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Original Research Article

The Effect of Preoperative Nebulisations with Ketamine and Magnesium Sulfate on Incidence of Postoperative Sore Throat

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Abstract

Introduction: Postoperative sore throat (POST) is a common entity following general anesthesia with endotracheal intubation with incidence ranging from 21%–65%. Variousm non-pharmacological and pharmacological trials have been tried for decreasing the incidence of POST with no proven single modality. Ketamine and magnesium sulfate are NMDA antagonists and available studies suggest that both drugs decrease the incidence of POST.

Study Design: A prospective randomised double blind comparative clinical study conducted over a period of 8 months.

Materials and Methods: 120 subjects who are between 18–65 years of age, either sex belonging to ASA physical status I-II undergoing elective surgery in supine position requiring General anesthesia with endotracheal intubation with duration of the surgery upto 2 hours were randomised into three groups namely

Group S: Received nebulisation of normal saline (NS) 5ml

Group K: Received nebulisation of 50mg ketamine diluted to 5ml using NS

Group M: Received nebulisation of 250mg of magnesium sulfate diluted to 5ml using NS.

Primary aim was to compare the incidence of POST in all three groups and secondary aim was observation of hemodynamic effects.

Statistical Analysis: Chi-square and ANOVA were used as test of significance for qualitative and quantitative data respectively.

Results: demographic data were similar in all three groups. Incidence of POST in group N - 57.5%, group M - 25% and group K - 10%.

Conclusion: Ketamine and magnesium sulfate both decreased the incidence of postoperative sore throat after endotracheal intubation with ketamine 50mg nebulistion being more effective than magnesium sulfate 250mg nebulisation.

Keywords: Postoperative Sore Throat, Ketamine, Magnesium Sulfate.

Introduction

Postoperative sore throat (POST) is a common entity following general anesthesia with endotracheal intubation with incidence ranging from 21%–65%. [1,2]. It increases the length of

hospital stay especially in day care surgeries [1]. Irritation and inflammation of the airway are considered to be the causes of POST [3].

Various non-pharmacological and pharmacological trials have been tried for decreasing the incidence of POST with no proven single modality. Among the nonpharmacological methods, the use of smaller endotracheal tubes, careful airway instrumentation, minimizing the number of laryngoscopy attempts, intubation after the full relaxation of the larynx, gentle oropharyngeal suctioning, minimizing intracuff pressures <20 mm Hg, and extubation when the tracheal tube is fully deflated, have been reported to decrease the incidence of POST. [4,5]

The pharmacological methods include the use of beclomethasone gel [3], lidocaine gel and spray, gargling with azulene sulphonate[6], Ketamine gargle & nebulisation [7,8], magnesium sulfate nebulisation, topical, gargle & intravenous route [5,9-11] intravenous dexamethasone [11,12], licorice, local spray of benzydamine hydrochloride, and intracuff administration of alkalized lignocaine [13]

N-methyl-D-aspartate (NMDA) receptors have a role in nociception and inflammation [14]. NMDA receptors are found not only in the central nervous system but also in the peripheral nervous system [15]. Ketamine and magnesium sulfate are NMDA antagonist [2,5,8-11,18] and the available studies suggest that they both are potential agents in reducing the incidence of POST [2,5,7,8,18,19] however there are limited studies comparing these two drugs, hence this study is undertaken to compare these two drugs on the incidence of POST.

The primary aim of our study is to measure and compare the incidence of POST with ketamine and magnesium nebulisation given preoperatively and secondary objective being the effect on hemodynamic parameters and evaluation of side effects – nausea, vomiting, cough, hoarsness and dry mouth.

Materials and Methods

- A prospective randomised double blind comparative clinical study conducted over a period of 8 months from October-2019 till may-2020 at Shimoga Institute of Medical Sciences, Shimoga after obtaining clearance from Institutional Ethical Committee. We have conducted the study on 120 subjects who are between 18–65 years of age, either sex belonging to ASA physical status I-II undergoing elective surgery in supine position requiring General anesthesia with endotracheal intubation with duration of the surgery upto 2 hours. The Sample size was calculated based on the incidence of POST of 65% from previous study [1.2] and by assuming a 50% reduction in the incidence after intervention at α-error of 0.05 and power 80% and we required a sample size of 36 patients per group. Considering 10% loss of follow-up 40 subjects were recruited in each group.

- Exclusion criteria included patients with pre-operative sore throat or cold, oral surgeries and neck surgeries, Asthma, chronic obstructive pulmonary disease, known allergies to study drug, Recent non-steroidal anti-inflammatory drug medication, more than one attempt of laryngoscopy and if the duration of laryngoscopy exceeds 15seconds, Difficult or traumatic intubations and Pregnant women.

Informed consent was obtained from

patients' day before the surgery after a detailed pre anaesthetic evaluation and explaining the procedure. Nil per orally guidelines were advised.

By using computer-generated random number and sealed envelope technique, study population were divided into three groups.

Group S: received nebulisation of normal saline (NS) 5ml.

Group K: received nebulisation of 50mg ketamine diluted to 5ml using NS.

Group M: received nebulisation of 250mg of magnesium sulfate diluted to 5ml using NS.

After the completion of nebulisation (for 15 minutes) in preoperative room patient was shifted to operating room (OR). ASA standard monitors were attached, and large bore intravenous cannula was secured. Intraoperative monitoring included blood pressure, heart rate, oxygen saturation, continuous electrocardiogram and end tidal CO2. General anesthesia (GA) was induced 10 minutes after the completion of nebulisation with injection midazolam 0.02 mg/kg, injection fentanyl 2 μg/kg, and injection propofol 2mg/kg after preoxygenation with 100% oxygen for 3 min through face mask. Tracheal intubation was facilitated with injection vecuronium 0.1 mg/kg. All male patients were intubated with sterile cuffed Portex polyvinyl chloride tubes of size 8.0–8.5 mm ID and female patients with 7.0–7.5 mm ID. The tracheal cuff was then inflated with air and with cuff pressure maintained at 20 cm H2O by cuff pressure manometer and thereafter for every 15 min till the end of surgery.

After confirmation of tracheal tube position by bilateral chest auscultation anaesthesia was maintained with 50% oxygen in nitrous oxide, isoflurane 1-2% and intermittent doses of vecuronium (1/4th of induction dose every half an hourly). Thirty minutes before the end of procedure injection ondansetron 4mg IV was given.

At the end of the surgery gentle suctioning of the oropharynx was done and Isoflurane was turned off. Then inspiratory oxygen concentration was kept at 100% and nirous oxide turned off. The residual neuromuscular block was reversed with 50 mics/kg of neostigmine and 10mics/kg of glycopyrolate after spontaneous ventilation was returned.

