Journal of Society Medicine
Research & Review Articles on Diseases
Journal of Society Medicine. 2022; 1(3)

Antisialogogue Effect of Atropine Sulfate at Dosages of 0.25 Mg and 0.5 Mg Under General Anesthesia with Ketamin

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ARTICLE INFO

Article history:
Received
15 December 2022

Accepted
30 December 2022

Manuscript ID:
JSOCMED-221217-3-4

Checked for Plagiarism: Yes

Language Editor:
Rebecca

Editor-Chief:
Prof. dr. Aznan Lelo, PhD

ABSTRACT

Introduction: Excessive saliva production can becomes an airway problem in conditions of decreased consciousness where there is impaired swallowing function. It increases the risk of aspiration of saliva into the airways that can result in choking. The use of premedication drugs to reduce the incidence of drug-induced hypersalivation can be done as a prevention. The anticholinergic drug class is the drug of choice for the management of hypersalivation in general anesthesia patients who have been given ketamine and ether. Ketamine as a sedating agent will provide a side effect of hypersalivation, where hypersalivation can cause laryngospasm or aspiration, as a form of prevention, anticholinergic drugs such as atropine can be given. The aim of this research was to compare the effect of antisialagogue on the administration of atropine sulfate at a dose of 0.25 mg and 0.5 mg in intravenous general anesthesia patients without ETT with ketamine at Haji Adam Malik General Hospital Medan and Putri Hijau Hospital Medan.
Method: This study used a double blind RCT design. A total of 60 patients with intravenous general anesthesia without ETT with ketamine (1-2 mg/kg BW) were divided into 2 groups of Atropine Sulfas doses (0.25 and 0.5 mg) then the total salivary volume of each patient was measured and analyzed.
Results: There was a significant difference between the treatment groups of 0.25 mg and 0.5 mg in the volume of saliva that had been collected (P-value = 0.008).
Conclusion: There was a significant comparison between the use of 0.25 mg and 0.5 mg atropine in patients at Haji Adam Malik Hospital and Putri Hijau Hospital Medan.

Keywords: General Anesthesia, Ketamine, Atropine Sulfate, Volume of Saliva

How to cite: Hasibuan MR, Lubis AP, Wijaya DW. Antisialogogue Effect of Atropine Sulfate at Dosages of 0.25 Mg and 0.5 Mg Under General Anesthesia with Ketamin. Journal of Society Medicine. 2022;1(3): 91-95

INTRODUCTION

General anesthesia is the most commonly used anesthetic technique. This technique works by putting the patient to sleep through the administration of induction and maintenance drugs through intravenous injection or the use of inhalation agents.[1] This technique is generally used in procedures with a relatively long operating duration, wide operating sites or neurosurgical operations. This aims to increase patient and operator comfort during the procedure and improve outcome and postoperative satisfaction.

Atropine is one of the drugs in the WHO List of Essential Medicines, which is an anticholinergic group that works as a non-selective MAChR inhibitor so that it eliminates parasympathetic effects. Atropine is a synthetically derived form of an endogenous alkaloid isolated from the plant Atropa belladonna. These agents are widely used for cardiovascular resuscitation and emergency management, in intensive therapy at the time of intubation and for reducing preoperative salivary production. This agent is also used in the treatment of

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acute sinus nodal dysfunction associated with bradycardia, complete atrioventricular block, and organophosphate poisoning and beta blockers. Atropine does not cross the blood-brain barrier.[2]

At our center, namely Haji Adam Malik General Hospital Medan, the premedication agent for general anesthesia that is routinely used daily is atropine sulfate at a dose of 0.25 given intravenously. So far there has been no study comparing the effectiveness of using atropine sulfate premedication at a dose of 0.25 mg which is commonly used in our center with the recommended dose of 0.4 – 0.6 mg.

METHOD

This study is an analytical experimental study which aims to determine the comparison of 0.25 atropine sulfate premedication and 0.5 mg administration related to salivary secretion in intravenous anesthetic patients. The subjects of this study were divided into 2 groups namely the 0.25 mg atropine sulfate group and the 0.5 mg atropine sulfate group which would be given TIVA general anesthesia without ETT with Ketamine. This study used an RCT (Randomized Clinical Trial) design with double blind, meaning that neither the research subjects nor the researchers had to know about the treatment or intervention given.

The resample used was a portion of the population that meets the inclusion and exclusion criteria. The sampling technique is the non-probability sampling method, by using consecutive sampling where the research subjects will be taken sequentially until the minimum sample size is met. RCT studies with consecutive sampling have been widely carried out and are considered the best among other non-probability sampling methods. Samples will then be randomly assigned to 2 groups, the first group given 0.25 mg and the other group 0.5 mg of atropine sulfate premedication.

