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EFFECTIVENESS OF NEBULISED DEXMEDETOMIDINE IN COMPARISON TO NEBULISED KETAMINE, IN ALLEVIATING POST OPERATIVE SORE THROAT IN PATIENTS UNDERGOING THYROIDECTOMY: A RANDOMISED, COMPARATIVE STUDY

Anesthesiology

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ABSTRACT

Background: Ketamine is already in use in the nebulised form, for attenuating POST, Dexmedetomidine, on the other hand is known to cause sedation and analgesia. The aim of our study was to assess the respective incidence and severity of POST and compare the effectiveness of nebulised dexmedetomidine and nebulised ketamine in reducing or alleviating POST in adult patients undergoing thyroidectomy under GA.

Method: A prospective, randomized, double-blinded, comparative study was conducted on a total of 96 patients, further divided into two age and gender-matched groups, in Super Specialty Hospital, GMC Jammu, over a period of 1 year. Patients in the age group of 18-60 years, who were scheduled to undergo elective thyroid surgery under general anaesthesia (GA) with endotracheal intubation, were included in the study. First group received ketamine 50mg (1mL) with saline (4mL) nebulisation and second group received dexmedetomidine 50µg (1mL) with saline (4mL) nebulisation.

Results: No significant difference in the mean age (in years), mean weight, gender ratio and duration of surgery between the two groups. Incidence of POST was 14.58% (7/48) in ketamine and 16.66% (8/48) in dexmedetomidine group, at 2 Hour interval. Severity was moderate for two patients in each group at 2 hour interval. POST persisted for a longer duration in Ketamine group as compared to Dexmedetomidine group. Significant reduction in the severity of sore throat in both groups at all time points during 24 Hours.

Conclusion: Nebulised dexmedetomidine may be considered as a safe alternative to nebulised ketamine for alleviating POST.

KEYWORDS

General Anaesthesia, Ketamine, Dexmedetomidine, Nebulisation, Post Operative Sore throat, Thyroidectomy

INTRODUCTION

Patients receiving general anaesthesia often complain of: nausea and vomiting, sore throat or hoarseness, dry mouth, shivering or chills, sleepiness, muscle aches, malignant hyperthermia, etc. Postoperative sore throat (POST) is considered to be quite common complaint.[1,2] For a treating physician, POST is of a lesser concern, but it can cause significant agony to the patient and displeasure with the quality of recovery after anaesthesia.[3] Symptoms of POST tend to improve with time, however prevention of POST will be useful in post-operative management, improve patient satisfaction and may economize the hospital stay by reducing the duration of stay.

Several pharmacological and non-pharmacological remedies have been tried, with numerous trials conducted in the past, with varying degree of success.[4-8] As the incidence of POST following GA varies between 20-74%,[9] it is found higher in post thyroidectomy patients.[10]

Nebulisations are better accepted nowadays, and tolerated by the patients than gargle, as it spares them from the bitter taste of the drug. The chance of aspiration is also less likely as only a reduced volume is administered when compared to the volume needed for gargle.[11]

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist, which has already been in use in the nebulised form, for attenuating POST, due to its anti-nociceptive and anti-inflammatory properties.[12] Dexmedetomidine is a colorless, tasteless and odorless drug with a selective α-2 adrenergic agonistic action, which causes sedation and analgesia.[13]

There is minimum literature and studies available, evaluating the effectiveness of nebulised dexmedetomidine in decreasing POST, more specifically on Indian population. Nevertheless, dexmedetomidine has already been in use in a nebulized form, and being a highly lipid soluble agent, with known and good systemic absorption on transmucosal administration.

Therefore, the aim of our study was to evaluate and compare the effectiveness of nebulised dexmedetomidine and nebulised ketamine in reducing or alleviating POST in adult patients undergoing thyroidectomy under GA, and also to assess the incidence and severity of POST among the two groups.

The secondary aims involved the monitoring of side-effects such as cough, dry mouth, post-operative nausea and vomiting (PONV), hallucinations, respiratory depression and haemodynamic instability in both the groups.

METHODS

A prospective, randomized, double-blinded, comparative study was conducted on a total of 100 patients, GMC Jammu, over a period of 1 year. The study group was further divided into two groups with age and gender-matched 48 patients each. A written informed consent was obtained from all participants. Ethical approval was duly obtained from institutional ethical committee. Randomization, for selection, was achieved using computer-generated random code number and sealed envelope method to create separate two groups. The code was maintained till the completion of study.