During extubation if the patient had excessive coughing or bucking IV lignocaine 1.5mg/kg was admistered and such patient were excluded from the study. After extubation patient was shifted to recovery room where patients were assessed for sorethroat at 0th hour. Postoperative analgesia was provided by IV paracetamol 8th hourly.

Measurement and recording of study parameters.

Sore throat incidence and severity was assessed at O, 2, 4, 8, 12 and 24hours and were graded as follows (0-III) [19]

0 = no sore throat.

I = mild (pain with deglutition)

II = moderate (pain present constantly and increasing with deglutition),

III = severe (pain interfering with eating and requiring analgesic medication)

Vital parameters – heart rate, BP and spo2 were recorded prenebulisation, post nebulisation, just before and after intubation and 5min after intubation.

Statistical analysis: [20-22]

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. ANOVA (Analysis of Variance) or Kruskal Wallis test was the

test of significance to identify the mean difference between more than two groups for quantitative and qualitative data respectively.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, column diagram and line diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results

Table 1: Mean Age Comparison between three groups

	Group						p value
	Group N		Group M		Group K		
	Mean	SD	Mean	SD	Mean	SD	
Age	41.35	12.97	39.55	11.6	39.3	12.36	0.72

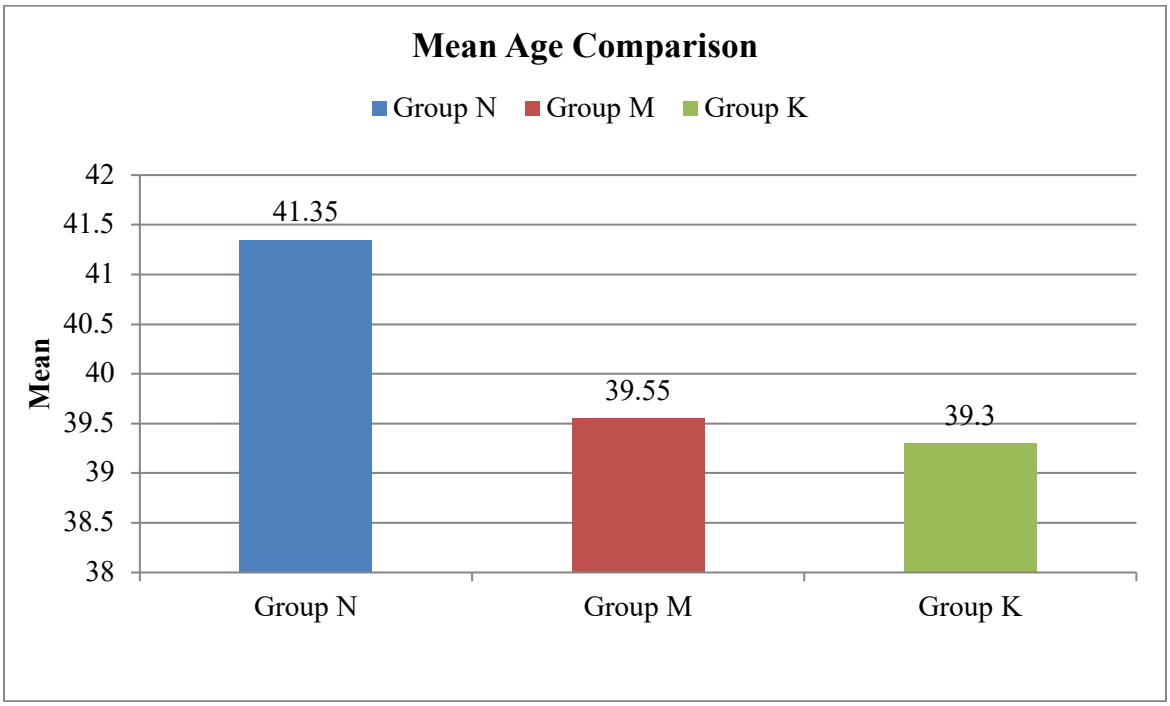

Figure 1: Bar Diagram Showing Mean Age Comparison between three groups.

Table 2: Sex Distribution between three groups

		Group					
		Group N		Group M		Group K	
		Count	%	Count	%	Count	%
Sex	Female	24	60.00%	25	62.50%	24	60.00%
	Male	16	40.00%	15	37.50%	16	40.00%

$\chi 2 = 0.07$, df = 2, p = 0.966

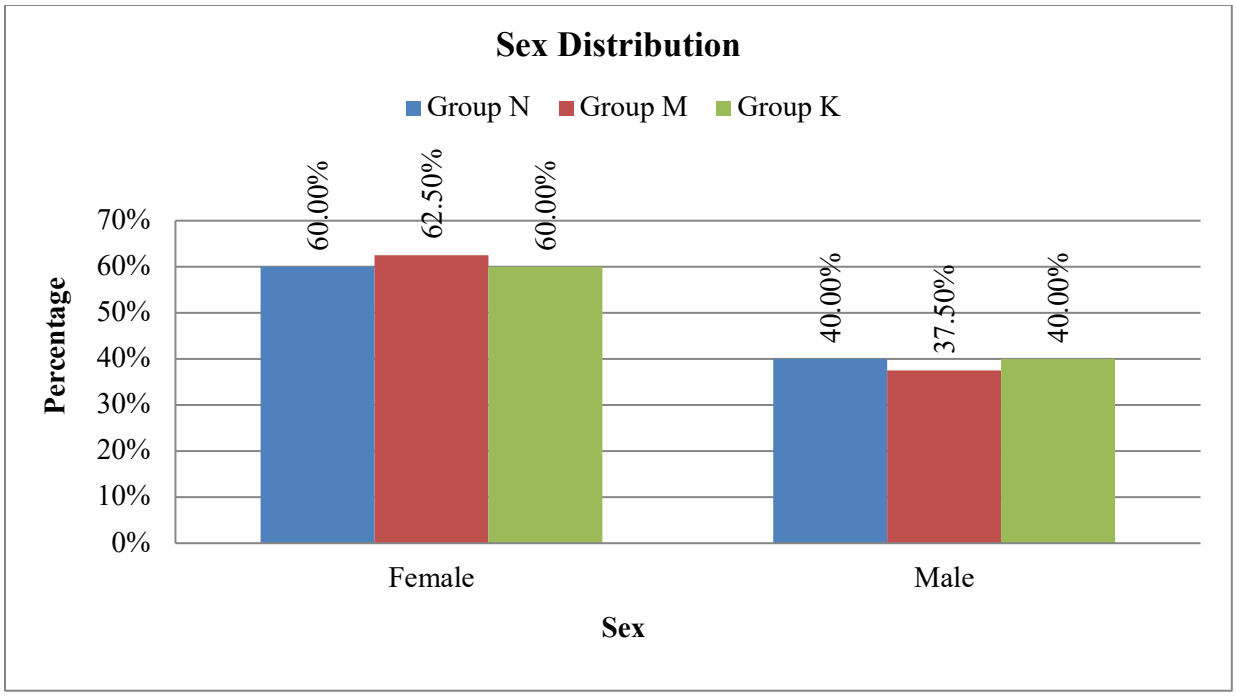

Figure 2: Bar Diagram Showing Sex Distribution between two groups.