RESULTS

This research is an experimental analytical research with RCT design. This study aims to determine the comparison of atropine sulfate premedication 0.25 mg and 0.5 mg related to salivary secretion in intravenous anesthetic patients. The subjects of this study were divided into 2 groups that is the 0.25 mg atropine sulfate group and the 0.5 mg atropine sulfate group which would be given TIVA general anesthesia without ETT with Ketamine. This research was carried out after passing the Ethical Clearance and the number of research subjects who met the inclusion and exclusion criteria was 60 patients.

Table 1 Table of Data Characteristics.

Characteristics	Sample Group				Total	
	0.25 mg		0.5 mg			
Age	n	%	n	%	n	%
16-25 years	2	6,67	4	13,33	6	10
26-35 years	4	13,33	9	30	13	21.67
36-45 years	10	33,33	9	30	19	31.67
46-55 years	11	36,67	7	23,33	18	30
56-60 years	3	10	1	3,34	4	6,66
Gender						
Man	12	40	17	56,67	29	48,33
Woman	18	60	13	43,33	31	56,67
PS-ASA						
I	13	43,33	18	60	31	56,67
II	17	56,67	12	40	29	48,83
Total	30	100	30	100	60	100

From Table 4.1 we can see there were 6 patients in the 16-25 years group (10%), with 2 patient in the 0.25 mg treatment group (6.67%) and 4 patient in the 0.5 mg group(13.33%). There were 13 patients aged 26-35 years (21.67%), with 4 patients in the 0.25 mg group (13.33%) and 9 patient in the 0.5 mg group (30%). A total of 19 patients in the 36-45 years age group (31.67%) with 10 patient in the 0.25 mg treatment group

(33.33%) and 9 patients in the 0.5 mg treatment group (30%). In the 46-55 years age group a total of 18 patients were counted (30%) with 11 patient in the 0.25 mg group (36.67%) and 7 patient in the 0.5 mg group (23.3%). Patients aged 56-60 years total for 4 patients (6.66%) and with 3 patientss in the 0.25 mg group (10%) and 1 patient in the 0.5 mg group (3.34%).

In this study, the total number of male subjects was 29 patients (48.33%), with the 0.25 mg group total of 12 patients (40%) and the 0.5 mg group total of 17 patients (56.7%). While the female sex acounted to 31 patients (56.67%) and the 0.25 mg group totaled 18 patients (60%) and the 0.5 mg group totaled 13 patients (43.3%). A total of 31 Patients Patients with PS-ASA 1 Classification was enrolled in this study (56.67%) with 13 patientsr from 0.25 mg group (43.3%) and 18 patients from 0.5 mg group (60%). While 29 subjects with PS-ASA 2 Classification (43.83%) with 17 Patients in the 0.25 mg group (56.67%) and 12 patients in the 0.5 mg group (40%)

The results of descriptive data analysis were processed out using SPSS to determine the distribution of research data. In this study, Kolmogorov-Smirnov data analysis was carried out to determine the normality of the data.

Table 2. Descriptive Analysis and Data Normality Test Results.

Data	Median	Min	Max	Means	±SD	p-values
Age (years)	43	17	57	41,32	10.53	0.047*
Weight (kg)	60	40	70	58,22	10.94	0.005*
Saliva (cc)	2	1	5	2,22	0.80	0.000*

Note: Kolmogorov-Smirnov test, *significant α<0,05

Based on the results of the normality test above, it is known that age is the only data on age, body weight and saliva not normally distributed. Data is declared normally distributed if the p-value of the normality test is > 0.05 and declared not normally distributed if the p-value of the normality test is <0.05.

Based on Table 4.2, it is known that the data on age, body weight, and the amount of saliva are not normally distributed. It is known that the median (min-max) age of the research subjects is 43(17-57) and the mean and standard deviation are 41.32+10.53. It is known that the median (min-max) weight of the research subjects is 60 (40-70) and the mean and standard deviation is 58.22+10.94. It is known that the median (min-max) value of the study subject's saliva is 2(1-5) and the mean and standard deviation are 2.22+0.8.

Table 3 Results of Data Analysis and Data Normality

Data	Sample Group	Median	Min	Max	Means	±SD	p-values
Saliva(cc)	0.25 mg	2	1	5	2,5	0.94	0.008*
	0.5 mg	2	1	3	1.93	0.52	

Note: The Mann Whitney test, *significant α<0,05

Based on the results of the analysis in Table 4.3, it was found that there was a significant difference between the 0.25 mg and 0.5 mg treatment groups in the volume of saliva that had been collected (p-value = 0.008). It is known that the median(min-max) value of the 0.25 mg group is 2(1-5) and the mean and standard deviation are 2.5 ± 0.94. It is known that the median(min-max) value of the 0.5 mg group is 2(1-3) and the mean and standard deviation are 1.93 ± 0.52.

