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Comparison of hemodynamic response between propofol and thiopental as an induction agent in neurosurgery anesthesia at Haji Adam Malik General Hospital Medan-Indonesa

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ABSTRACT

Introduction: The neuro anesthesia technique is the only anesthetic technique used today in craniotomy surgery, the anesthetic doctor must pay attention to the components of CBF and ICP which depends on the hemodynamic parameters of patient. Such condition is influenced by anesthetic drugs used in the technique. Intravenous anesthetic drugs that can decrease ICP and CBF from induction drug classes are thiopental, propofol, etomidate, and midazolam. Aim of this study is to obtain comparison of hemodynamic response after administration of propofol and thiopental as an induction drug in brain surgery with general anesthesia.

Methods: Study design using double-blinded randomized clinical trial with a total sample of 40 research subjects performed elective brain surgery using general anesthesia techniques. The sample was divided into two groups, the patients were induced with propofol 2 mg /kg for group A and thiopental 4.5 mg /kg for group B in 1 minute. Measurements of hemodynamic response (systolic blood pressure, diastolic blood pressure, heart rate, mean arterial pressure and RPP score) were tested. The results were tested using independent sample t-test, with a significance level of 95% ($p < 0.05$).

Results: The results showed that mean systolic blood pressure, diastolic blood pressure, mean arterial pressure and RPP score between group A and B was significantly different from T1, T2, T3 ($p < 0,05$). Meanwhile, for heart rate, there were no significant differences ($p > 0.05$).

Conclusions: There were significant hemodynamic differences in the administration of thiopental and propofol drugs in brain surgery patients. Thiopental drug administration showed lower systolic blood pressure, diastolic blood pressure and mean arterial pressure compared to propofol for induction drugs.

Keywords: Induction, Propofol, Thiopental, Hemodynamic, Craniotomy

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INTRODUCTION

Indonesia is one of the developing countries which has undergone many changes in various fields from time to time including the lifestyle of the people in it. This change makes Indonesia experiencing an epidemiological transition in which the pattern of disease shifts from infectious diseases to degenerative diseases. Before this infectious disease problem can be solved, non-communicable diseases are already emerging. One example of non-infectious diseases are tumors or brain cancer. Cancer is one of the diseases included in the group of non-communicable diseases (NCD). [1]

Non-communicable disease deaths are projected to rise 15% globally between 2010 and 2020, to 44 million deaths. The highest increase (estimated at 20%) will occur in the countries of Africa, Southeast Asia and the Eastern Mediterranean. However, countries estimated to have the highest number of deaths by 2020 are Southeast Asia (10.4 million deaths) and the Western Pacific (12.3 million deaths). In the next decade, cancer is predicted as an increasingly important cause of illness and death worldwide. The challenge for cancer control is enormous, coupled with population characteristics with increasing age. Therefore, increased prevalence of cancer is difficult to avoid. It is estimated that in 2008 there were 12.7 million new cases of cancer, and this number is predicted to be 21.4 million cases by 2030. Two-thirds of those cases are found in countries with low-to-medium socioeconomic condition.[2]

The most common treatment of these brain diseases is to utilize craniotomy. This craniotomy is a surgical action performed by opening the cranium to access the brain. Craniotomy means making a hole in the skull to evaluate and repairing brain damage. Craniotomy surgery is usually performed in a hospital that has a neurosurgery department and an intensive care unit (ICU). Also, this craniotomy action is almost the same as any other operative action, which has a risk of death.[3]

Craniotomy procedure is the most often performed for surgical removal of brain tumors. Also, craniotomy can be performed with two indications of head trauma and non head trauma. This procedure may also be aimed at removing hematoma, controlling bleeding from ruptured blood vessels (aneurysm of cerebral), repairing arteriovenous malformations (abnormal blood vessels), eliminating cerebral abscesses, decrease intracranial pressure, to perform biopsy, and to treat hydrocephalus.[4] Among the two indications of craniotomy mentioned, most indication of craniotomy is non traumatic. The most non-traumatic cause of craniotomy action is due to tumor or malignancy. In addition to brain tumors, there are other examples which can be an indication for craniotomy with a non-traumatic etiology such as hydrocephalus. Hydrocephalus itself occurs 2 per 1.000 births. In general, the incidence of hydrocephalus is similar in men and women with incidence in adults is about 40%. In addition to tumors and hydrocephalus, there are many more non-traumatic indications for craniotomies such as cerebral aneurysms, and so on.[4, 5]