Table 3: ASA Distribution between three groups

		Group					
		Group N		Group M		Group K	
		Count	%	Count	%	Count	%
ASA-PS	I	27	67.50%	24	60.00%	25	62.50%
	II	13	32.50%	16	40.00%	15	37.50%

$\chi 2 = 0.502$, df = 2, p = 0.778

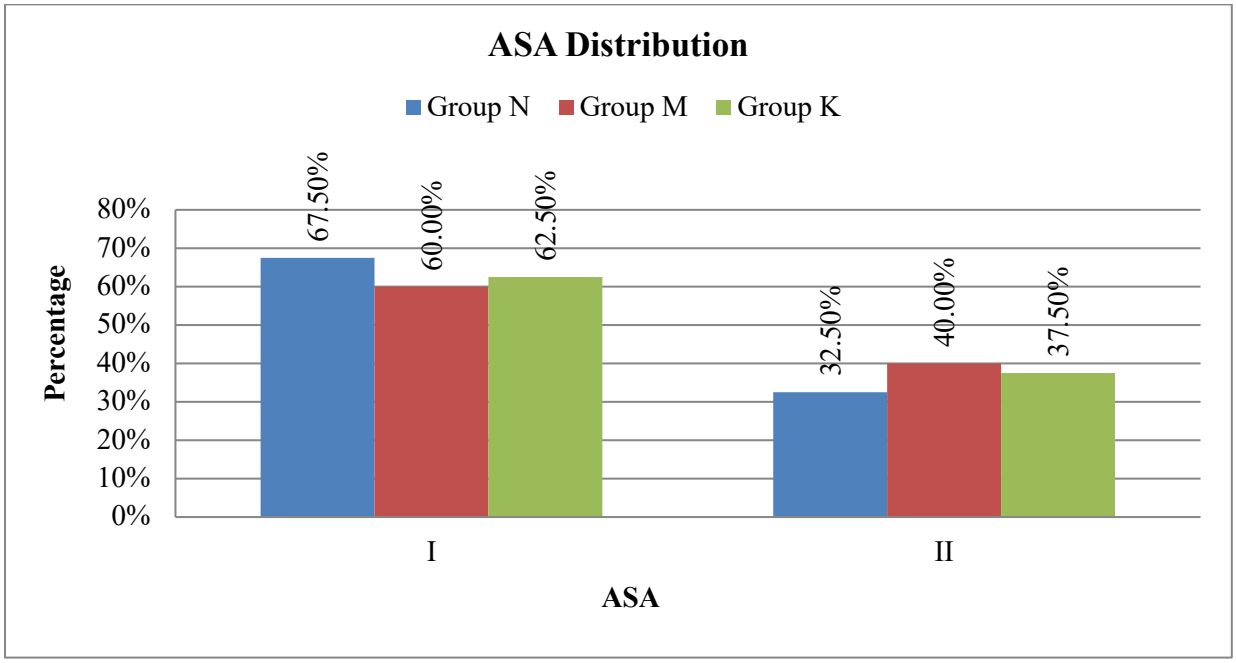

Figure 3: Bar Diagram Showing ASA Distribution between two groups.

Table 4: Mean Weight Comparison between three groups

	Group						p value
	Group N		Group M		Group K		
	Mean	SD	Mean	SD	Mean	SD	
Weight	60.75	7.89	59.03	11.29	59.73	7.45	0.693

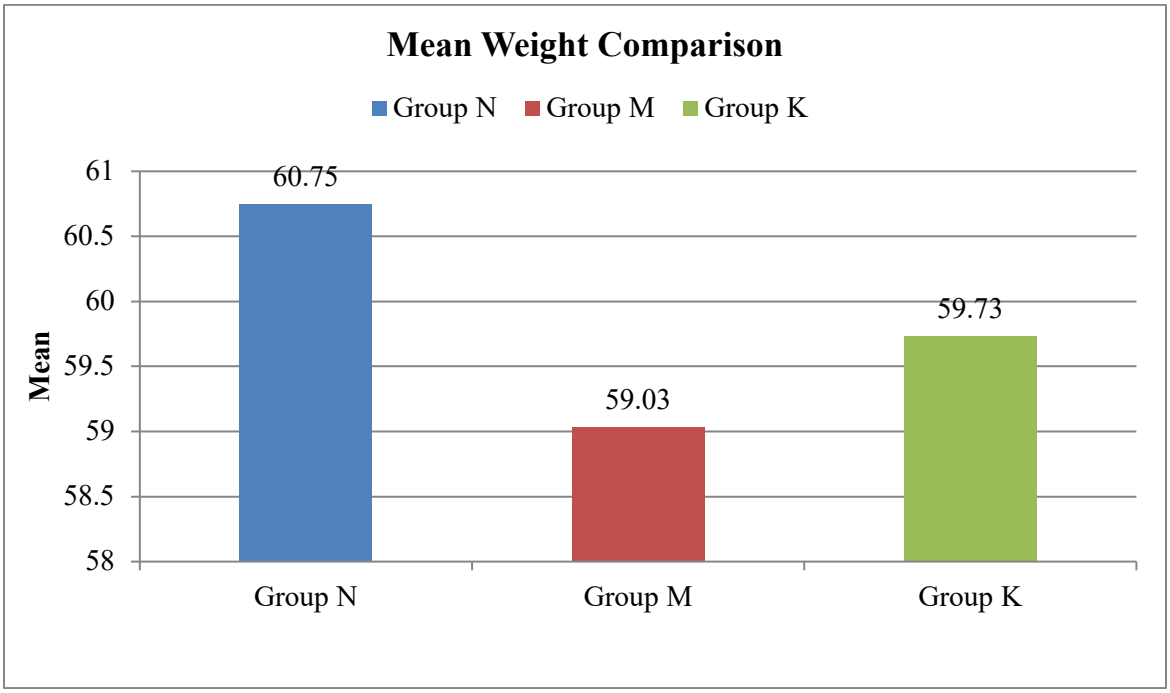

Figure 4: Bar Diagram Showing Mean Weight Comparison between three groups

Table 5: Mean Time Taken for Laryngoscopy Comparison between three groups

	Group						**p value**
	Group N		**Group M**		**Group K**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Time Taken For Laryngoscopy	12.33	2.4	11.75	2.3	11.7	2.24	0.409