Inclusion Criteria:

Patients between the age group of 18 to 60 years were included. Patients with ASA Physical Status of I and II, who were scheduled to undergo elective thyroid surgery under general anaesthesia (GA) with endotracheal intubation, were included in the study.

Exclusion Criteria:

Habitual smokers, pregnant women, patients with a recent history of sore throat or upper respiratory tract infection, known allergy to study drug, chronic obstructive pulmonary disease and patients with Malampatti grade (MPG) greater than II were excluded from the study. The enlisted patients, who needed more than one intubation attempt or developed any intra-operative or post-operative complication, were also excluded from further evaluation and analysis.

The patients drafted for the study remained fasted for 6 hours prior to surgery. Anaesthesia protocol was standardized for all patients. Patients were randomly allocated into two groups with the help of a computer-formulated randomization technique, using consecutively numbered opaque sealed envelopes, which were arranged by an anaesthesiologist who did not take part in the study. After opening those envelopes, the nebulisation solution was made ready by an anaesthesia assistant according to the assigned group. As, according to the study protocol, a double-blind clinical trial is one in which both the recipient and the administrator does not know if the recipient is receiving the actual drug, thus all the study-group patients were kept blinded as both the study preparations were colorless and tasteless. The anaesthesia assistant who prepared the solution was also not allowed to take part in the subsequent analysis of these patients.

The participants were randomized into two groups of 48 each:

Group A received ketamine 50mg (1mL) with saline (4mL) nebulisation.

Group B received dexmedetomidine 50µg (1mL) with saline (4mL) nebulisation.

The drug was delivered using a nebulization mask for 15 min, with the help of a oxygen driven source (8L, 50psi). Fifteen minutes after finishing nebulisation, GA was induced with intravenous (IV) tramadol 1mg/kg and IV propofol 2 mg/kg. Laryngoscopies were performed on both groups and laryngoscopic view of glottis was classified using Cormack–Lehane classification. Duration of laryngoscopy (time from opening mouth to the placement of the endotracheal tube) and the intubation time (the interval between the insertion of the laryngoscope blade into the mouth to the inflation of the endotracheal tube cuff) was recorded in all patients. The cuff pressure of the endotracheal tube was adjusted every 30 min, using a handheld pressure gauge and maintained between 20 and 22 cm of H_2O.

Three minutes after giving vecuronium bromide 0.1 mg/kg IV, a swift and a gentle laryngoscopy was performed by a well experienced anaesthesiologist. A sterile single lumen cuffed polyvinyl chloride (PVC) endotracheal tube with an inner diameter of 7-7.5mm in females and 8-8.5mm in males and the intubation time (the interval between the insertion of the laryngoscope blade into the mouth to the inflation of the endotracheal tube cuff) was recorded in all patients. The use of steroids and anti-inflammatory drugs was recorded.

Anesthesia was maintained with 1.1% isoflurane in 60% N2O and 40% O2 mixture. For pain relief, paracetamol 1g IV was administered during surgery, followed by 6- hourly in the post-operative period. Ondansetron 4mg IV was given 30 min preceding the end of surgery and thereafter every eight hours post-operatively. The patients were extubated upon completion of surgery; the oropharynx was gently suctioned using a soft suction catheter and reversal of the neuromuscular blockade was done with neostigmine 50 µg/kg IV and glycopyrrolate 10µg/kg IV. After regaining complete consciousness, the patient was extubated.

In the post anaesthesia care unit (PACU), sore throat was evaluated at 0, 2, 4, 6, 12 and 24 hours after extubation. And grading of POST was done using a four-point scale (0-3): 0 score was given for no sore throat; 1 for mild sore throat (complains of sore throat only when asked); 2 for moderate sore throat (complains of sore throat even without asking); and 3 for severe sore throat (with change of voice or hoarseness, and/or throat pain).

After 24 hours, if patients still complained of moderate or severe POST, lukewarm saline gargle as well as decongestants were prescribed. And if the symptoms persisted, an otorhinolaryngology consultation was ensured. Haemodynamic variables such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MABP) were also recorded at pre-nebulisation, pre-induction, and at intervals of 0,2,4,6,12 and 24 hours after extubation.

The statistical calculations were performed using the software MS Excel 2010. Student t-test, paired t-test and chi-square test was applied to find the incidence and to compare the data extracted. P< 0.05 was considered significant.

