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COMPARISON BETWEEN NEBULISATION OF MGSO4 20 MG/KGBW WITH KETAMINE 0.5 MG/KGBW ON THE INCIDENT OF POST-OPERATIVE SORE THROAT DUE TO ENDOTRACHEAL INTUBATION IN PATIENTS UNDERGOING GENERAL ANESTHESIA IN DR. HASAN SADIKIN HOSPITALS BANDUNG

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ABSTRACT

Post Operative Sore Throat (POST) is a Symptoms often experienced by patients after surgery under general anesthesia and endotracheal intubation. The incidence of POST is between 21-71.8%. *POST causes discomfort to patients which can prolong hospital stay. In this study, a comparison was made between MgSO4 nebulization* 20 *mg/ KgBW and ketamine nebulization* 0.5 *mg/ KgBW on the incidence of POST after general anesthesia at* RSUP Dr. Hasan Sadikin Bandung . *This study used a double blind randomized controlled trial design.* 72 *elective surgery patients were randomly divided into* 2 *groups. Group M was given MgSO4 nebulization while group K was given ketamine nebulization. Nebulization was performed* 15 *minutes before induction of general anesthesia. POST monitoring was performed at* 1, 4 *and* 24 *hours after extubation using POST scoring. In this study, it was found that the incidence of POST in group M, namely the 1st hour of* 13.5%, *the 4th hour of* 10.8% *and the 24th hour of* 0% *was lower than that in group K, namely the 1st hour of* 28.5%, *the 4th hour of* 32.5% *and the 24th hour of* 0% . *Statistical test results* p=0.033 *showed a significant difference in group M better than group K at the 4th hour in reducing the incidence of POST. MgSO4 and ketamine have antinociceptive and anti-inflammatory effects with the mechanism of action of blocking NMDA receptors that inhibit calcium influx that avoids central sensitization. MgSO4 also has a muscle relaxing effect and reduces airway mucus secretion, thus reducing the risk of trauma during endotracheal intubation. The conclusion of this study is that MgSO4 nebulization shows a lower incidence of POST than ketamine nebulization.*

Key words: *General anesthesia, Endotracheal intubation, Ketamine, MgSO4, POST nebulization.*

INTRODUCTION

Postoperative throat pain or *Postoperative sore throat* (POST) is often considered the most common complication often occur after intubation endotracheal . Intubation endotracheal often linked with various degree of trauma to the mucosa airway which can cause irritation and inflammation · Although POST generally is effect side mild recovery with by itself , it can cause dissatisfaction patient so that can prolong hospital stay .[1 - 4]

Incidence of postoperative sore throat after intubation endotracheal ranged from 21-71.8 % . In Indonesia itself, research comparing the incidence of post-operative throat pain using a laryngeal mask and tracheal tube reported that 62.3% of the incidence of throat pain was caused by ETT and 12.9% was caused by LMA. The incidence of postoperative sore throat may be associated with the size endotracheal tube , endotracheal tube balloon pressure , prolonged duration of anesthesia and use of double lumen endobronchial tubes . The size of the endotracheal tube balloon pressure that exceeds 25 cmH2O can increase the pressure effect on the tracheal mucosa with consequent ischemia and inflammatory changes increases the risk of postoperative sore throat .[5 - 8]

Various pharmacological and non-pharmacological methods have been tried to reduce the incidence of POST with varying degrees of success. Several studies used non-pharmacological methods shows varying results but is considered less significant in reducing the incidence of POST. Among various pharmacological interventions, the use of magnesium sulfate and ketamine mouthwash has the highest success rate. However, problems that can arise from using mouthwash or throat lozenges are the bitter taste of the medicine and the risk of aspiration when gargling which can cause serious complications. Therefore, administering drugs via the aerosol route has become popular among anesthesiologists because it provides a good response from patients and reduces complications that can occur with the use of mouthwash .[9 - 13]

