THE COMPARISON OF ATRACURIUM DOSES IN PRODUCING INTUBATION QUALITY, ONSET, DURATION OF MUSCLE RELAXATION IN SURGERIES WITH GENERAL ANESTHESIA

I Gede Juli Suastika[1*], Bianca Jeanne[2], IGP Sukrana Sidemen[3], IGAG Utara Hartawan[4], Tjokorda Gde Agung Senapathi[5], I Made Gede Widnyana[6], I Putu Pramana Suarjaya[7], I Dewa Ayu Mas Shintya Dewi[8], Kadek Agus Heryana Putra[9], Tjahya Aryasa EM[10]

Resident of at Department of Anesthesiology, Pain Management, and Intensive Care, Udayana *University, Sanglah General Hospital* Bali[1,2,3,4,5,6,7,8,9,10]

**Corresponding Author :* gjsbius2021@gmail.com

ABSTRAK

Relaksan otot secara rutin digunakan selama anestesi umum untuk memfasilitasi intubasi endotrakeal dan mempertahankan kondisi kerja bedah yang optimal. Atracurium merupakan alternatif yang banyak digunakan dibandingkan rokuronium dan paling sering digunakan dalam anestesi umum untuk memfasilitasi intubasi endotrakeal serta memberikan relaksasi otot rangka selama ventilasi atau ventilasi mekanis. Pemberian atracurium dalam dosis tinggi yaitu 1 mg/kgBB (4ED95) dibandingkan dengan dosis umum 0,5 mg/kgBB (2ED95) dapat memberikan waktu onset intubasi yang lebih cepat, durasi kerja obat yang lebih lama, kualitas intubasi yang lebih baik, serta kondisi hemodinamik yang cukup stabil. Penelitian ini merupakan penelitian eksperimental murni yang dilakukan di ruang operasi Bedah Sentral sebuah rumah sakit pendidikan, dimulai pada Juli 2024 hingga jumlah sampel penelitian terpenuhi. Populasi penelitian adalah pasien berusia 18–65 tahun yang akan menjalani operasi elektif dengan anestesi umum menggunakan laringoskopi intubasi endotrakeal. Analisis data dilakukan dengan bantuan SPSS versi 26, termasuk uji normalitas Shapiro-Wilk, uji Chi-square, dan uji berpasangan. Jumlah total subjek dalam penelitian ini adalah 38 pasien ASA I dan ASA II yang menjalani intubasi endotrakeal. Rerata waktu onset obat pada kelompok perlakuan adalah 133,21 ± 7,86 detik dan pada kelompok kontrol adalah 230,05 ± 33,45 detik. Rerata durasi kerja obat pada kelompok kasus adalah 72,95 ± 8,50 menit, sedangkan pada kelompok kontrol adalah 34,00 ± 5,42 menit. Tidak terdapat perbedaan signifikan pada stabilitas hemodinamik dan denyut nadi selama proses intubasi yang baik pada kedua kelompok. Kualitas intubasi sangat baik ditemukan pada 19 pasien (100%) di kelompok perlakuan dibandingkan dengan 4 pasien (21,1%) di kelompok kontrol.

Kata kunci : anestesi, atracurium, kualitas intubasi, perioperatif

ABSTRACT

Muscle relaxants are routinely used during general anesthesia to facilitate endotracheal intubation and to maintain optimal surgical working conditions. Atracurium is a widely used alternative to rocuronium and is commonly administered in general anesthesia to aid endotracheal intubation and provide skeletal muscle relaxation during spontaneous or mechanical ventilation. Administering atracurium at a higher dose of 1 mg/kg body weight (4ED95) compared to the standard dose of 0.5 mg/kg body weight (2ED95) can result in a faster onset of intubation, longer duration of action, better intubation quality, and relatively stable hemodynamic conditions. A total of 38 ASA I and II patients undergoing endotracheal intubation participated in the study. The mean onset of action in the treatment group was 133.21 ± 7.86 seconds, while in the control group it was 230.05 ± 33.45 seconds. The mean duration of action in the treatment group was 72.95 ± 8.50 minutes, compared to 34.00 ± 5.42 minutes in the control group. There was no significant difference in hemodynamic stability and pulse rate during intubation between the two groups. However, very good intubation quality was observed in 19 patients (100%) in the treatment group compared to only 4 patients (21.1%) in the control group.

