacological trials have been used for attenuating POST with variable success. The aim of the present study was to compare the effect of ketamine, tramadol and 1.5% saline gargle in prevention of post-operative sore throat.

Methods and Material: Following institutional ethical committee approval and written informed consent, a prospective randomized double-blinded study was conducted in 100 cases divided into four groups of 25 patients in each group. Patients included in the study were of age group 18- 60 years, ASA grade I-II, undergoing elective surgeries with duration of surgery approximately 2 hrs or more requiring tracheal intubation. Patients were allocated randomly to four groups, Group A, Group B, Group C and Group D. After shifting patient to operation theatre 5 mins prior to induction of anesthesia, Group A received 30ml of normal saline, Group B preservative free ketamine 1ml (50 mg) in 29 ml of normal saline, Group C received tramadol 1ml(50 mg) in 29ml normal saline and Group D received 30ml of 1.5% saline to gargle for 30 seconds. Postoperatively presence of sore throat was noted at rest and on swallowing immediately after extubation, at 2 h, 4 h, and 24 h.

Statistical Analysis Used: IBMSPSS_21 was used for statistical analysis.

Results: There was no significant difference in POST at rest (Figure 1) at 0 hr, 4 hr and 24 hr postoperatively among the four groups. Incidence of POST at rest at 2hr was significantly lower in ketamine group. Ketamine caused significant reduction in POST at swallowing (Figure 2) at 2 & 4hrs. Tramadol caused significant reduction at 2 & 4 hrs. 1.5% saline caused significant reduction in POST at swallowing at 2hrs.

Conclusions: Among all the groups ketamine was found to be most effective in prevention of POST followed by tramadol. Based on the risk estimate analysis even 1.5% saline reduces incidence of POST.

Keywords: Postoperative; Complication; Endotracheal Intubation.

Introduction

Postoperative sore throat (POST) is a frequent complaint following endotracheal intubation with incidence rates varying from 14.4% to 61%. It ranks along nausea as the most common complaint after endotracheal intubation for general anaesthesia [1]. Regardless of the incidence or duration, POST is rated as a patient's 8th most undesirable outcome in the postoperative period, [2] and is certainly an opportunity to improve patient outcomes [3].

Various non-pharmacological and pharmacological trials have been used for attenuating POST with variable success. Among the non-pharmacological

Corresponding Author: Monu Yadav, Associate Professor, Department of Anaesthesiology and Critical Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana 500082, India.
E-mail: monubalbir@yahoo.co.in

Received on 23.01.2018, **Accepted on** 17.02.2018

methods, smaller-sized endotracheal tubes, lubricating the endotracheal tube with water-soluble jelly, careful airway instrumentation, intubation after full relaxation, gentle oropharyngeal suctioning, minimizing intracuff pressure (<20mmhg), and extubation when the tracheal tube cuff is fully deflated have been reported to decrease the incidence of POST [4]. The pharmacological methods include inhalation of beclomethasone, fluticasone and gargling with azulenesulphonate, aspirin and licorice [5-7].

Preemptive application of locally active anti-inflammatory and analgesic agents may reduce the discomfort associated with airway inflammation. In this regard ketamine(phencyclidine derivative) and benzydine hydrochloride (topical NSAID) have been used independently as preoperative gargle and have been noted to decrease the incidence and severity of POST [7]. Role of n-methyl-d-aspartate (NMDA) in nociception and inflammation is already known [8,9]. NMDA receptors are found in peripheral nerves and in the central nervous system [10,11]. Hence NMDA antagonists such as ketamine and tramadol act on peripheral nerve endings in pharyngeal mucosa and can reduce the incidence of sore throat [12]. Although no literature is available about role of hypertonic saline for reducing POST. It has been hypothesized that similar to its role for providing symptomatic relief in acute bronchiolitis and sore throat due to upper respiratory tract infections it may be beneficial in POST too [13]. In view of making it palatable we diluted hypertonic saline to 1.5% saline. In our study we plan to compare the efficacy of ketamine, tramadol, 1.5% saline and normal saline gargles to reduce the incidence of POST.