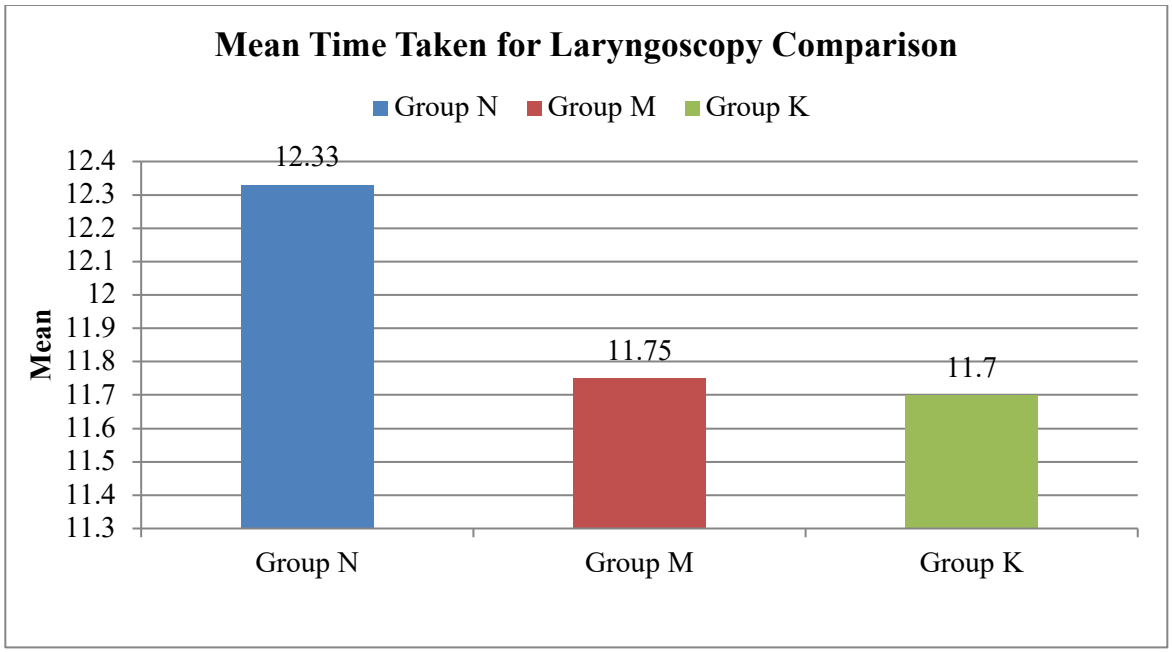

Figure 5: Bar Diagram Showing Mean Time Taken for Laryngoscopy Comparison between three groups.

Table 6: Mean Duration of Surgery Comparison between three groups

	Group						p value
	Group N		Group M		Group K		
	Mean	SD	Mean	SD	Mean	SD	
Duration of Surgery	67.53	29.46	63.13	26.29	65.5	28.05	0.787

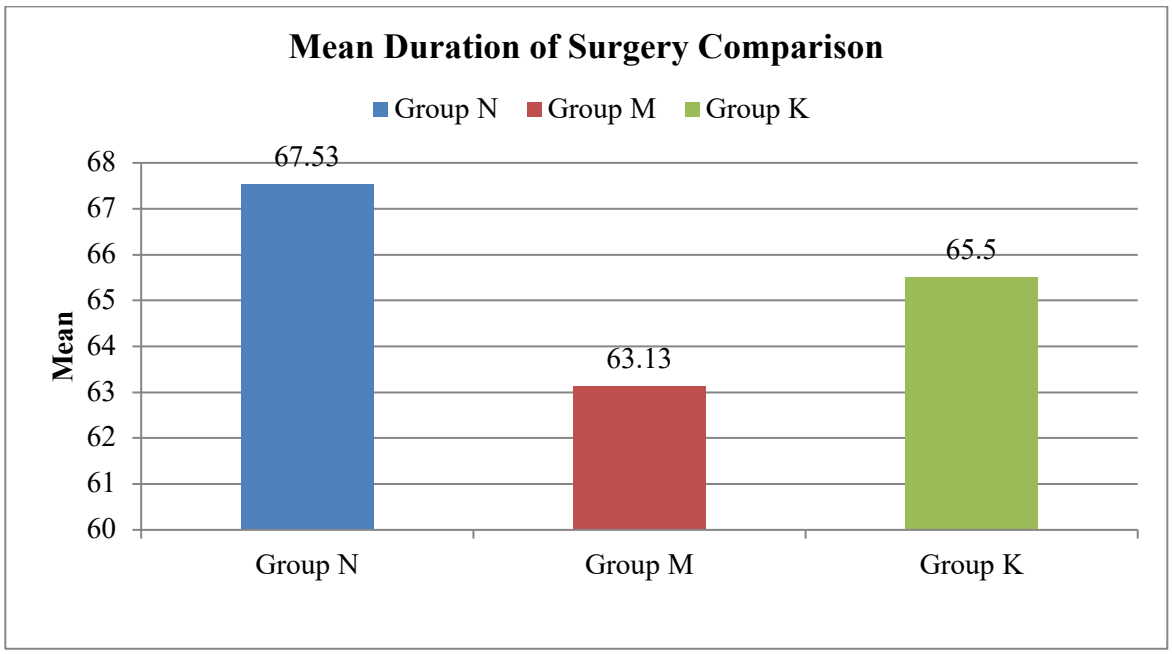

Figure 6: Bar Diagram Showing Mean Duration of Surgery Comparison between three groups.

Table 7: Mean SBP Comparison between three groups at different intervals of time

SBP	Group						p value
	Group N		Group M		Group K		
	Mean	SD	Mean	SD	Mean	SD	
Pre Neb	117.6	38.1	123.25	34.2	122.2	10.19	0.673
Post Neb	126.8	10.73	132.4	6.89	129	9.47	0.025*
Before Intubation	113	19.83	110.2	16.29	109.7	14.32	0.645
Just After Intubation	129.6	39.59	134.2	15.49	142.7	12.07	0.07
3 Min	124	13.22	117.4	14.12	124.7	7.16	0.012*
5 Min	114.8	13.92	110.4	14.66	119.9	6.85	0.003*
10 Min	113.2	9.29	110.5	9.45	117.4	9.49	0.005*