RESULTS

Out of the 104 patients screened for the study, 8 patients were excluded, due to various reasons and excluding criteria. A total of 96 patients were recruited. 96 patients were then assigned to the two equal groups: Group A receiving ketamine and Group B receiving dexmedetomidine. All the selected patients duly completed the study and were subsequently followed up and analysed.

The comparable distribution of demographic characteristics showed that there was no significant difference in the mean age (in years), mean weight, gender ratio and duration of surgery as well. (Table 1) However, it was quite evident that the females were the predominant gender among the selected patients.

Table 1: Demographic Characteristics Of Both Groups

Characteristics	Group A (Ketamine)	Group B (Dexmedetomidine)	p-value
Age in years (Mean ± SD)	47.13 (±10.65)	46.87 (±9.43)	0.733
Weight in kg (Mean ± SD)	67.72 (±13.54)	67.16 (±12.62)	0.645
Gender : Males:	18	19	0.808
Females:	30	29	
Duration Of Surgery In Minutes (Mean ± SD)	109.32 (±35.48)	104.92 (±31.45)	0.209

*P<0.05 = significant

The (maximum) incidence of POST was comparable in the two groups: POST was experienced by 7 patients (14.58%) in ketamine and 8 patients (16.66%) in dexmedetomidine group, at 2 Hour interval (P = 0.682). However, at all time intervals of observation and study, postoperatively, no statistically significant difference was noticed among the two groups. [Table 2].

Table 2: Incidence Of POST

Time (Hours-Interval)	POST (Whether Present or Absent)	Group A (Ketamine)	Group B (Dexmedetomidine)	p-value
0	Absent	47	46	0.771
	Present	1	2	
2	Absent	41	40	0.682
	Present	7	8	
4	Absent	41	42	0.706
	Present	7	6	
6	Absent	42	44	0.434
	Present	6	4	
12	Absent	42	45	0.283
	Present	6	3	
24	Absent	42	46	0.119
	Present	6	2	

*P<0.05 = significant

Grading of POST at all time intervals showed that no patient encountered a severe sore throat. The severity was moderate for two patients in each group at 2 hour interval. [Table 3]

Table 3: Severity Of POST

Time (Hours-Interval)	Grading of POST	Group 1 (Ketamine)	Group 2 (Dexmedetomidine)	p-value
0	0	47	46	0.329
	1	1	1	
	2	0	1	
	3	0	0	
2	0	41	40	0.772
	1	5	6	
	2	2	2	
	3	0	0	
4	0	41	42	0.696
	1	6	5	
	2	1	1	
	3	0	0	
6	0	42	44	0.188
	1	5	4	
	2	1	0	
	3	0	0	
12	0	42	45	0.283
	1	6	3	
	2	0	0	
	3	0	0	
24	0	42	46	0.119
	1	6	2	
	2	0	0	
	3	0	0	

*P<0.05 = significant

Observations made regarding the incidence and severity of POST showed that the POST persisted for a slightly longer duration in Ketamine group as compared to Dexmedetomidine group, however not significant.

Statistically significant rise in Heart Rate and Diastolic Blood Pressure, with p-value being 0.026 and 0.002 respectively was observed in Group A (ketamine group), when pre-nebulisation and pre-induction values were compared. [Table 4]

Table 4: Comparison Of Haemodynamic Parameters Among Two Groups

	Pre Nebulisation	Pre Induction	P-value
Heart Rate			
Group A	79.72 ± 12.65	85.69 ± 10.12	0.026*
Group B	80.33 ± 11.84	78.96 ± 12.45	0.081
Systolic Blood Pressure (mmHg)			
Group A	130.37 ± 14.22	136.44 ± 20.25	0.054
Group B	133.81 ± 16.26	134.83 ± 22.76	0.169
Mean Arterial Blood Pressure (mmHg)			
Group A	91.55 ± 12.83	96.92 ± 14.06	0.463
Group B	93.46 ± 12.42	98.77 ± 15.21	0.112
Diastolic Blood Pressure (mmHg)			
Group A	77.19 ± 9.24	84.48 ± 11.85	0.002*
Group B	78.49 ± 11.67	79.09 ± 10.61	0.765

*P<0.05 = significant

DISCUSSION

Postoperative sore throat (POST) has a reported incidence of up to 62% following general anaesthesia. Adults undergoing tracheal intubation, females, young children, pre-existing lung disease and prolonged duration of anesthesia are considered to be greatest risk factors. Tracheal intubation without neuromuscular blockade, use of double-lumen tubes, as well as high tracheal tube cuff pressures may also increase the risk of postoperative sore throat. [14]