Keywords *: atracurium, quality of intubation, perioperative, anesthesia*

INTRODUCTION

Atracurium is the primary and most common choice used in general anesthesia to facilitate endotracheal intubation and provide skeletal muscle relaxation during surgery or mechanical ventilation. Atracurium is a non-depolarizing neuromuscular blocker from the benzylisoquinolinium class. This drug competes with acetylcholine for binding sites. However, its longer onset compared to rocuronium and succinylcholine makes atracurium less preferred in patients who require immediate muscle paralysis onset, such as in patients with indications for rapid sequence intubation (RSI) and patients with difficult airways (Hampton et al., 2023). The use of atracurium offers several advantages over succinylcholine or rocuronium, including its availability, relatively lower cost, ease of access, and the availability of a reversal agent. Atracurium is quite safe for patients with liver and kidney diseases because it is spontaneously eliminated in the plasma and tissues at normal body pH and temperature. Research has shown that the drug has an average onset of about 3–5 minutes. Its effects are reversed by anticholinesterase drugs and it has few side effects (Butterworth et al., 2020; Koh & Chen, 1994; Lennon et al., 1986).

To date, there are still few studies evaluating the use of high-dose atracurium and assessing its intubation quality and onset of action compared to the usual dosage. The onset of action for atracurium doses used for tracheal intubation is around 3 minutes. The speed of onset of NMBA (neuromuscular blocking agents) is inversely correlated with its potency. Therefore, a higher dose of atracurium, around 3–4 times the ED95 (Effective Dose), will facilitate rapid tracheal intubation comparable to high-dose rocuronium (Bartkowski et al., 1993; Man et al., 2002). In previous studies using high-dose atracurium boluses, satisfactory results were obtained for rapid tracheal intubation. The study was divided into three groups receiving different doses of atracurium: 0.6 mg/kg (2ED95), 0.75 mg/kg (3ED95), and 1 mg/kg (4ED95). The best results were obtained at a dose of 1 mg/kg, which showed a significant difference in vocal cord and diaphragm paralysis (Chalermkitpanit et al., 2020; Holkunde et al., 2022).

Therefore, the author is interested in evaluating the differences between high-dose atracurium using 1 mg/kg body weight compared to the standard dose of 0.5 mg/kg body weight to assess intubation quality, onset, duration of muscle relaxation, and hemodynamic fluctuations during intubation (Xue et al., 1999).

METHODS

This study is a pure experimental research with a double-blind randomized control trial design. The subjects in this study were divided into two groups: one group received general anesthesia with atracurium at a dose of 1 mg/kg body weight, while the control group received atracurium at a dose of 0.5 mg/kg body weight. To assign the subjects into either the first treatment group or the second treatment group, randomization was conducted, and blinding was applied to both the subjects and the researcher. The study was conducted in the operating room of the Central Surgical Installation of a teaching hospital from May to October 2024. Inclusion criteria for this study included adult patients aged between 18 and 65 years who were scheduled to undergo surgery with general anesthesia. Only patients classified as ASA physical status I or II and requiring endotracheal intubation using laryngoscopy were eligible to participate.

Exclusion criteria encompassed patients with a known history of allergy to atracurium, those with asthma, and individuals diagnosed with myasthenia gravis. Patients predicted to have difficult airways—based on a LEMON score greater than 5, a body mass index (BMI) exceeding 30 kg/m², or other indicators of intubation difficulty—were also excluded. Furthermore, patients with hemodynamic instability or with severe cardiac or pulmonary

disease were not included. Lastly, patients who declined to participate, as indicated by refusal to sign the informed consent form, were excluded from the study. Dropout criteria were established to ensure patient safety and study consistency. Patients were withdrawn from the study if complications such as allergic reactions or anaphylactic shock occurred. Additionally, cases where the time required for laryngoscopy and intubation exceeded 30 minutes, or where more than three attempts at intubation were required, were excluded from the final analysis.

The anesthesia procedure began with pre-oxygenation for a duration of 3 to 5 minutes. Induction was performed using intravenous propofol at a dose of 2 mg/kg and fentanyl at a dose of 2 mcg/kg. Patients were then assigned to either the treatment or control group. In the treatment group, atracurium was administered intravenously at a dose of 1 mg/kg, while in the control group, atracurium was given at the standard dose of 0.5 mg/kg. Once the clinical onset of the muscle relaxant effect was observed, hemodynamic parameters—specifically mean arterial pressure (MAP) and heart rate—were immediately recorded from the monitor before intubation. Intubation was performed by an anesthesia resident using a McGRATH video laryngoscope. During intubation, the ease of laryngoscopy, vocal cord position, and the presence of any cough reflex or limb movement were assessed and documented using the Helbo-Hansen Raulo and Trap-Andersen intubation quality scoring system. If intubation exceeded three attempts or took longer than 30 minutes, the patient was excluded from the study. Following successful intubation, blood pressure and heart rate were recorded again as displayed on the monitor.