Aim of the Study

Primary aim is to compare the effect of ketamine, tramadol, 1.5% saline and normal saline gargle in prevention of post-operative sore throat.

Materials and Methods

Following institutional ethical committee approval and written informed consent, a prospective randomized double-blinded study was conducted in 100 cases divided into four groups of 25 patients in each group.

With the level of significance (alpha) = 0.05, and power of 80%, sample size required was 20 per group. To accommodate any exclusion, 25 patients from each group were selected.

Patients included in the study were of either gender, 18 to 60 years age belonging to physical status (American Society of Anesthesiologist) ASA grade 1 or 2, undergoing elective surgery of duration of approximately 2 h or more and requiring tracheal intubation. Patients with neuromuscular disease, allergy or hypersensitivity of drugs, on steroid therapy, undergoing oral cavity and pharynx surgeries with use of nasogastric tube were excluded.

Patients who required more than two attempts at intubation or had bucking or coughing during intubation were also excluded.

Patients were allocated randomly to four groups, Group A, Group B, Group C and Group D.

Simple randomization was done using SPSS software (IBM, SPSS Statistics 21).

All patients were kept fasting overnight and premedicated with oral alprazolam 0.5 mg and ranitidine 150 mg on night before surgery and on the morning of surgery. After shifting patient to operation theatre Group A received 30ml of normal saline, Group B received preservative free ketamine 1ml (50 mg) in 29 ml of normal saline, Group C received tramadol 1ml (50 mg) in 29ml normal saline and Group D received 30ml of 1.5% saline to gargle for 30 seconds, 5 mins prior to induction of anesthesia.

The solution for gargling was administered by anaesthesiologist not associated with the management of the case. The anaesthesiologist anesthetizing the case and those recording the scores were blinded to it. In the operation theatre, after connecting the patient to standard monitoring intravenous access was secured. Anesthesia was induced with fentanyl 2 mcg/kg and thiopentone 5 mg/kg. Tracheal intubation was facilitated by atracurium 0.6 mg/kg, and the trachea intubated with soft seal cuffed sterile polyvinyl chloride tracheal tube (Portex Limited CT 21, 6JL, UK) of 7 mm inner diameter in female and 8 mm in male patients. The tracheal tube cuff was inflated with air.

The cuff pressure was checked just after intubation using hand held endotracheal cuff pressure monitor (Portex Cuff Inflator/Pressure Gauge, SIMS Portex, Hythe, Kent, UK) and then every half hourly till end of surgery and maintained at 20 cm of H2O.

Ventilation was controlled, and no nasogastric tube was inserted. Anesthesia was maintained with 66% nitrous oxide in oxygen with 1% of isoflurane and intermittent doses of atracurium and fentanyl as required. The last dose of atracurium was given 20 min prior to extubation. At the end of surgery, the muscle relaxation was reversed with a combination

of neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. The patients were extubated after meeting regular extubation criteria (like return of consciousness, adequate muscle power, sustained head lift for 5 seconds, sustained hand grip for 5 seconds, spontaneous ventilation, and the ability to follow verbal commands with eye opening), and the patients were shifted to post anaesthesia care unit. Presence of sore throat was noted at rest (Figure 1) and on swallowing (Figure 2) immediately after extubation, and 2 h, 4 h, and 24 h postoperatively. In the postoperative ward, patients were also monitored for any drug-related side effects.

Statistical Analysis

Data was expressed as mean and 95% confidence interval of mean and tests of normality (Kolmogorov-smirnov, shapiro-wilk) for continuous variables (height, weight, age) were used. Categorical data (gender) was expressed as frequency of occurrence. Comparison of continuous data between groups was done using ANOVA of means. P value of <0.05 was considered statistically significant. Comparison of categorical data between groups was done using pearson chi- square, continuity correction, likelihood ratio, fishers exact test, P value of <0.05 was considered statistically significant. IBMSPSS_21 was used for statistical analysis.

