

Post Operative Sore Throat (POST), Comparison Between Nebulization with Ketamine and Placebo

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ABSTRACT

Objective: To compare the frequency of post-operative sore throat with nebulized ketamine versus nebulized placebo pre-operatively in patients undergoing elective surgery under general anaesthesia.

Study design; Randomized Controlled trial.

Setting; Department of Anesthesia, Hameed Latif Hospital, Lahore.

Duration of study; 08-05-2018 to 08-11-2018.

Methodology: In this study, the cases of either gender and age range of 18 to 40 years undergoing elective surgery under GA requiring endotracheal tube were selected. The cases in Group A were nebulized with Ketamine (50 mg) mixed with normal saline while those in group B with normal saline only for 15 minutes. They were assessed at 4 hours on the basis of verbal response scale (VRS) after extubation regarding cough and irritation in the throat and score of 4 or more on VRS was labelled as POST.

Results: In this study out of 40 cases in each group males were 23 (57.5%) vs 26 (65%) and mean age was 34.21±4.21 vs 32.57±4.67 years in group A and B respectively. Post operative sore throat was seen in 8 (17.5%) in group A and 18 (45%) in group B with p= 0.01. This difference was significant in terms of female gender where this was seen more in females in group B 64.28% vs 11.76% (p= 0.001). This difference was also significant in cases with duration of surgery more than 60 minutes where it was seen in 14.28% vs 44.34% in group A and B respectively (p= 0.01)

Conclusion; Ketamine nebulization is significantly better for POST than placebo and this difference is also significantly high in terms of female gender and duration of surgery > 60 minutes.

Keywords; POST, Ketamine, Placebo, nebulized ketamine.

INTRODUCTION

Postoperative sore throat (POST) is one of the commonest complaints that are being encountered in the post-operative area and although it is denoted as a minor and non-serious ailment; yet post a great concern to the patients and also to the surgeons in cases where cough is an extremely unwanted side effect especially in the neurosurgical cases. the prevalence is highly variable and is usually seen in 21-65% cases.^{1,2}

There are multiple factors that can contribute to its development and these include naso-gastric tube placement, pharyngo-laryngeal mucosal trauma during laryngoscopy, repeated suction etc. Number of modalities have been tried in the past to prevent the occurrence of this untoward complication and can be both pharmacological and non pharmacological with different degree of success rate and side effect profiles.³ The pharmacological measures include, beclomethasone inhalation, ketamine, clonidine and gargling with azulene sulfonate. There are always concerns regarding the safety profile, cost, availability of the agent, that's why a simple, safe, and inexpensive intervention to prevent POST is always required.⁴⁻⁶

Ketamine, is an anesthetic agent and works as NMDA receptor antagonist and has the property of anti-nociception and anti-inflammatory effects and for this purpose it is used via various routes and purposes. According to a randomized controlled trial, the incidence of POST was 46% patients in placebo group and 20% patients in nebulized ketamine group (P = 0.01).⁶

The data regarding the prevention of Postoperative sore throat in cases managed by nebulized ketamine and even nebulized placebo was deficient in the local populations for which this study was planned.

Objective: To compare the frequency of postoperative sore throat with nebulized ketamine versus nebulized placebo before intubation in patients undergoing elective surgery under general anaesthesia

Operational Definitions

Postoperative sore throat: It was labelled as yes if patient

complained about cough and itching (assessed subjectively) in throat assessed at 4 hours after surgery. Verbal rating scale (VRS) was used at score of 4 or more was labelled as POST where 0 had no sore throat and 10 had maximum score.

Sample selection:

Inclusion Criteria:

- Patients aged between 18-40 years,
- Either gender undergoing elective surgery under general anaesthesia with endotracheal tube
- Surgery in supine position

Exclusion Criteria:

- ASA III & IV
- Mallampati score III & IV as assessed on pre operative assessment
- Patients with sore throat before surgery (on clinical examination)
- Patients having tonsillitis (on clinical examination)
- Pregnant patients
- BMI >30

METHODOLOGY

The cases were divided into two groups by sealed opaque envelope method, labelled as A and B. The cases selecting group A were nebulized with ketamine 50mg (1.0 ml) with 4.0 ml of saline nebulization for 15 minutes and Group B were nebulized with placebo (saline nebulization 5.0ml) for 15 minutes before general anaesthesia. Then all patients underwent respective surgery. General anaesthesia was induced 10 min after completion of nebulization. All patients underwent intravenous induction of anaesthesia with propofol (2 -3mg/kg), atracurium (0.5- 1mg/kg) followed by maintenance on sevoflurane 3%. Trachea was intubated with a soft seal cuffed sterile polyvinyl chloride tracheal tube with an internal diameter of 7–7.5 mm for women and 8–8.5 mm for men. A researcher performed tracheal intubation after ensuring maximum neuromuscular blocking effect as assessed by

train of four (TOF) count <2. At the end of procedure, after gain of consciousness, patients were shifted in post-anesthesia care unit and were followed-up there for 2 and 4 hours. After 4 hours, patients were asked and assessed for the presence of cough and irritation in throat as per operational definition of POST.