Bilateral lung sounds were auscultated to confirm equal air entry on both sides. The endotracheal tube was then secured, and the cuff was inflated to a pressure of 20 cmH_2O to ensure adequate sealing. Neuromuscular transmission was monitored using the train-of-four (TOF) technique by placing a transducer along the ulnar nerve to stimulate the adductor pollicis muscle with a current of 50 mA. Stimulation was applied every 12 seconds from the start of induction until all four muscle twitches disappeared. The time at which the post-tetanic count (PTC) reached zero was noted, marking the onset of maximum neuromuscular blockade. TOF monitoring continued every 5 minutes thereafter until the return of two twitches, which was used to determine the total duration of muscle relaxation. Anesthesia was maintained using a combination of oxygen and compressed air at a 2:2-liter ratio, along with continuous intravenous infusion of propofol at 0.075 mg/kg/min. Intermittent doses of fentanyl, ranging from 0.5 to 1 mcg/kg intravenously, were administered as needed if signs of pain were observed, such as increases in heart rate or blood pressure (MAP) exceeding 20% of baseline. Additional doses could be given until hemodynamic parameters returned to baseline. If two twitches were observed on the TOF monitor, indicating a decrease in the level of muscle relaxation, an additional dose of atracurium at 0.1 mg/kg was administered to maintain the desired neuromuscular blockade.

Statistical Analysis

The normality test aims to assess whether variables such as age (years), height (cm), weight (kg), BMI (kg/m^2), and surgery duration follow a normal distribution. This analysis was conducted using the Shapiro-Wilk test at a significance level of 0.05, where data is considered normal if $p > 0.05$. The homogeneity test is used to evaluate whether the variances between groups are homogeneous. The homogeneity of variance is tested using Levene's test. Variances are considered homogeneous if $p > 0.05$ and not homogeneous if $p \leq 0.05$. Differences in intubation quality, onset, muscle relaxant duration, and hemodynamics during intubation between the control and treatment groups are normally distributed, so an independent t-test was used. If the data between the control and treatment groups are not normally distributed, the Mann-Whitney test is applied in the data analysis. Percentages and figures are used to represent qualitative data such as gender, ASA physical status, and intubation conditions using 2x2 cross-

tabulation analysis. The statistical test applied is the Chi-Square test. The results will be presented as Relative Risk (RR). Conclusions are drawn based on a 95% Confidence Interval (CI) and a P-value with a significance level of $\alpha < 0.05$. The entire data analysis process is performed using SPSS statistical software.

RESULT

The sample's charatheristic can be seen in table 1. All the subjects between the case and the control group were comparable.

Table 1 Subject Characteristics

Characteristics Patient	Group		p-value
	Case	Control	
Age (years) , mean ± SD	37.21±10.91	43.79±12.06	0.086 [a]
Gender			0.148 [a]
Female, n (%)	12 (63.2%)	16 (84.2%)	
Male , n (%)	7 (36.8%)	3 (15.8%)	
Height (cm) , mean ± S D	162.32±6.29	159.84±6.55	0.186 [a]
Body Weight (kg) , r eaver ± S D	63.63±9.83	59.47±11.37	0.293 [a]
BMI (kg / m ^{2}) , mean ± S D	24.06±4.19	23.27±3.72	0.544 [a]
Thin (<18.5 kg/m ^{2})	1 (5.3%)	1 (5.3%)	
Normal (18.5-24.9 kg/m ^{2})	12 (63.2%)	11 (57.9%)	
Obese (>25 kg/m ^{2})	6 (31.6%)	7 (36.8%)	
ASA Physical Status			1,000 [a]
I, n (%)	8 (42.1%)	8 (42.1%)	
II, n (%)	11 (57.9%)	11 (57.9%)	

Description : a = *Independent T- te s t,* it is said significant if $p < 0.05$

Comparison of Mean Intubation Quality, Onset and Duration of Muscle Relaxant, and Hemodynamic Conditions in the Case and Control Groups