The N-methyl-D-aspartate (NMDA) receptor plays a role in nociception and inflammation . NMDA receptors are found not only in the system nerve center but also in the system nerve edge and marrow bone behind . Antinociceptive and anti-inflammatory properties from ketamine and magnesium sulfate with available data show that both of them own role potential in reduce POST.[14 - 16]

A studies compare nebulization ketamine 50 mg with nebulized normal saline 5 ml shows results decline significant incidence of POST at 2 and 4 hours postoperatively . In another study that compared nebulized MgSO4 225 mg with nebulized normal saline 3 ml shows results MgSO4 nebulization is proven safe , simple , and effective reduce POST events are compared with nebulized normal saline 3 ml.[3,12,16]

With this background, the author wants to know the comparison of 20 mg / kgbb MgSO4 nebulization with nebulization ketamine 0.5 mg / kgbb on the incidence of throat pain after general anesthesia surgery Intubation *Endotracheal* at Dr. RSUP. Hasan Sadikin Bandung .

SUBJECT AND METHOD

This research uses design study analytic comparative experimental , with design *double blind randomized controlled trial* to second group study . Retrieval technique sample study done with consecutive sampling method , namely with take every subject adequate research criteria inclusion and exclusion based on order arrival patient .

Study has done at Dr. RSUP. Hasan Sadikin Bandung (RSHS) Data collection was carried out after get agreement from Committee Ethics and permits from Director of RSUP Dr. Hasan Sadikin until with data collection and processing is complete .

Study done of 71 subjects who underwent operation in general anesthesia anesthesia which has fulfil criteria inclusion and exclusion criteria exclusion . The population used sample will done randomization in block permutation into 2 groups , namely group M was carried out nebulization with MgSO4 20mg/ KgBW a total of 37 subjects whereas group K was carried out nebulization with Ketamine 0.5mg/ KgBB as many as 35 subjects . There is n't any excluded subject in this research .

Taking sample use formula $n1 = n2 = \left(\frac{Z_\alpha\sqrt{2p(1-p)}+Z_\beta\sqrt{p1(1-p1)+p2(1-p2)}}{(p1-p2)}\right)^2$. Based on formula the with choose level 95% confidence with hypothesis One direction (Zα = 1.64) and power test 80% (Zβ = 0.84). Based on journal study previously obtained For proportion exists complaints in group I (nebulization ketamine) by 25% (p1=0.22) and in group II (nebulized Mgso4) by 50% (p2=0.55). Total proportion p=(p1+p2)/2 =(0.22+0.55)/2=0.385. With thereby amount minimum sample for each group is 33 people, plus with a 10% (3 people) chance experienced samples *dropped out* so that amount samples of each group drug is 36 people. Determination allocation which treatment is given to patient A double blind randomized controlled trial was used against second group study . Results data study analyzed and presented in form table in accordance with identified variables during study . This research has get agreement ethics with number LB.02.01/X.6.5/361/2023.

How research works First all over the patient who becomes subject study done anesthesia general and intubated . The population used sample will done randomization in block permutation into 2 groups , namely group in group M was carried out nebulization with MgSO4 20 mg/ kgbb added Nacl 0.9% up to 5 cc, Group K is performed nebulization with ketamine 0.5 mg/ kgbb added Nacl 0.9% up to 5 cc. Randomization carried out by residents anesthesia is not involved in the research process , results randomization will given in sealed envelope

Patients fasted for six hours before surgery . After the patient arrives in the operating room waiting room, the patient is re-examined for identity, diagnosis, anesthesia action plan and infusion access . Done inspection track patient's intravenous and infusion flow fluent. The patient is then given nebulization for 10 -15 minutes according to the previously randomly determined treatment group. The research drug has been prepared assistant study with share into two groups that is group M and group K.