Statistical Analysis: Data was entered & analyzed by using SPSS version 20.0. Mean and SD were calculated for quantitative variables and frequency and percentage for qualitative variables. Both the groups were compared by using chi-square test and effect modifiers were controlled through stratification and P-value ≤ 0.05 was taken as significant

RESULTS

In this study there were total 80 cases (40 cases in each group). There were 23 (57.5%) vs 26 (65%) males in group A and B. The mean age of the participants was 34.21 ± 4.21 vs 32.57 ± 4.67 years, mean BMI in group A and B was 24.37 ± 3.13 vs 24.11 ± 2.97 as shown in table I. Post operative sore throat (POST) was seen in 8 (17.5%) in group A and 18 (45%) in group B with $p = 0.01$ as shown in table II. This difference was significant in terms of female gender where this was seen more in females in group B 64.28% vs 11.76% ($p = 0.001$) as in table III. There was no significant difference in terms of age groups and BMI (tables IV & V). POST was also significant in cases with duration of surgery more than 60 minutes where it was seen in 14.28% vs 44.34% in group A and B respectively ($p = 0.01$) as in table VI.

Table 1: Demographics n= 80 (40 in each group)

Gender	Treatment group	
	A	B
Male	23 (57.5%)	26 (65%)
Female	17 (42.5%)	14 (35%)
Age	34.21 ± 4.21	32.57 ± 4.67
BMI	24.37 ± 3.13	24.11 ± 2.97
Duration of surgery	71.37 ± 17.45	73.98 ± 20.14

Table 2: POST in study subjects with respect to both groups n= 80 (40 in each group)

POST	Treatment group		p
	A	B	
Yes	8 (17.5%)	18 (45%)	0.01
No	32 (82.5%)	22 (55%)	
Total	40	40	

Table 3: POST in both groups with respect to gender n= 80 (40 in each group)

GENDER	POST	Treatment group		p
		A	B	
Male	Yes	6 (26.09%)	9 (34.61%)	0.78
	No	17 (73.81%)	17 (65.39%)	
Female	Yes	2 (11.76%)	9 (64.28%)	0.001
	No	15 (88.24%)	5 (35.72%)	
Total	40	40		

Table 4: POST in both groups with respect to age n= 80 (40 in each group)

AGE	POST	Treatment group		p
		A	B	
18-29	Yes	5 (23.81%)	8 (40%)	0.67
	No	16 (76.19%)	12 (60%)	
30-40	Yes	3 (15.79%)	10 (50%)	0.09
	No	16 (84.21%)	10 (50%)	
Total	40	40		

Table 5: POST in both groups with respect to BMI n= 80 (40 in each group)

BMI	POST	Treatment group		p
		A	B	
<25	Yes	4 (19.04%)	7 (35%)	0.58
	No	17 (80.96%)	13 (65%)	
25 or more	Yes	4 (21.05%)	11 (55%)	0.07
	No	15 (78.95%)	9 (45%)	
Total	40	40		

Table 6: POST in both groups with respect to duration of surgery n= 80 (40 in each group)

Duration of surgery	POST	Treatment group		p
		A	B	
>60	Yes	4 (14.28%)	8 (44.4%)	0.01
	No	28 (85.72%)	10 (55.6%)	
60 or less	Yes	4 (50%)	10 (45.5%)	0.92
	No	4 (50%)	12 (54.5%)	
Total	40	40		

DISCUSSION

In the present study Post operative sore throat was seen in 8 (17.5%) in group A managed with nebulized ketamine and 18 (45%) cases in group B managed with normal saline nebulization (placebo) with p value of 0.01.

These results were similar to the findings of the studies done in the past where ketamine has shown good efficacy in prevention of post operative sore throat. According to a study done by Ahuja et al they carried out a randomized controlled trial and also compared Ketamine with placebo and it was seen that the premedication with these agents led to POST in 46% patients in placebo group and 20% patients in nebulized ketamine group ($P = 0.01$).⁶

In another randomized controlled trial done by Jain S et al, they compared nebulized Ketamine and ketamine with clonidine for prevention of POST and it was observed that combination group had efficacy significantly higher than Ketamine nebulization only at all the interval assessed at 4,8,12 and 24 hours with p values of 0.0002.¹

In a study conducted by Aditya AK et al also compared ketamine and nebulized normal saline in similar protocol as our study and it was seen that the incidence of post operative sore throat was only better in cases with ketamine group but also its severity was lesser with p values of less than 0.05.⁷

In other studies, it has been shown that the incidence of post operative sore throat and its severity were better in cases that were administered Lignocaine local spray or they were given lozenges or liquorice and have shown significant better results as compared to the placebo drugs ($p < 0.05$).⁸⁻¹⁰

The other studies have also shown variable results but ultimately with better efficacy of ketamine in prevention of POST. The reason of this can be explained by the factor that they have NMDA-antagonist activity which has shown an anti-inflammatory effect that reduces the risk of sore throat when administered locally via nebulization.¹¹⁻¹²

The effect of Ketamine in prevention of POST was significantly better in terms of female gender where this was seen more in females in group B 64.28% vs 11.76% ($p = 0.001$) in the present study while in males this was seen as 6 (26.09%) in Ketamine and 9 (34.61%) in placebo group. The results of the previous studies were variable but have shown that the incidence of POST was over all higher in females as compared to males and hence the efficacy of Ketamine was more seen in those. The female prevalence of POST was seen in nearly 2:1 ratio in the studies done by Chan L and Marland S et al.^{13,14}

In the present study the frequency of POST was also significant in cases with duration of surgery more than 60 minutes where it was seen in 14.28% vs 44.34% in group A and B while those with surgery duration of 60 minutes or less this was seen in 50% of cases in Ketamine and 45.5% of cases with saline group respectively with a significant p value 0.01.