This study focuses on comparing the intubation quality, onset, and duration of muscle relaxation, as well as the hemodynamic conditions, with different doses of atracurium in the case group (atracurium dose of 1 mg/kg body weight) and the control group (atracurium dose of 0.5 mg/kg body weight). A significant difference in intubation quality was found between the two groups, with a p-value of 0.000 ($p < 0.05$). In the case group, all 19 patients (100%) who received an atracurium dose of 1 mg/kg body weight demonstrated excellent intubation quality with scores of 3-4. In contrast, in the control group, the majority of patients who received an atracurium dose of 0.5 mg/kg body weight showed good intubation quality with scores of 5-8, amounting to 15 patients (78.9%), while 4 patients (21.1%) exhibited excellent intubation quality with scores of 3-4.

Table 2. 2Table of Intubation Quality, Onset and Duration of Muscle Paralysis

Characteristics Patient	Group		p-value
	Case	Control	
Intubation Quality, n (%)			0.000 [b]
Good (score 5-8)	0 (0.0%)	15 (78.9%)	
Very Good (score 3-4)	19 (100%)	4 (21.1%)	
Onset (seconds) , mean ± S D	133.21±7.86	230.05±33.45	0.000 [a]
Duration (minutes) , mean ± S D	72.95±8.50	34.00±5.42	0.000 [a]

Description : a = Independent T- te s t, it is said significant if $p < 0.05$ and b = Mann-Whitney test, it is said significant if $p < 0.05$

Onset is determined as the time required for the muscle relaxant to take effect, measured using the train-of-four (TOF) and post-tetanic count (PTC). A significant difference was found

with a p-value of 0.000 ($p < 0.05$), where the mean onset time for the case group was 133.21 ± 7.86 seconds, or approximately 2.2 minutes, while the mean onset time for the control group was 230.05 ± 33.45 seconds, or about 3.8 minutes. Duration is defined as the length of time for muscle relaxation after administering the muscle relaxant, also measured using TOF stimulation. A significant difference was found between the case and control groups with a p-value of 0.000 ($p < 0.05$), where the mean duration for the case group was 72.95 ± 8.50 minutes, and the mean duration for the control group was 34.00 ± 5.42 minutes.

Relationship Between Gender, ASA Physical Status, Intubation Quality, and POST Scale in the Case and Control Groups

In the case group, where a dose of 1 mg/kg of atracurium was administered, 12 patients (63.2%) were female, while in the control group with a dose of 0.5 mg/kg, 16 patients (72.2%) were female. In the case group, 7 patients (36.8%) receiving 1 mg/kg of atracurium were male, while in the control group, 3 patients (15.8%) receiving 0.5 mg/kg were male. To examine the relationship between atracurium dosage and gender, a Chi-square test was conducted. Table 3 shows no significant relationship between atracurium dosage and patient gender, with a p-value of 0.141 ($p > 0.05$).

Table 3 Relationship between Atracurium Dose Administration and Gender

Gender	Group		RO	IK 95%	P Value
	Case n (%)	Control n (%)			
Woman	12 (63.2%)	16 (72.2%)	3,111	0.663-14.596	0.141 [a]
Man	7 (36.8%)	3 (15.8%)			

a = *Chi-square test*, it is said significant if $p < 0.05$

Table 4 outlines the proportion of ASA physical status of patients in the case and control groups. To determine the relationship between the administration of atracurium dosage and ASA physical status, a Chi-square analysis was conducted. Table 5.4 shows that there is no significant relationship between atracurium dosage and the ASA physical status of patients, with a p-value of 1.000 ($p > 0.05$). This indicates that systemic diseases do not affect the administration quality of atracurium dosage during surgery.

Table 4 Relationship between Atracurium Dose Administration and ASA Physical Status

ASA Physical Status	Group		RO	IK 95%	P Value
	Case n (%)	Control n (%)			
I	8 (42.1%)	8 (42.1%)	1,000	0.276-3.625	1,000 [a]
II	11 (57.9%)	11 (57.9%)			

Description : a = *Chi-square test*, it is said significant if $p < 0.05$

Table 5. Relationship between Atracurium Dose Administration and Intubation Quality Score

Intubation Quality Score	Group		RO	IK 95%	P Value
	Case n (%)	Control n (%)			
Good	0 (0.0%)	15 (78.9%)	5,750	2,360-14,012	0.000 [a]
Very good	19 (100%)	4 (21.1%)			

a = *Chi-square test*, it is said significant if $p < 0.05$

Table 5 outlines the relationship and proportion of intubation quality scores with the administration of atracurium dosage in both the case and control groups. To determine the relationship between atracurium dosage and intubation quality, a Chi-square analysis was conducted. Table 5 shows a significant relationship between atracurium dosage and the ASA physical status of patients, with a p-value of 0.000 ($p < 0.05$). The administration of 1 mg/kgBW of atracurium resulted in a 5,750 times better intubation quality compared to the 0.5 mg/kgBW dose (odds ratio [OR] = 5.750; 95% confidence interval [CI] = 2.360-14.012; p = 0.000).