In various studies conducted worldover, the overall incidence of POST after GA, was reported to be between 20-74%,[9] whereas following total thyroidectomy, the incidence of POST was as high as 80%. Kadri et al.[10] have proposed that POST was even dependent on the types of thyroid surgery and he noticed that 59.6% of patients had POST following partial thyroidectomy, 87.7% following subtotal thyroidectomy and 100% following total thyroidectomy. In our study majority of the patients underwent total thyroidectomy, only 9 patients had subtotal thyroidectomy.

Keeping the demographic characteristics of our study groups comparable, our study showed no significant difference in the mean age (in years), mean weight, gender ratio and duration of surgery between the two groups. The incidence of POST was 14.58% (7/48) in ketamine and 16.66% (8/48) in dexmedetomidine group, at 2 Hour interval, which was comparable to major studies conducted earlier. [11,12] However, at all time intervals of observation and study, postoperatively, no statistically significant difference was noticed among the two groups. Grading of POST at all time intervals showed that no patient encountered a severe sore throat. The severity was moderate for two patients in each group at 2 hour interval. It was however observed that the POST persisted for a slightly longer duration in Ketamine group as compared to Dexmedetomidine group. There was no statistically significant difference in the incidence of POST between the two groups at 0, 2, 4, 6, 12 and 24h post-operatively. Significant reduction in the severity of sore throat was noticed in both groups at all time points during the first post-operative day.

Chan et al.[15] in his study using ketamine gargle, have shown that the topical action of ketamine reduced the incidence of POST more than the systemic effect. Also, Ahuja et al.[12] and Thomas et al.[11] proposed that pre-operative administration of nebulised ketamine significantly declined the incidence and severity of sore throat in the post-operative period, this observation is similar to our results.

Similarly, Zhang et al.[16] had also concluded in their study that dexmedetomidine decreased inflammatory responses, thereby reducing the chances of cerebral injury following cardio pulmonary bypass dexmedetomidine observed a rapid and efficient absorption of dexmedetomidine when administered intranasally. Therefore, the significant decline in the incidence and severity of POST that we noted in our dexmedetomidine group can be attributed to the significant reduction in the inflammatory mediators caused by nebulised dexmedetomidine when administered pre-operatively, along with its analgesic action.

Pharyngeal, laryngeal, or tracheal irritation leading to inflammation may be the reason for POST, but it may also occur in absence of tracheal intubation. It generally occurs as a consequence of injury to the mucosa of pharynx during laryngoscopy or as an injury to tracheal tissues either during intubation or extubation, which may trigger an aseptic inflammatory reaction in the tracheal mucosa.[17]

Ketamine nebulisation, which abated the local inflammation and also triggered a peripheral analgesic effect, with its NMDA-antagonistic and anti-inflammatory actions can be the reason for the significant attenuation of POST in our ketamine group.[18,19] Statistically significant rise in Heart Rate and Diastolic Blood Pressure, with p-value being 0.026 and 0.002 respectively were also observed in Group A (ketamine group) of our study, when pre-nebulisation and pre-induction values were compared. This may be attributed to the systemic absorption of ketamine. Similar results were also obtained by Segaran et al.[20] in the ketamine group in their study, while comparing and evaluating the efficacy of nebulised magnesium sulphate with nebulised ketamine in diminishing POST.

Zhu et al [21] and Li et al [22] had also concluded that when administered along with GA, dexmedetomidine produced remarkable reduction in the levels of serum IL-6, IL-8 and TNF-α, post-operatively. In view of these anti-inflammatory effects shown by dexmedetomidine, many authors are now advocating its pre-emptive administration, in isolation or in combination with ketamine, for better results.

Adverse effects such as PONV, dry mouth, cough, hoarseness, hallucinations or respiratory depression were absent during the entire period of observation, in the present study, but, absence of sedation scale and absence of follow up after 24 hours, may be considered as a limitation to the present study.

CONCLUSION

This study was a good demonstration towards showing the effectiveness of pre-operatively administered dexmedetomidine nebulisation in comparison to ketamine nebulisation for reducing POST, with lesser haemodynamic derangement. More such studies may be requiring proving the point; however, nebulised dexmedetomidine may be considered as a safe alternative to nebulised ketamine for alleviating POST.

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