Group M was carried out nebulization with MgSO4 20 mg/ kgbb added Nacl 0.9% up to 5 cc with use 5cc syringe . After that this solution was transferred into the container on the nebulization mask and carried out nebulization for 10-15 minutes . Group K was carried out nebulization with ketamine 0.5 mg/ kgbb added Nacl 0.9% up to 5 cc with use 5 cc syringe . After that this solution was transferred into the container on the nebulization mask and carried out nebulization for 10-15 minutes . After that is done recording hemodynamics patient form pulse heart , pressure blood and saturation patient before nebulization and after nebulization .

Statistic test For compare scale painful between the 2 groups with categorical data type done with the Mann Whitney test. After results the analysis show that second group the homogeneous so that worthy For compared and can be Hypothesis testing is carried out in a way statistics more carry on . Whereas analysis statistics for categorical data that has a 2x2 table is tested with the chi-square test if Chi-Square condition is met if not fulfilled so Fisher's Exact test is used for 2 x 2 tables and Kolmogorov Smirnov for tables other than 2 x 2. The Chi Square condition is non- existent the expected value is less from 5 as much as 20% of the table. There are no types of data in this study numeric so it does not use the data normality test . Data obtained noted in form special Then processed through the Statistical Product and Service Solutions (SPSS) program version 25.0.

RESULTS

Based on results inspection comparison Characteristics subject study based on age , type gender , weight , height , BMI, ETT size , duration anesthesia , cuff pressure , ASA and level education between group M and group K were not found difference significant (p>0.05; Table 1). Group M has mean age 36.7±11.0 years with man as many as 16 people and women as many as 21 people, average body weight 56.4 ± 7.9 kg whereas average height 156.9 ± 6.2 cm and average BMI 22.9 ± 3.1 kg/m2 . For the size of the ETT used was an average of 7.2 ± 0.3, duration anesthesia 135.3±25.9 minutes and cuff pressure 23.1±1.3. The ASA assessment found ASA 1 as many as 11 people and ASA 2 as many as 26 people . Meanwhile in group K, the average age was 38.6 ± 12.5 years with man as many as 19 people and women as many as 16 people, average body weight 59.9 ± 10.4 kg whereas average height 158.9 ± 5.4 cm and average BMI 23.7 ± 3.8 kg/m2 . For the size of the ETT used was an average of 7.3 ± 0.3, duration anesthesia 134.4±30.3 minutes and cuff pressure 23.2±0.9. The ASA assessment found ASA 1 as many as 13 people and ASA 2 as many as 22 people.

Table 1 General Characteristics of Subjects Study

Variable	Group		P value *
	M = nebulized $MgSO_4$ 20 mg/ kgbb	**K = nebulization ketamine 0.5 mg/ kgbb**	
	n = 37	**n = 35**	
Age			0.528
Mean±SD	36.7±11.0	38.6±12.5	
Median (Min-Max)	38 (17 – 56)	40 (17 – 59)	
Gender [n (%)]			0.349
Man	16 (43.2%)	19 (54.3%)	
Woman	21 (56.8%)	16 (45 . 7 %)	
Education Level [n (%)]			
JUNIOR HIGH SCHOOL	10 (52.6%)	9 (47.4%)	
SENIOR HIGH SCHOOL	9 (52.9%)	8 (47.1%)	0.278
D3	8 (50%)	8 (50%)	
S1	11 (45.8%)	13 (54.2%)	
Weight			0.120