DISCUSSION

In this study, significant differences and correlations were found between the quality of intubation in the case group, which received 1 mg/kgBW of atracurium, and the control group, which received 0.5 mg/kgBW of atracurium. Intubation quality was measured using the criteria designed by Helbo-Hansen, Raulo, and Trap Anderson, which included the ease of laryngoscopy access, vocal cord opening, and the presence or absence of coughing or involuntary limb movement. The administration of a higher dose of atracurium (1 mg/kgBW) resulted in satisfactory intubation quality, with a score of 3–4 (very good). The 1 mg/kgBW dose showed a very good intubation quality, 5.750 times greater than the 0.5 mg/kgBW dose (odds ratio [OR] = 5.750; 95% confidence interval [CI] = 2.360–14.012; p = 0.000). However, the administration of 0.5 mg/kgBW still showed good intubation quality, with a score of 5–8 (good). This study aligns with the findings of Xue et al. (1999), where higher doses of atracurium provided good intubation quality without coughing or bucking by assessing vocal cord and diaphragm movements during intubation (Xue et al., 1999). Similar results were found in the study by Chalermkitpanit et al. (2020), which also stated that a 1 mg/kgBW dose was very effective and significant for successful intubation (Chalermkitpanit et al., 2020).

The onset of muscle relaxation required for the neuromuscular blocker to work was measured using train-of-four (TOF) and post-tetanic count (PTC) and showed significant differences with a p-value of 0.000 ($p < 0.05$). The average onset in the case group was 133.21 ± 7.86 seconds, while in the control group, it was 230.05 ± 33.45 seconds. This indicates that muscle relaxation onset with a 1 mg/kgBW dose of atracurium was faster, around 2.22 minutes, compared to 0.5 mg/kgBW, which took about 3.83 minutes. This aligns with previous research by Staals et al. (2010, as cited in Butterworth et al., 2020), where the potency of a high dose of atracurium (1 mg/kgBW) was equivalent to 1.2 mg/kgBW of rocuronium (Butterworth et al., 2020). Another study by Holkunde et al. (2022) stated that atracurium at a dose of 1 mg/kgBW provided good intubation quality without coughing or bucking, which might occur with lower doses like 0.75 mg/kgBW (Holkunde et al., 2022).

The duration of muscle relaxation, defined as the length of time muscle relaxation lasted after the administration of a neuromuscular blocker, was measured using TOF stimulation and showed significant differences between the case and control groups with a p-value of 0.000 ($p < 0.05$). The average duration in the case group (1 mg/kgBW) was 72.95 ± 8.50 minutes, while in the control group (0.5 mg/kgBW), it was 34.00 ± 5.42 minutes. In the study conducted by Chalermkitpanit et al. (2020), it was also stated that a 1 mg/kgBW dose of atracurium had a faster onset and longer duration of action compared to lower doses, where 0.6 mg/kgBW and 0.75 mg/kgBW were used for comparison (Chalermkitpanit et al., 2020). These results are consistent with the study by Chalermkitpanit et al. (2020), which found no serious side effects such as desaturation, bronchospasm, or severe hypotension with the administration of a high dose of atracurium. This is likely due to the good intubation quality achieved with the higher dose, where the fast onset of relaxation prevents pain from inflammation or trauma caused by the laryngoscopy procedure and the insertion of the endotracheal tube (Chalermkitpanit et al., 2020; Hampton et al., 2023).

ACKNOWLEDGMENT

The author sincerely acknowledges Udayana University for its continuous support and contribution throughout the course of this research. Special thanks are extended to the Faculty of Medicine and all the lecturers, mentors, and staff who provided valuable guidance, encouragement, and access to necessary resources. Their expertise and assistance played a crucial role in the successful completion of this study.