These results were in line with the results of the past studies which have also shown that the incidence of POST had linear association with the duration of surgery i.e. longer the duration and higher is the likelihood of POS; though there were no such studies that used such cut off as were used in the present study. The reason of this can be explained by the factor that longer duration of tube and furthermore, difference in cuff pressures can increase the chances of local inflammation and the chances of irritation and then cough and sore throat in the post operative period.^{15,16}

CONCLUSION

Ketamine nebulization is significantly better for POST than placebo and this difference is also significantly high in terms of female gender and duration of surgery > 60 minutes.

Conflict of interest: The author has no conflict of interest.

REFERENCES

1. Jain S, Bendwal HP, Gohiya S, Alwani N, Pancholi S, Romday R. Comparison of nebulized ketamine and ketamine with clonidine in postoperative sore throat. *Int Surg J*. 2017;4(5):1579-83.
2. Salama AK, El-badawy AM. Does nebulized dexamethasone decrease the incidence of postextubation sore throat?: a randomized controlled study. *Ain-Shams J Anaesth*. 2016;9(1):104.
3. Rajkumar G, Eshwori L, Konyak PY, Singh LD, Singh TR, Rani MB. Prophylactic ketamine gargle to reduce post-operative sore throat following endotracheal intubation. *J Med Soc*. 2012;26(3):175.
4. Romero TR, Galdino GS, Silva GC, Resende LC, Perez AC, Côrtes SF, et al. Ketamine activates the L-arginine/nitric oxide/cyclic guanosine monophosphate pathway to induce peripheral antinociception in rats. *Anesth & Analg*. 2011;113(5):1254-59.
5. Niciu MJ, Henter ID, Luckenbaugh DA, Zarate Jr CA, Charney DS. Glutamate receptor antagonists as fast-acting therapeutic alternatives for the treatment of depression: ketamine and other compounds. *Annual Rev Pharmacol and Toxicol*. 2014;54:119-39.
6. Ahuja V, Mitra S, Sarna R. Nebulized ketamine decreases incidence and severity of post-operative sore throat. *Indian J Anaesth*. 2015;59(1):37.
7. Aditya AK, Das B, Mishra DK. Assessment of nebulized ketamine for reduction of incidence and severity of post operative sore throat. *Int J Med Health Res*. 2017;9(3):130-32.
8. D'Aragon F, Beaudet N, Gagnon V, Martin R, Sansoucy Y. The effects of lidocaine spray and intracuff alkalinized lidocaine. on the occurrence of cough at extubation: A double-blind randomized controlled trial. *Can J Anaesth* 2013; 60:370-6.
9. Gupta D, Agrawal S, Sharma JP. Effect of preoperative licorice lozenges on incidence of postextubation cough and sore throat in smokers undergoing general anesthesia and endotracheal intubation. *Middle East J Anaesthesiol*. 2013; 22:173-8.
10. Aydin GB, Ergil J, Polat R, Sayin M, Akelma FK. Comparison of Siccoral® spray, Stomatovis® gargle, and Strefen® lozenges on postoperative sore throat. *J Anesth*. 2014; 28:494-8.
11. Hirota K, Lambert DG. Ketamine: New uses for an old drug? *Br J Anaesth*. 2011;107:123-6.
12. Zhu MM, Qian YN, Zhu W, Xu YM, Rong HB, Ding ZN, et al. Protective effects of ketamine on allergen-induced airway inflammatory injury and high airway reactivity in asthma: Experiment with rats. *Zhonghua Yi Xue Za Zhi*. 2007;87:1308-13
13. Chan L, Lee ML, Lo YL. Postoperative sore throat and ketamine gargle. *Br J Anaesth*. 2010;105:97.
14. Marland S, Ellerton J, Andolfatto G, Strapazzon G, Thomassen O, Brandner B, et al. Ketamine: Use in anesthesia. *CNS Neurosci Ther*. 2013;19:381-9.
15. Khatavkar SS, Bakhshi RG. Comparison of nasal midazolam with ketamine versus nasal midazolam as a premedication in children. *Saudi J Anaesth*. 2014;8:17-21.
16. Nitta R, Goyagi T, Nishikawa T. Combination of oral clonidine and intravenous low-dose ketamine reduces the consumption of postoperative patient-controlled analgesia morphine after spine surgery. *Acta Anaesthesiol Taiwan*. 2013;51(1):14-7.