Table 8: Post Hoc Bonferroni Test

Dependent Variable	(I) Group	(J) Group	P value
Pre NEB	Group N	Group M	1.000
		Group K	1.000
	Group M	Group K	1.000
Post NEB	Group N	Group M	0.022*
		Group K	0.856
	Group M	Group K	0.300
Before Intubation	Group N	Group M	1.000
		Group K	1.000
	Group M	Group K	1.000
Just After Intubation	Group N	Group M	1.000
		Group K	0.070
	Group M	Group K	0.417
3 Min After Intubation	Group N	Group M	0.044*
		Group K	1.000
	Group M	Group K	0.021*
5 Min After Intubation	Group N	Group M	0.339
		Group K	0.200
	Group M	Group K	0.002*
10 Min After Intubation	Group N	Group M	0.606
		Group K	0.145
	Group M	Group K	0.004*

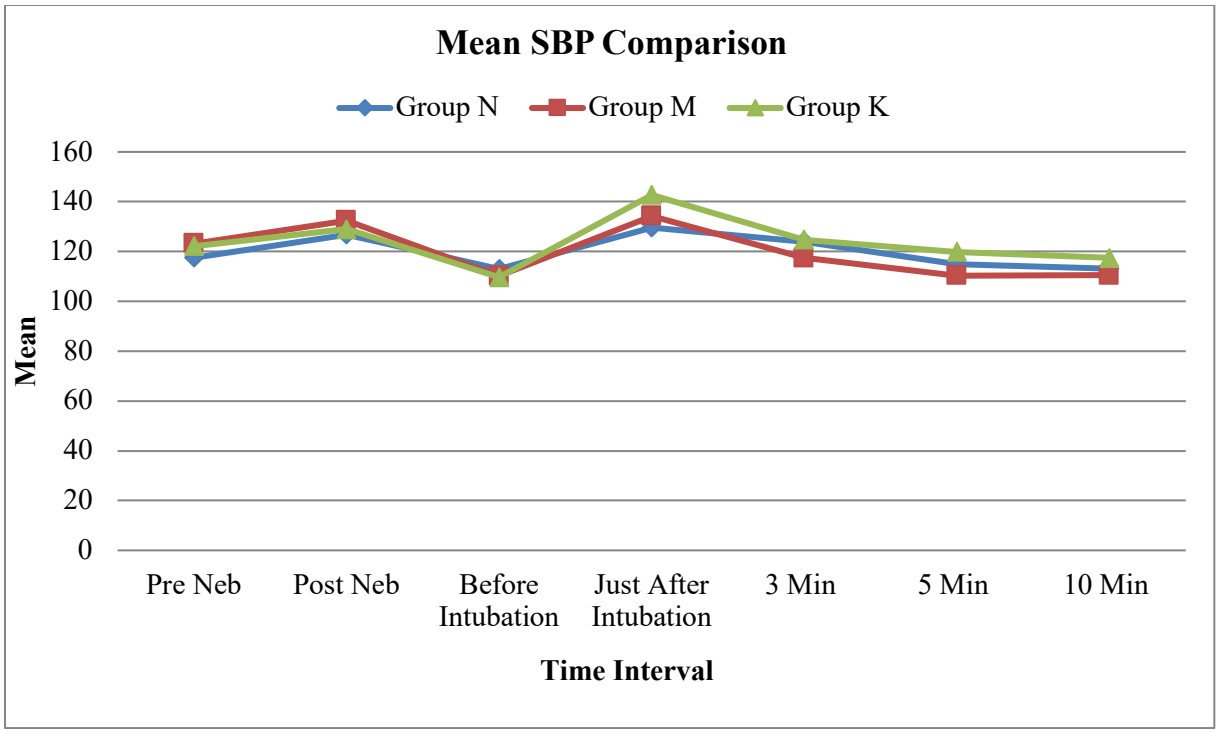

Figure 7: Line Diagram Showing Mean SBP Comparison between three groups at different intervals of time.

Table 9: Mean DBP Comparison between three groups at different intervals of time

DBP	Group						p value
	Group N		Group M		Group K		
	Mean	SD	Mean	SD	Mean	SD	
Pre Neb	82.4	9.14	82.4	9.27	78.1	8.53	0.051
Post Neb	79.8	7.49	82.6	6.9	79.8	8.23	0.165
Before Intubation	70.2	12.27	68	10.95	68.6	11.1	0.675
Just After Intubation	92.2	9.69	86.2	7.66	87.4	11.63	0.017*
3 Min	81.2	12.26	76.4	12.54	76.9	7.39	0.104
5 Min	74.4	8.39	70.8	9.51	74.6	8.44	0.098
10 Min	72.6	7.74	70	8.1	74.5	9.32	0.06

Table 10: Post Hoc Bonferroni Test

Dependent Variable	(I) Group	(J) Group	P value
Pre NEB	Group N	Group M	1.000
		Group K	0.103
	Group M	Group K	0.103
Post NEB	Group N	Group M	0.301
		Group K	1.000
	Group M	Group K	0.301
Before Intubation	Group N	Group M	1.000
		Group K	1.000

	Group M	Group K	1.000
Just After Intubation	Group N	Group M	0.021*
		Group K	0.091
	Group M	Group K	1.000
3 Min After Intubation	Group N	Group M	0.160
		Group K	0.248
	Group M	Group K	1.000
5 Min After Intubation	Group N	Group M	0.209
		Group K	1.000
	Group M	Group K	0.167
10 Min After Intubation	Group N	Group M	0.509
		Group K	0.944
	Group M	Group K	0.055