Variable	Group		P value *
	M = nebulized $MgSO_4$ 20 mg/ kgbb	**K = nebulization ketamine 0.5 mg/ kgbb**	
	n = 37	**n = 35**	
Mean±SD	56.4±7.9	59.9±10.4	
Median (Min-Max)	56 (35 – 80)	58 (43 – 100)	
Height			0.294
Mean±SD	156.9±6.2	158.9±5.4	
Median (Min-Max)	158 (140 – 168)	160 (150 – 170)	
BMI			0.460
Mean±SD	22.9±3.1	23.7±3.8	
Median (Min-Max)	22.7 (12.9 – 28.3)	23.4 (17.5 – 35.0)	
ETT size			0.352
Mean±SD	7.2±0.3	7.3±0.3	
Median (Min-Max)	7 (7.0 – 7.5)	7.3 (7.0 – 7.5)	
Duration Anesthesia			0.848
Mean±SD	135.3±25.9	134.4±30.3	
Median (Min-Max)	120 (100 – 180)	120 (90 – 180)	
Cuff Pressure			0.991
Mean±SD	23.1±1.3	23.2±0.9	
Median (Min-Max)	24 (20 – 25)	23 (21 – 25)	
ASA [n (%)]			0.505
1	11 (29.7%)	13 (37.1%)	
2	26 (70.3%)	22 (62.9%)	

Description: For numeric data p values are tested with unpaired T test if the data is normally distributed with Alternative *Mann Whitney* test if the data is not normally distributed . Categorical data p value is calculated based on the *Chi-Square* test with alternative *Kolmogorov Smirnov* and *Fisher's Exact tests* if condition from *Chi-Square* is not met . Meaningful value based on p value <0.05.

Analysis results bivariate comparison incident painful throat between group M and group K at the 1st hour, the 4th hour and the 24th hour were obtained difference significant on scale painful throat on both group in the 4th hour with p value <0.05. By the 4th hour, the majority group M has painful throat with scale 0 is 89.2% and the majority group K has painful throat with scale 0 is 68.6%. At the 1st hour and 24th hour it was not found difference significant scale painful throat between group M and group K (P>0.05; Table 2)

Table 2 Comparison Group M and Group K against Throat Pain Occurrence

Throat Pain	**Group**		**p-value***
	M= nebulized $MgSO_4$ 20 mg/ kgbb	**K= nebulization ketamine 0.5 mg/ kgbb**	
	n = 37	**n=35**	
At 1 o'clock			0.120
0	32 (86.5%)	25 (71.4%)	
1	4 (10.8%)	8 (22.9%)	
2	1 (2.7%)	2 (5.7%)	
3	0 (0.0%)	0 (0.0%)	
4 o'clock			**0.033 ***
0	33 (89.2%)	24 (68.6%)	

Throat Pain	Group		p-value*
	M= nebulized $MgSO_4$ 20 mg/ kgbb	K= nebulization ketamine 0.5 mg/ kgbb	
	n = 37	n=35	
1	3 (8.1%)	8 (22.9%)	
2	1 (2.7%)	3 (8.6%)	
3	0 (0.0%)	0 (0.0%)	
24 hours			-
0	37 (100.0%)	35 (100.0%)	
1	0 (0.0%)	0 (0.0%)	
2	0 (0.0%)	0 (0.0%)	
3	0 (0.0%)	0 (0.0%)	

Description *:* * For numeric data p values are tested with unpaired T test if the data is normally distributed with Alternative *Mann Whitney* test if the data is not normally distributed . Meaningful value based on p value <0.05

Analysis results bivariate comparison incident cough between group M and group K at the 1st hour, the 4th hour and the 24th hour can seen that number incident cough in group M was 10.8% and group K was 7%. Incident cough post-operatively in group M and group K both at the 1st, 4th and 24th hours P value > 0.05 which means it doesn't exist difference significant incident cough post-operatively on both group . (Table 3)

Table 3 Comparison Group M and Group K against Coughing Occurrence

Cough	Group		p value*
	M= nebulized $MgSO_4$ 20 mg/ kgbb	K= nebulization ketamine 0.5 mg/ kgbb	
	n = 37	n=35	
At 1 o'clock			0.252
0	33 (89.2%)	28 (80.0%)	
1	4 (10.8%)	5 (14.3%)	
2	0 (0.0%)	2 (5.7%)	
3	0 (0.0%)	0 (0.0%)	
4 o'clock			0.281
0	36 (97.3%)	3 (91.4%)	
1	1 (2.7%)	3 (8.6%)	
2	0 (0.0%)	0 (0.0%)	
3	0 (0.0%)	0 (0.0%)	
24 hours			-
0	37 (100.0%)	35 (100.0%)	
1	0 (0.0%)	0 (0.0%)	
2	0 (0.0%)	0 (0.0%)	
3	0 (0.0%)	0 (0.0%)	

Description: * For numeric data p values are tested with unpaired T test if the data is normally distributed with Alternative *Mann Whitney* test if the data is not normally distributed . Meaningful value based on p value <0.05.