DISCUSSION

In this study, the age of patients ranged from 16 to 60 years. The median of the patients age in this study was 43 years old, with the highest number of patients in the range of 36-45 years. The subjects of this study were patients being treated at H. Adam Malik Hospital in Medan and Putri Hijau Hospital in Medan. Patients with various age ranges will be grouped into groups that treated with 0.25mg and 0.5mg sulfas atropine with a double blind method, thus eliminating the possibility of bias in this study. The Age data in this study were found to be normally distributed through the data normality test (p=0.2). The 46-55 year old group was dominant in the 0.25 mg group, the 26-35 year old and 36-45 year old group was dominant in the 0.5 mg

group.[2] Although there was a difference in the median age of patients treated, both studies found that age was not a relevant variable. In Saleh and Elazzazi's study, a p-value of 0.428 was obtained, so there was no statistically significant difference ($p>0.05$). However, their research results did not include whether the ages were normally distributed or not.[3]

The saliva assessed in this study is the saliva produced during the operation, that is, from the administration of the drug until the operation is complete. Saliva measurement is carried out using a suction prepared with a measuring tube as a reservoir for saliva and will be measured after the saliva is obtained. From the results of the saliva measured, a median of 1 cc was obtained with a minimum amount of 2 cc and a maximum of 5 cc. Data on saliva volume obtained in this study were not normally distributed ($p<0.05$), having a significant difference between the amount of saliva secreted by the 0.25mg and 0.5mg groups. Research by Kessell J. also found hypersalivation problems in 5 patients out of 125 patients in his study. This complication occurred during the post-operative period, and was not of significant value. Data on patient distribution in Kessel J.'s study were not included in the study, so they could not be compared with ours.[4] Saleh and Elazzazi found increased secretions in 18 patients from all three groups. The 0.5 mg group was found in 1 patient, the 0.3 mg group was found in 2 patients, and 0.1 mg in 15 patients. In Saleh and Elazzazi's study, a comparison was made between the 3 groups, where a significant value was obtained in the comparison between the 0.3mg and 0.1 mg and 0.5 mg and 0.1 mg groups with p-values respectively $p=0.003$ and $p=0.001$. Data on the distribution of patients in the Saleh and Elazzazi studies were not included in the study, so they could not be compared with ours.[5]

There was a significant difference between the volume of saliva in the 0.25 mg group and the 0.5 mg group ($p=0.008$). In the 0.25 mg group it was obtained with a minimum volume of 1 cc and a maximum of 5 cc with a median of 2 cc, while in the 5mg group it was obtained with a minimum volume of 1 cc and a maximum of 3 cc with a median of 2 cc. Saleh and Elazzazi in their research also obtained significant value from comparisons between the 0.5 mg, 0.3 mg and 0.1 mg groups. The values obtained between the comparisons between groups 0.3mg with 0.1mg and 0.5mg with 0.1 mg with p values respectively $p=0.003$ and $p=0.001$.

Anticholinergic drugs are the drugs of choice in the management of hypersalivation. Ketamine-induced hypersalivation can be treated by premedication with anticholinergic agents such as atropine sulfate and glycopyrrolate.[3] In this study, all patients were premedicated with an anticholinergic agent either 0.25 mg atropine or 0.5 mg atropine sulfate approximately 30 minutes before induction of anesthesia. The treatment carried out by Saleh and Elazzazi was given atropine 0.5 mg, 0.3 mg and 0.1 mg, but the difference lies in when the atropine was given. In Saleh and Elazzazi's study it was given after the patient was induced with ketamine, whereas in this study, atropine was given before the patient was induced with ketamine.[4]

The limitation of this study is not including other descriptive data, such as systolic and diastolic blood pressure, heart rate, respiratory rate, and others. In addition, this study did not record comorbidities in our patients, so we could not assess whether the effects occurred because of the drugs given or because of the patient's comorbidities.

CONCLUSION

There is a significant comparison ($p = 0.008$) in the comparison between the use of atropine 0.25 mg and 0.5 mg in patients at the HAM Hospital and Putri Hijau Hospital Medan. The volume of saliva in patients given atropine 0.25 mg ranged from 1 cc to 5 cc with a mean of 2.5 cc. The volume of saliva in patients given atropine 0.5 mg ranged from 1 cc to 3 cc with a mean of 1.93 cc. The salivary volume of the patients in this study ranged from 1 cc to 5 cc with a median of 2 cc.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

FUNDING

This research has received no external funding.

AUTHORS' CONTRIBUTIONS

MHRS collects the data and writes the initial manuscript. ERD provided contribution and revision regarding the data analysis and imaging aspect of the discussion. RH provided contribution and revision regarding the data analysis and clinical aspect of the discussion. All authors read and approved the final manuscript.

ACKNOWLEDGMENTS

Not applicable.

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