Results

There were hundred patients were enrolled into 4 groups of the present study. There were no significant differences between four groups in terms of age, sex, and weight.

1. No significant differences between the groups were observed by one way ANOVA for continuous variable, age and weight and chi-square test for categorical variable, gender. P<0.05 was considered statistically significant. Demographic data was presented as either, mean with 95% confidence interval for mean or as numbers (Table 1).
2. There was no significant difference in POST at rest (Figure 1) at 0 hr (Table 2), 4 hr (Table 4) and 24hrs (Table 5) among the four groups. Incidence of POST at rest at 2hr (Table 3) was significantly lower in ketamine group.
3. Incidence of POST at swallowing (Figure 2) at 0hrs (Table 6) and 24hrs (Table 9) was not significantly different among the groups.

   Significant difference in POST at swallowing was seen at 2hrs (Table 7) with ketamine, tramadol and 1.5% saline as compared to normal saline. But based on relative risk assessment ketamine

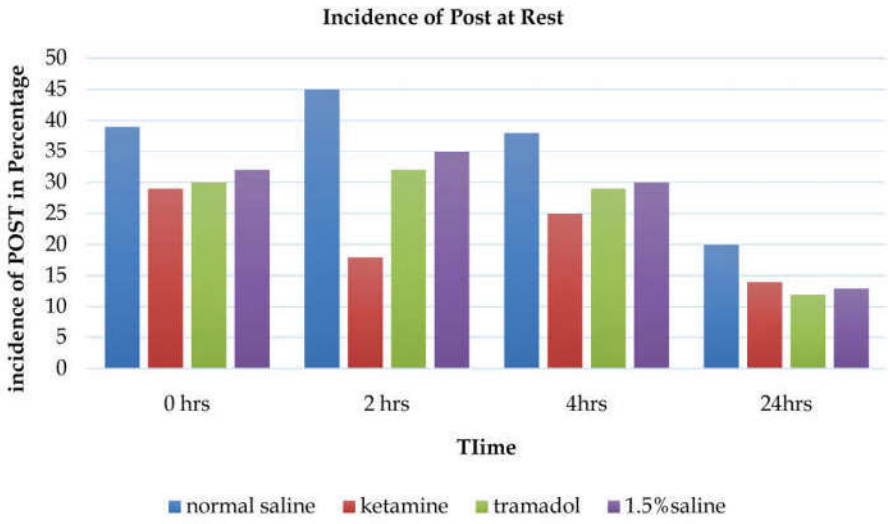

Fig. 1: Incidence of POST at rest

Table 1: Demographic data

Variables	Group A (normal saline)	Group B (ketamine)	Group C (tramadol)	Group D (1.5% saline)	P Value
Age(years)	50.8±11.9	51.5±12.7	52.3±12.4	52.48±10.18	0.325
Sex(male/female)	14/11	13/12	15/10	12/13	0.46
Weight (Kgs)	68±9.08	61±9.06	60±9.45	63±9.1	0.09