From the results calculations in Table 4 can be seen that on the second group intervention , not found exists effect side like nausea , tachycardia , bradypnea , sedation , etc hypotension and hypertension . By statistics, all over effect this side can't see degrees its meaning because all data is valuable the same.

Table 4 Comparison Effect Side in groups M and K

Effect Side	Group		p value*
	M = nebulized $MgSO_4$ 20 mg/ kgbb	K = nebulization ketamine 0.5 mg/ kgbb	
	n (%)	n (%)	
Nauseous	0 (0.0%)	0 (0.0%)	-

Effect Side	Group		p value*
	M = nebulized $MgSO_4$ 20 mg/ kgbb	K = nebulization ketamine 0.5 mg/ kgbb	
	n (%)	n (%)	
Tachycardia	0 (0.0%)	0 (0.0%)	-
Bradypnea	0 (0.0%)	0 (0.0%)	-
Sedation	0 (0.0%)	0 (0.0%)	-
Hypotension	0 (0.0%)	0 (0.0%)	-
Hypertension	0 (0.0%)	0 (0.0%)	-

Description *: *)* Categorical data p value is calculated based on the *Chi-Square* test with alternative *Kolmogorov Smirnov* and *Fisher's Exact tests* if condition from *Chi-Square* is not met . Meaningful value based on p value <0.05.

DISCUSSION

Study done of 72 patients who underwent operation elective in anesthesia general compliance criteria inclusion and exclusion . This research and shared into two groups that is group M who used intervention nebulized MgSO4 at a dose of 20 mg/ kgbb as many as 37 patients and group K with intervention nebulization ketamine at a dose of 0.5 mg/ kgbb as many as 35 patients

The characteristics of research subjects in group M and group K based on age, body mass index (BMI), ETT size, duration of anesthesia, ASA status and ETT balloon pressure based on statistical test results (p>0.05) did not show significant differences.

Based on study previously researched *Postoperative throat complications after tracheal intubation* , figures POST incidence was 46%. This is when compared to with results research conducted by researchers with giving Nebulization MgSO4 20mg/ kgbb preoperatively, occurs decline number POST incidence was 16.2%. The results of this research are also lower the previous study, Which comparing between nebulization MgSO4 225 mg with Nacl 0.9% where obtained results POST incident on the group administration of MgSO4 225 mg by 44%. This is expected because in this study , the dose used based on weight so considered more proportional For each subject study .[7,12,29]

According to the results of this research figures POST incidence in group M was more low compared to with group K at the 1st and 4th hours after surgery. Found that the incidence in group M, namely the 1st hour, was 13.5%, whereas group K was 28.5%, however based on statistical test results mark p= 0.120 (p>0.05) so it doesn't show difference significant between second group. At the 4th hour number the incidence of POST in group M was 10.8%, meanwhile group K was 32.5% with statistical test results mark p= 0.033 (p<0.05) shows that there is difference significant group M more low from inner K group lower POST event . At the 24th hour, no more POST incidents were found in the second time group .