As already mentioned, craniotomy action has a risk of death. Before getting to that stage, there must be a stage where the occurrence of hemodynamic disturbances. Therefore, this craniotomy act is closely related to the patient's hemodynamic problems. This is in line with research conducted by Winarno et al. (2010), where it is said that hemodynamic monitoring in neurosurgery surgery is essential. The hemodynamics that is monitored in these neurosurgical operations are standard blood pressure monitoring, electrocardiogram (ECG), heart rate, and peripheral oxygen saturation (SpO2).[6]

In craniotomy surgery, anesthesia techniques commonly used are neuro anesthesia techniques. The neuro anesthesia technique is the only anesthetic technique used today in craniotomy surgery. It needs to consider cerebral blood flow (CBF), intracranial pressure (ICP), and cerebral perfusion pressure (CPP), and autoregulation in patients. Among the components to note in the technique, the CBF and ICP elements are the two components most affected by the anesthetic drugs used in the neuro anesthesia technique.

According to Bisri et al. (2012), intravenous anesthesia that can reduce ICP and CBF from induction drug classes are pentotal, propofol, etomidate, and midazolam. Also, a study from Yazici et al. (2013) also showed that one of the side effects of the propofol class was that it could decrease the hemodynamic parameters more significantly than other anesthetic agents. Propofol is known to cause hypotension, hypertriglyceridemia, and propofol infusion syndrome (PRIS). However, this propofol has proven to be an effective drug for regulating intracranial pressure (ICP). Propofol is shown to decrease ICP in normal subjects and also in patients with increased ICP. This can reduce the cerebral metabolism rate by 40% by relying on the dose and decreasing cerebral blood flow.[7] However, from the whole class of induction drugs mentioned, the most commonly used option is pentothal. Thiopental is one of the intravenous anesthetics derived from barbiturates. The onset of action of this drug is very short. Also, intravenous administration of thiopental doses may result in decreased blood pressure and elevation of the heart rate. In high doses, thiopental will cause a decrease in arterial pressure, recurrence and cardiac output).[8,9]

Propofol and thiopental, it is known that both affect one's hemodynamic when induced. However, among the two classes of drugs, from Safee et al. (2007) studies show that propofol causes less hemodynamic changes when compared with thiopental. Also, studies conducted by Yang et al. (2001) also show that the induction of propofol produces hemodynamics which is more stable than induction from thiopental.[10]

These ICP and CBF components are the two components that play a role in craniotomy surgery. As we know, both elements (ICP and CBF) are also strongly influenced by propofol and thiopental anesthesia drugs. Therefore, this study was conducted to determine whether there are differences in the effect of propofol and thiopental on hemodynamics on craniotomy surgery.

METHOD

Study design using double-blind randomized clinical trial. The study was conducted from June to October 2017 at Haji Adam Malik General Hospital, Medan, Indonesia. Subject search is done through consecutive sampling method. Inclusion criteria in this study were patients aged 18-65 years, physical status ASA I-II, patients undergoing elective craniotomy surgery and non head trauma, patients were not difficult for intubation. The study involved 40 subjects and randomly divided into two groups by trained volunteers.