REFERENCES

Bartkowski, R. R., Witkowski, T. A., Azad, S., Lessin, J., & Marr, A. (1993). *Rocuronium onset of action: A comparison with atracurium and vecuronium. Anesthesia & Analgesia, 77*(3), 574–578. https://doi.org/10.1213/00000539-199309000-00025

Butterworth, J. F., Mackey, D. C., Wasnick, J. D., Morgan, G. E., Mikhail, M. S., & Morgan, G. Edward. (2020). *Morgan & Mikhail's clinical anesthesiology*. McGraw-Hill Education.

Chalermkitpanit, P., Rodanant, O., Thaveepunsan, W., & Assavanop, S. (2020). *Determination of dose and efficacy of atracurium for rapid sequence induction of anesthesia: A randomised prospective study. Journal of Anaesthesiology Clinical Pharmacology, 36*(1).

Hampton, J. P., Hommer, K., Musselman, M., & Bilhimer, M. (2023). *Rapid sequence intubation and the role of the emergency medicine pharmacist: 2022 update. American Journal of Health-System Pharmacy, 80*.

Holkunde, R., Masur, S., Patil, B. A., Patil, C., Naik, D., & Lamani, S. (2022). *Comparison of different doses of atracurium for quality of muscle relaxation during modified rapid sequence induction in emergency laparotomy: A prospective randomised double blind study. Indian Journal of Anaesthesia, 66*(12).

Koh, K. F., & Chen, F. G. (1994). *Rapid tracheal intubation with atracurium: The timing principle. Canadian Journal of Anaesthesia, 41*, 688–693.

Lennon, R. L., Olson, R. A., & Gronert, G. A. (1986). *Atracurium or vecuronium for rapid sequence endotracheal intubation. Anesthesiology, 64*, 510–513.

Man, T. T., Cheng, J. K., Wong, K. L., Chen, C. C., Rau, R. H., Wu, K. H., et al. (2002). *Tracheal intubation condition--a comparison between one minute after rocuronium alone, one minute after rocuronium combined with atracurium and one minute after atracurium with rocuronium at one minute priming interval. Acta Anaesthesiologica Sinica, 40*, 179–183.

Pajeko, G. F., Diartama, A. A. A., & Darmita, I. M. P. (2023). Analisis Pengaruh Variasi Rekonstruksi Slice Thickness Dan Rekonstruksi Increment Terhadap Informasi Citra Anatomi Pemeriksaan MSCT Scan Sinus Paranasal Potongan Coronal Pada Kasus Rhinosinusitis Kronis Di RSUP Prof. Dr. IGNG Ngoerah. *Journal of Educational* Penelitian menggunakan etika sebagai berikut menurut Loiselle (2004, dalam Iman 2012)

Putri, Luh Gede Yunda Rustika, I. Putu Eka Juliantara, and I. Made Purwa Darmita. "*The Effect of Slice Thickness Variation on The Anatomical Information of CT Scan Paranasal Sinus Coronal Section in Clinical Rhinosinusitis.*" *Jurnal EduHealth* 14.03 (2023): 1376-1381.

Rahayu, K. L. F ., & Hartanto, D. (2022). Seorang Laki-laki Usia 28 Tahun dengan Rinosinusitis Kronis: Laporan Kasus. *Proceeding Book Call for Papers* Fakultas Kedokteran Universitas Muhammadiyah Surakarta, 638-647.

Ramadhani, Tezar Ridho, Siti Masrochah, and Ary Kurniawati. "Efektifitas Variasi Window Width Terhadap Informasi Anatomi CT Scan Sinus Paranasal Citra Jaringan Lunak Pada Kasus Sinusitis." Jurnal Imejing Diagnostik (JImeD) 9.2 (2023): 80-87.

Samara, Anggita Putri, Budi Budi Sutikno, and Reny I'tishom. "Gambaran Derajat Keparahan Gejala Pasien Rinosinusitis Kronik di RSUD Surabaya Dr. Soetomo." *Care* Jurnal Ilmiah

Ilmu Kesehatan 8.2 (2020): 235-245.

Utami, A. D. (2019). Identifikasi Mikrobiom pada penderita Rinosinusitis Kronis dengan dan tanpa polip (telaah berdasarkan pemeriksaan Next Generation 16S Sequencing).

Xue, F. S., Zhang, Y. M., Liao, X., Liu, J. H., & An, G. (1999). *Influences of age and gender on dose response and time course of effect of atracurium in anesthetized adult patients. Journal of Clinical Anesthesia, 11*, 397–405.