The results of this study are appropriate with a number of study previously also compared administration of MgSO4 with ketamine in lower POST event. Based on study previously show in a way significant lower more POST events lower in the MgSO4 group compared with group ketamine at 2 hours (p=0.023), 4 hours (p=0.001), and 8 hours (p=0.044).[15]

On research there was one before difference significant more POST incidents low in the group magnesium compared with group ketamine at 2 hours (P=0.032), 4 hours (P=0.02) and 24 hours (P=0.01) after surgery , however incident Sick throat post-operatively on two groups after use drug magnesium gargle or ketamine is no different in a way significant moment arrived at the room recovery at hour 0 (P = 0.085).[28]

Other research also found significant difference in pain throat moment use drug magnesium sulfate gargle and medication gargle ketamine on the NRS scale . From the results research , there is difference meaningful between drug gargle magnesium sulfate and ketamine at the 1st hour (p = 0.01) and 6th hour (p = 0.022). Differences from previous research done that is giving MgSO4 and ketamine drugs given in a way gargle or throat lozenge often causes a bitter taste of the drug and the risk of aspiration when gargling which can cause serious complications. Therefore, in this study, drug administration via the aerosol route became popular among anesthesiologists and provided a good response from patients and this method ensures that drug distributed in a way evenly and effectively throughout the pharynx beginning respiratory tract.[9]

MgSO4 and ketamine own effect antinociceptive and anti-inflammatory with block NMDA receptor so that inhibits calcium ions enters intracellularly cause prevention sensitization central caused by injury network peripheral. NMDA receptors are found not only in the system nerve center but also in the system nerve edge. Antinociceptive properties and anti-inflammatory from ketamine and magnesium sulfate with available data show that both of them own role potential in reduce POST event.[24,29]

Magnesium sulfate is antagonist NMDA receptor ion channels that have effect anti- inflammatory and antinociceptive properties consequence contact direct $Mg2^{+}$ with pharyngeal wall so lower release of inflammatory mediators like leukotrienes, thromboxane, and histamine. MgSO4 own effect anti-inflammatory with hinder release substance P by end nerve which lowers leakage microvascular so that reduce oedema tract and mucus hypersecretion.[16,24]
Mechanism of action of ketamine in reduce POST estimated consequence effect topical from nebulization inhibitory ketamine inflammation local and because effect analgesic ketamine peripheral. Using ketamine through route nose, medicine gargle and route rectal more show effect peripheral rather than effects systemic. On research previously related nebulization ketamine for reduce POST done gauge rate Intraoperative serum ketamine results show rate low serum ketamine. This shows that decline level more POST events big consequence effect topical ketamine rather than effects systemic ketamine.[12,16]

In this research, whole number incident coughing in group M was 4 people (10.8%) while in group K there were 7 people (20.0%) with details, events Grade 1 cough in the 1st hour in group M was 4 people (10.8%) while in group K there were 5 people (14.3%) and in grade 2 there were 2 people (5.7%). Then at the 4th hour it was discovered Grade 1 cough in group M was 1 person (2.7%) and 3 people (8.6%) in group K. In both groups not found patient with cough heavy. Incident cough post operation on both groups does not exist significant difference based on statistical test results with p value = 0.281 ($p>0.05$). This is also appropriate with study previously compared giving magnesium sulfate gargle and gargle ketamine in lower incident cough extubation endotracheal was obtained results patient magnesium sulfate group experience cough (30.4%) and 7 patients the ketamine group experienced cough (30.4%), statistical test obtained p=1,000 ($p>0.05$). [9]

In this study it was not found to exist effect side like bradycardia, tachycardia, hypertension or hypotension (20% pressure blood onset), nausea, bradypnea, hallucinations or bitter taste . This is appropriate with study administration of Mgso4 or ketamine nebulization previously. Bradycardia, hypotension, sedation often found in giving intravenously, while the taste is bitter and hallucinations can occur in giving other agents such as ketamine.[9,16,28]

Limitations this research because in this research, it was not carried out grouping patient in accordance type surgery certain, so can influence mark painful throat of the patient.

CONCLUSION

There is difference significant where nebulized MgSO4 20 mg/ kgbw lower incident of painful throat post-operative anesthesia generally done intubation endotracheal rather than nebulization ketamine 0.5 mg/ kgbw at RSUP Dr. Hasan Sadikin Bandung

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