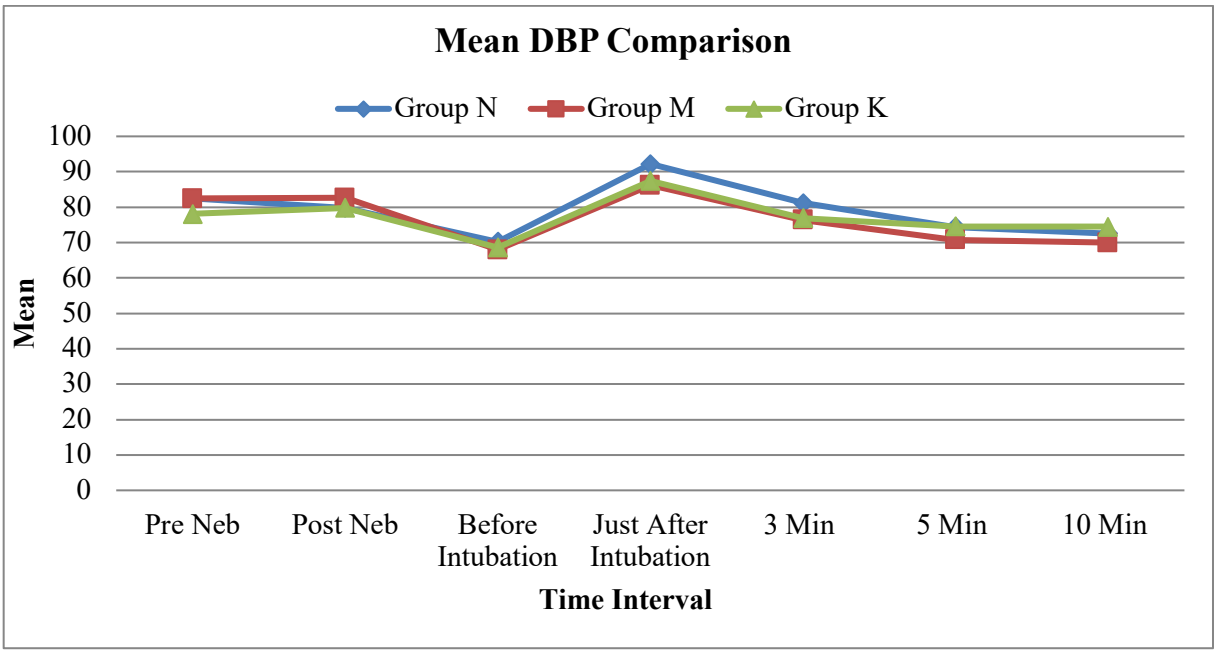

Figure 8: Line Diagram Showing Mean DBP Comparison between three groups at different intervals of time.

Table 9: Mean MAP Comparison between three groups at different intervals of time

	Group						p value
	Group N		Group M		Group K		
	Mean	SD	Mean	SD	Mean	SD	
Pre Neb	89.7	11.4	93.8	13.23	90.6	12.14	0.712
Post Neb	87.3	8.76	92.8	13.04	89	13.59	0.115
Before Intubation	77.6	15.61	80.8	13.16	79.1	12.29	0.583
Just After Intubation	98.8	11.82	102	8.5	100.3	14.22	0.478
3 Min	88.2	9.08	89.4	10.91	87	10.02	0.566
5 Min	80.7	7.3	81.9	11.39	83.3	9.69	0.482
10 Min	78.4	4.13	79.2	9.47	81.2	9.89	0.299

Dependent Variable	(I) Group	(J) Group	P value
Pre NEB	Group N	Group M	0.481
		Group K	0.773
	Group M	Group K	0.036*
Post NEB	Group N	Group M	0.128
		Group K	1.000
	Group M	Group K	0.478
Before Intubation	Group N	Group M	0.901
		Group K	1.000
	Group M	Group K	1.000
Just After Intubation	Group N	Group M	0.677
		Group K	1.000
	Group M	Group K	1.000
3 Min After Intubation	Group N	Group M	1.000
		Group K	1.000
	Group M	Group K	0.860
5 Min After Intubation	Group N	Group M	1.000
		Group K	0.686
	Group M	Group K	1.000
10 Min After Intubation	Group N	Group M	1.000
		Group K	0.396
	Group M	Group K	0.843

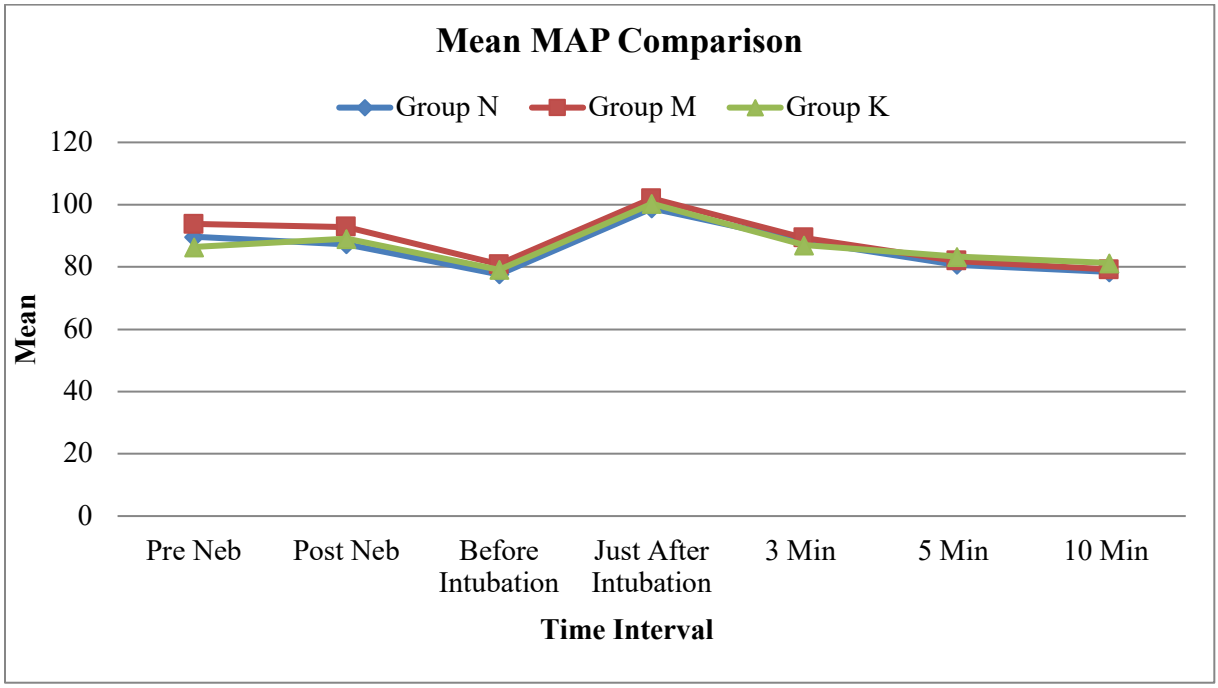

Figure 9: Line Diagram Showing Mean MAP Comparison between three groups at different intervals of time.

Table 10: Number of attempts Distribution between three groups

		Group					
		Group N		Group M		Group K	
		Count	%	Count	%	Count	%
No of attempts	1	40	100.00%	39	97.50%	39	97.50%
	2	0	0.00%	1	2.50%	1	2.50%