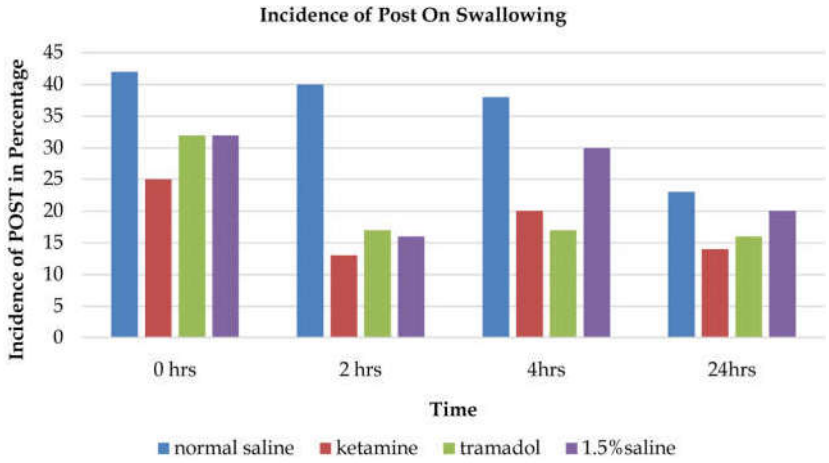

Fig. 2: Incidence of POST on swallowing

Table 2: Incidence of POST at rest at 0 hour

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. When N.S is Used
N.S (n=25)	36%			
Ketamine (n=25)	28%	0.135	0.261	1.64
Tramadol (n=25)	28%	0.614	0.315	1.23
1.5% SALINE (n=25)	32%	0.025	0.013	1.12

Table 3: Incidence of POST at rest at 2hrs

Drug	POST	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS Used
N.S (n=25)	44%			
Ketamine (n=25)	16%	0.04	0.03	3.61
Tramadol (n=25)	32%	0.08	0.12	1.57
1.5% Saline (n=25)	36%	0.23	0.32	1.32

Table 4: Incidence of POST at rest at 4hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS used
N.S (n=25)	36%	-	-	-
Ketamine (n=25)	24%	0.13	0.24	1.67
Tramadol (n=25)	28%	0.45	0.32	1.43
1.5% Saline (n=25)	32%	0.23	0.26	1.32

Table 5: Incidence of POST at rest at 24hrs

Drug	Post	Pearson Chi Square p value	Fishers Exact Test	R.R. when N.S IS Used
N.S (n=25)	20%			
Ketamine (n=25)	16%	0.09	0.12	1.22
Tramadol (n=25)	12%	0.34	0.46	1.54
1.5% saline (n=25)	12%	0.21	0.25	1.46

Table 6: Incidence of POST on swallowing at 0hr

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS used
N.S (n=25)	44%			
Ketamine (n=25)	24%	0.13	0.09	1.89
Tramadol (n=25)	32%	0.37	0.32	1.41
1.5% saline (n=25)	32%	0.26	0.30	1.32

Table 7: Incidence of POST on swallowing at 2hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S is used
N.S (n=25)	40%			
Ketamine (n=25)	12%	0.02	0.03	3.34
Tramadol (n=25)	16%	O.03	0.03	2.56
1.5% saline (n=25)	16%	0.03	0.04	2.64

Table 8: Incidence of POST on swallowing at 4hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S IS used
N.S (n=25)	36%			
Ketamine (n=25)	20%	0.04	0.04	4.3
Tramadol (n=25)	16%	0.03	0.04	2.6
1.5% saline (n=25)	28%	o.14	0.09	1.8

Table 9: Incidence of POST on swallowing at 24hrs

Drug	Post	Pearson Chi square P Value	Fishers Exact Test	R.R. when N.S Is Used
N.S (n=25)	24%	-	-	-
Ketamine (n=25)	12%	0.24	0.13	2.3
Tramadol (n=25)	16%	0.47	0.35	1.9
1.5% Saline (n=25)	20%	0.51	0.62	1.2

caused more decrease in incidence of POST at swallowing at 2hrs compared to tramadol and 1.5% saline. At 4 hrs (Table 8) only ketamine caused significant difference. The other variations observed are due to chance error.

4. With respect to age and gender, there was no significant difference in POST "at rest" and "on swallowing" between the four groups.

Discussion

General anesthesia with endotracheal intubation can result in sore throat and hoarseness which may be considered to be minor by some and troublesome by others. Therefore, identification of risk factors and prevention of these symptoms would add to patient satisfaction. Present study compared the efficiency of preoperative gargle with ketamine, tramadol, 1.5% saline and normal saline in reducing the incidence of post-operative sore throat following general anaesthesia with endotracheal tube for elective surgeries in ASA 1 or 2 cases aged between 18-60 years.

In our study we did not find any significant difference between groups in terms of age, gender and weight. Patient sex, age, gynaecological surgery, use of succinylcholine, larger tracheal tubes, cuff design and intracuff pressures have all been shown to contribute to POST [4,14,15]. Increased incidence of POST in females was reported by Biro et al [1] but in our study we did not find such association of POST with gender.