$\chi 2 = 1.017$, df = 2, p = 0.601

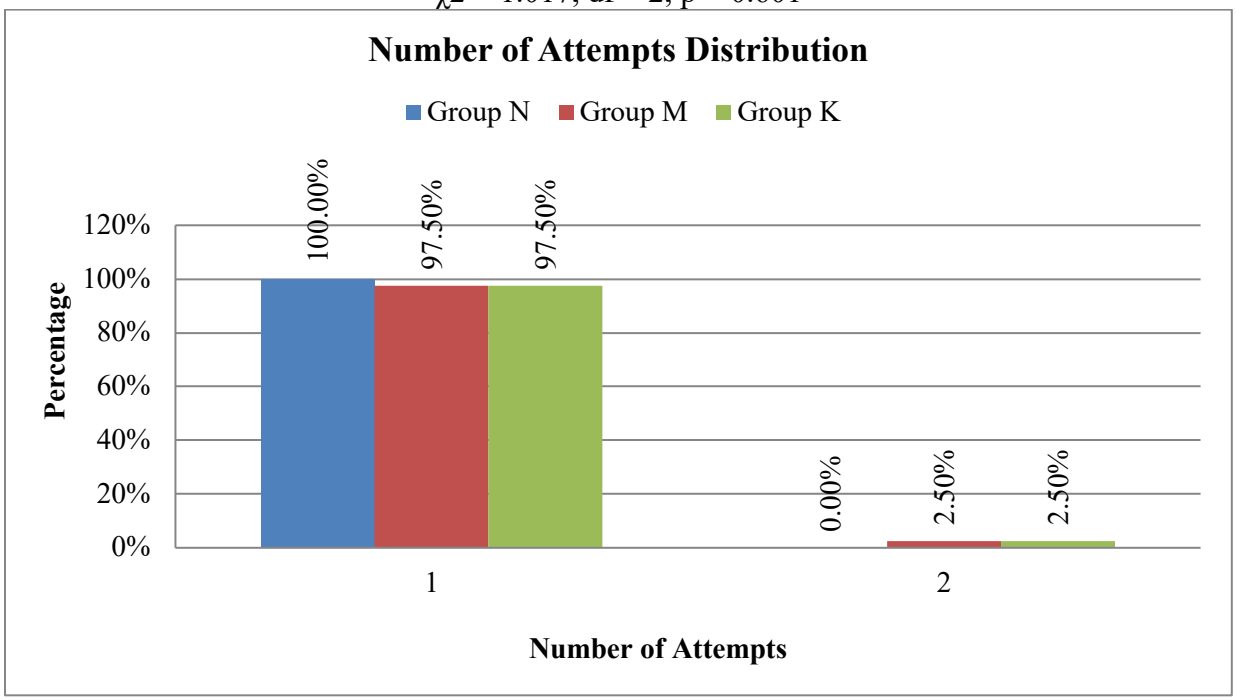

Figure 10: Bar Diagram Showing Number of Attempts Distribution between two groups

Table 11: Sore throat Distribution between three groups at different intervals of time

		Group						p value
		Group N		Group M		Group K		
		Count	%	Count	%	Count	%	
0th hour	No ST	40	100.00%	40	100.00%	40	100.00%	
2nd hour	Grade 1	3	7.50%	0	0.00%	0	0.00%	0.046*
	No ST	37	92.50%	40	100.00%	40	100.00%	
4th hour	Grade 1	10	25.00%	5	12.50%	2	5.00%	0.001*
	Grade 2	5	12.50%	0	0.00%	0	0.00%	
	No ST	25	62.50%	35	87.50%	38	95.00%	
6th hour	Grade 1	15	37.50%	6	15.00%	3	7.50%	< 0.001*
	Grade 2	6	15.00%	2	5.00%	0	0.00%	
	No ST	19	47.50%	32	80.00%	37	92.50%	
8th hour	Grade 1	9	22.50%	3	7.50%	2	5.00%	0.052
	Grade 2	2	5.00%	2	5.00%	0	0.00%	
	No ST	29	72.50%	35	87.50%	38	95.00%	
12th hour	Grade 1	2	5.00%	0	0.00%	0	0.00%	0.195
	Grade 2	0	0.00%	1	2.50%	0	0.00%	

	No ST	38	95.00%	39	97.50%	40	100.00%	
24th hour		0	0.00%	1	2.50%	0	0.00%	0.365
	No ST	40	100.00%	39	97.50%	40	100.00%	

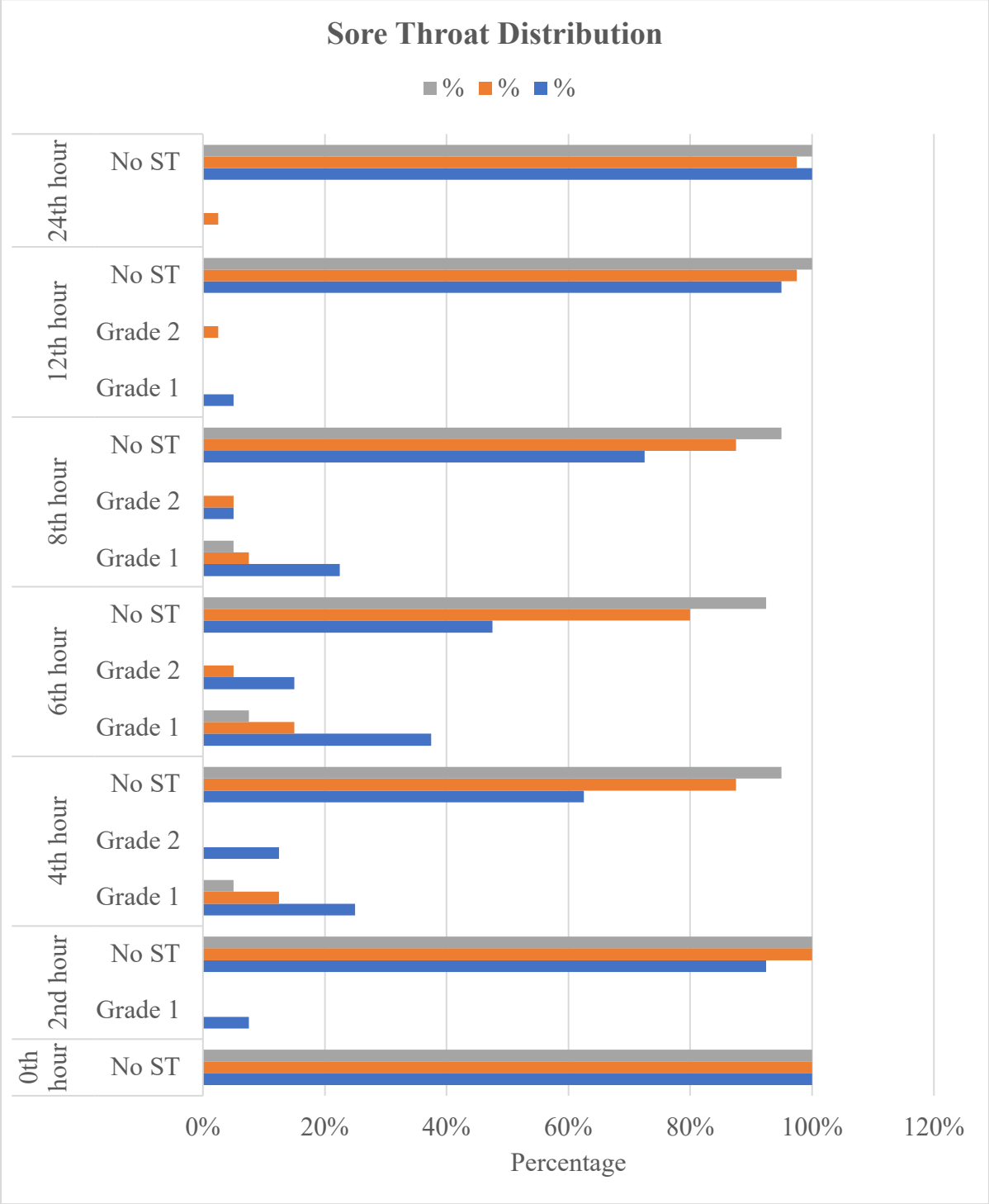

Figure 11: Column Diagram Showing Sore throat Distribution between three groups at different intervals of time