Similar to the results of study by Canbay et. al., no correlation was observed between incidence of POST, age, weight and duration of intubation [6]. Application of lignocaine jelly was avoided in our study as Maruyama et. al., Kori K et. al. found increased incidence of POST on application of 2% lignocaine jelly to the endotracheal tube [16,17].

Succinylcholine was found to increase incidence of POST by Higgins et. al. [14] Therefore to avoid any bias succinylcholine was not used in our study. Suzuki et al suggested that keeping the cuff pressure under 15mmHg (20.55cm of water) prevented postoperative hoarseness or sore throat at 24hrs. McHardy et al and Suzuki et al found that monitoring and adjustment of intracuff pressure reduces the incidence of POST [18,19]. Therefore in all our cases cuff pressure was maintained at 20mm of water and monitored every 30 min to reduce the effect of this confounding factor.

The incidence of POST in normal saline group was lower in our study as compared to incidence reported by Canbay et al and Agarwal et al respectively in their studies [3,6].

This could be because we standardized the cuff pressure to 20 cm of water, lignocaine jelly on endotracheal tube was avoided and succinylcholine was not used, all of which have been shown to

increase incidence of POST.

In study by canbay et. al. there was increase in incidence of POST at 24hrs. This could be because all patients had undergone septorhinoplasty which causes dryness and inflammation of oral cavity due to mouth breathing in the postoperative period, increasing the incidence of late onset POST [6].

In our study the incidence of POST at rest for Ketamine group was 29%, 18%, 25% and 14% at 0hr, 2hrs, 4hrs and 24hrs respectively.

Our results are comparable to the results of study by Rudra et al who also observed statistically significant reduction in the incidence of POST in ketamine group compared to control group [20].

The incidence of POST on swallowing for tramadol group was 32%, 17%, 17% and 16% at at 0hr, 2hrs, 4hrs and 24hrs respectively. The results are similar to study by Rashwan et al who showed reduction in incidence and severity of POST by tramadol gargle at 2hrs, 6hrs and 12hrs [21].

There are no studies to compare the effect of 1.5% saline on incidence of POST. It was hypothesized that similar to its role for providing symptomatic relief in acute bronchiolitis and sore throat due to upper respiratory tract infections it may be beneficial in POST too [13].

According to risk estimate tables the incidence of POST was significantly more frequent in normal saline group compared to the other three groups with the reduction being maximum in ketamine group. Sore throat after endotracheal intubation might be because of local trauma leading to aseptic inflammation of the pharyngeal mucosa leading to oedema congestion and pain.

NMDA receptors have a role in nociception and inflammation. Ketamine and Tramadol by antagonizing NMDA receptors reduce the inflammation [12].

This may be the reason for reduction of incidence of POST with preoperative ketamine and tramadol gargle in our study. The drawback of our study was absence of measurement of serum ketamine and tramadol levels to know the systemic effects of these drugs. But the doses were low and drugs were given as gargles. No adverse effects were observed.

Conclusion

The incidence of POST in the patients undergoing GA with endotracheal intubation for routine cases is quiet common and remains for next 24 hrs. There was no significant difference between the groups for age, weight and gender. Among all the groups ketamine was found to be most effective in prevention of POST followed by tramadol. Based on the risk estimate analysis even 1.5 % saline reduces incidence of POST. Therefore due to the cost effectiveness and efficacy of the treatment 1.5 % saline may be considered in practice for reducing POST.

Key Message

Due to cost effectiveness and efficacy of the treatment 1.5% saline may be considered in clinical practice for reducing POST.

References

1. Biro P, Seifert B, Pasch T. Complaints of sore throat after tracheal intubation: a prospective evaluation. Eur J Anaesthesiol 2005;22:307–11.
2. Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? The perspective of patients. AnesthAnalg 1999;89: 652–8.
3. Agarwal A, Nath SS, Goswami D, Gupta D, Dhiraaj S, Singh PK. An evaluation of the efficacy of aspirin and benzydamine hydrochloride gargle for attenuating postoperative sore throat: A prospective, randomized, single-blind study. Anesth Analg. 2006;103:1001–3.
4. Ratnaraj J, Todorov A, McHugh T, Cheng MA, Lauryssen C. Effects of decreasing endotracheal tube cuff pressures during neck retraction for anterior cervical spine surgery. J Neurosurg. 2002;97:176–9.
5. Ogata J, Minami K, Horishita T, et. al. Gargling with sodium azulene sulfonate reduces the postoperative sore throat after intubation of the trachea. Anesth Analg. 2005 Jul;101(1):290-3.
6. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. Br J Anaesth. 2008;100:490–3.
7. Agarwal A, Gupta D, Yadav G, Goyal P, Singh PK, Singh U. An evaluation of the efficacy of licorice gargle for attenuating postoperative sore throat: a prospective, randomized, single-blind study. . Anesth Analg. 2009 Jul;109(1):77-81.
8. Lin CY, Tsai PS, Hung YC, Huang CJ. L-type calcium channels are involved in mediating the anti-inflammatory effects of magnesium sulphate. Br J Anaesth. 2010;104:44–51.
9. Zhu MM, Zhou QH, Zhu MH, Rong HB, Xu YM, Qian YN, et al. Effects of nebulized ketamine on allergen-induced airway hyperresponsiveness and inflammation in actively sensitized Brown-Norway rats. J Inflamm (Lond) 2007;4:10.
10. Tan PH, Yang LC, Chiang PT, Jang JS, Chung HC, Kuo CH. Inflammation-induced up-regulation of ionotropic glutamate receptor expression in human

skin. Br J Anaesth. 2008;100:380–4.

11. Carlton SM. Encyclopedia of Pain. Berlin, Heidelberg: Springer; Inflammation, role of peripheral glutamate receptors; 2007.pp.984–7.
12. Chan L, Lee ML, Lo YL. Postoperative sore throat and ketamine gargle. . Br J Anaesth. 2010 Jul;105(1):97.
13. Yen-Ju Chen,Wen-Li Lee, Chuang-Ming Wang,Hsin-Hsu Chou.Nebulized Hypertonic Saline Treatment Reduces Both Rate and Duration of Hospitalization for Acute Bronchiolitis in Infants: An Updated Meta-analysis. Pediatr Neonatol 2014 Dec;55(6):431-8.
14. Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. Br J Anaesth. 2002;88:582–4.
15. Hu B, Bao R, Wang X, Liu S, Tao T, Xie Q, et. al. The size of endotracheal tube and sore throat after surgery: A systematic review and meta-analysis. PLoS One. 2013; 8:e74467.
16. Maruyama K, Sakai H, Miyazawa H, Iijima K, Toda N, Kawahara S, et al. Laryngotracheal application of lidocaine spray increases the incidence of postoperative sore throat after total intravenous anesthesia. J Anesth. 2004;18:237–40.
17. Kori K, Muratani T, Tatsumi S, Minami T. Influence of endotracheal tube cuff lubrication on postoperative sore throat and hoarseness. Masui. 2009;58:342–5.
18. McHardy FE, Chung F. Postoperative sore throat: cause, prevention and treatment . Anaesthesia. 1999;54 (5):444-53.
19. Suzuki N, Kooguchi K, Mizobe T et al. Postoperative hoarseness and sore throat after tracheal intubation: Effect of a low intracuff pressure of endotracheal tube and the usefulness of cuff pressure indicator. Masui 1999;48(10):1091-95.
20. Rudra A, Ray S, Chatterjee S, Ahmed A, Ghosh S. Gargling with ketamine attenuates the postoperative sore throat. Indian J Anaesth. 2009 Feb;53(1):40-3.
21. Rashwan S, Elmawgoud A A and Badawy AA. Effect of tramadol gargle on postoperative sore throat: A double blinded randomized placebo controlled study. Egyptian Journal of Anaesthesia. 2014;(30):235- 9.