Table12: Overall incidence of Sore throat

		Group						Group N vs M	Group N vs K	Group M vs K
		Group N		Group M		Group K				
		Count	%	Count	%	Count	%			
Over all Incidence of Sore throat	Yes	23	57.5%	10	25.0%	4	10.0%	0.003*	<0.001*	0.004*
	No	17	42.5%	30	75.0%	36	90.0%			

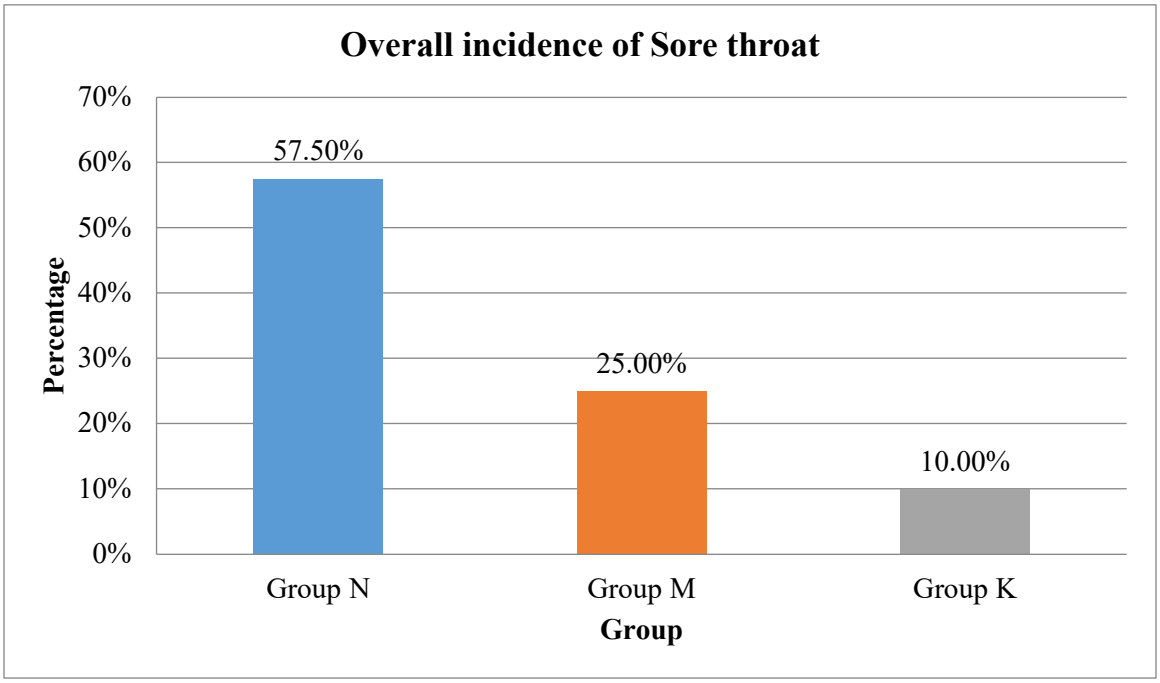

Figure 12: Bar diagram showing Overall incidence of Sore throat.

Discussion

All the three groups were similar in demographic data like age, sex, ASA status, weight. There was no significant difference in mean time taken for laryngoscopy, number of attempts of laryngoscopy and mean duration of surgery.

The overall incidence of POST in our study was 30.8% of which 57.5% in control group, 25% and 10% in group M and group K respectively.

In group N 23 patients had Sore Throat (ST) out of which 13 patients had grade II and 10 patients had grade I ST

In group M 11 patients had ST of which 5 patients had grade 2 sore throat and 6 grade I and in group K 4 patients had sore throat all grade I.

So, in the present study, we found that there was a significant difference in Sore Throat Distribution between three groups and attenuation of ST at 2nd hour, 4th hour and 6th hour.

Ahuja *et al* [8]., studied the effect of nebulized ketamine on incidence and severity of post-operative and concluded that Ketamine nebulization significantly attenuated the incidence and severity of POST, especially in 2nd and 4th hour with no adverse effects. Yadav M *et al* [5]., in their study reported that MgSO4 significantly

reduces the incidence of POST compared to normal saline.

Jain S *et al* [19]., compared preoperative Ketamine and MgSO4 nebulisation for incidence of POST after Endotracheal Intubation and concluded that the Incidence of ST was significantly less with ketamine and MgSO4 nebulisation. In a similar study conducted by Segaran S *et al* [2], the incidence of postoperative sorethroat was significantly decreased with ketamine nebulization 50 mg when compared to magnesium sulfate 250 mg. Also, Rajan S *et al* [18]., in their study concluded that Nebulization with ketamine 50 mg and magnesium sulfate 500 mg, reduce the incidence and severity of POST which stands in line with my study.

The proposed mechanism of action of both ketamine and magnesium sulfate is through NMDA receptors N-methyl-D-aspartate (NMDA) receptors have a role in nociception and inflammation [14] and are found both in the central nervous system and in peripheral nervous system [15]. Ketamine and magnesium sulfate are NMDA antagonist [2,5,8-11,18] and attenuate ST by their action on peripheral nerves in pharangeal mucosa. Both ketamine and magnesium sulfate are extensively used for their analgesic action but its systemic effects and also used in regional blocks to prolong the duration of analgesia.

Although no statistically significant difference in mean blood pressure between three groups post nebulisation and post intubation, it was found that magnesium attenuates the hemodynamic responses to laryngoscopy from SBP and DBP post hoc analysis.

No adverse effects were recorded in any of the groups.

Conclusion

Ketamine and magnesium sulfate both decreased the incidence of postoperative sore throat after endotracheal intubation with ketamine 50mg nebulistion being more effective than magnesium sulfate 250mg nebulisation.

We did not find any hemodynamic changes in either of the groups.

No complications were reported in any of the groups.

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