Intervention is done using general anesthesia method. Group A obtained intervention of propofol induction 2 mg/kg and group B received thiopental induction intervention 4.5 mg/kg. Monitoring of the hemodynamic parameters involved such as blood pressure, heart rate, MAP, and Rate Pressure Product (RPP). Assessment of RPP is a

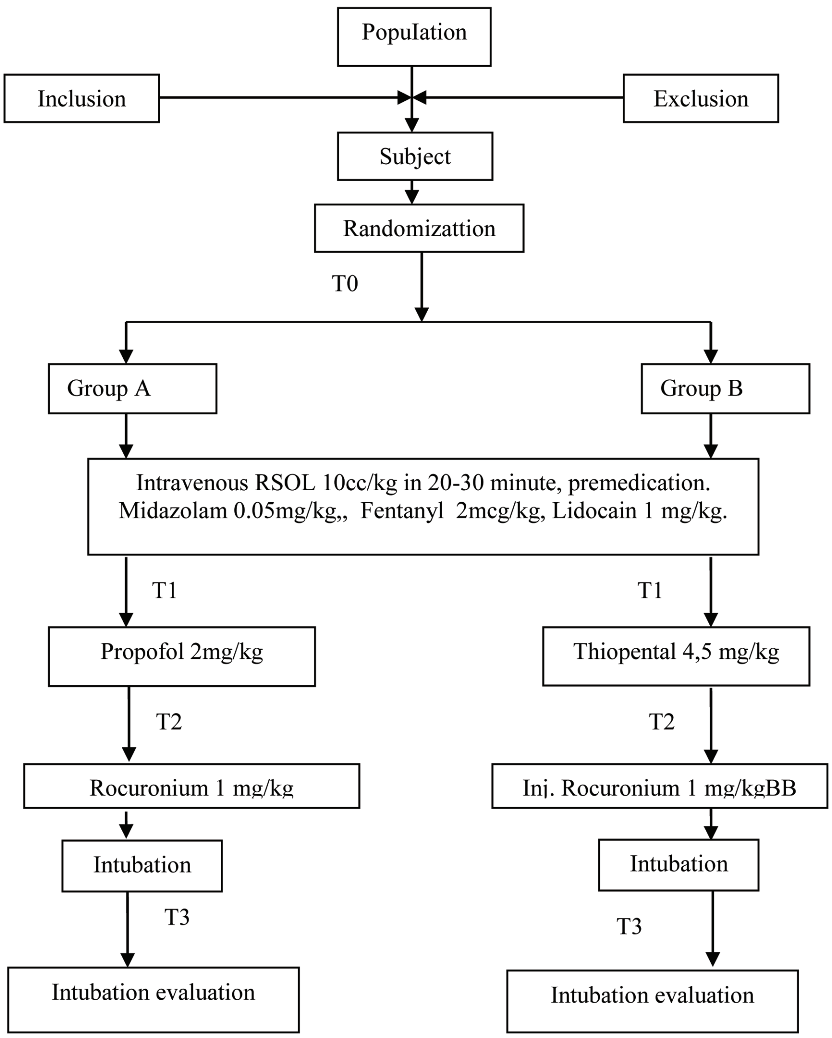

Figure 1 Flowchart of the research

Table 1 Subject characteristics

Characteristics	Induction drugs: Group A (Thiopental 4.5 mg/kg)	Induction drugs: Group B (Propofol 2 mg/kg)	Total	Nilai p*
Age (years)				
18 - 29	4 (20%)	3(15%)	7 (17.5%)	0.578
30 - 39	6(30%)	6 (30%)	12 (30%)	
40 - 49	6(30%)	6(30%)	12 (30%)	
50 - 59	1(5%)	4(20%)	15 (12.5%)	
60 - 65	3 (15%)	1(5%)	4(10%)	
Gender				
Male	10 (50%)	8 (40%)	18 (45%)	0.379
Female	10 (50%)	12 (60%)	22 (55%)	
ASA status				
ASA 1	8 (40%)	7 (35%)	15 (37.5%)	0.534
ASA 2	12 (60%)	13 (65%)	25 (62.5%)	
Total	**20 (100%)**	**20 (100%)**	**40 (100%)**	

measurement of stress on cardiac muscle based on heart rate per minute multiplied by systolic blood pressure, a proper measurement for indication of heart energy usage (RPP = HR x Systolic Blood Pressure). Evaluation of hemodynamic parameters and RPP scores were performed before the induction (T0), 3 min after premedication (T1), 30 s after induction (T2), and after intubation (T3). The analysis used independent sample t-test to compare blood pressure, MAP, pulse rate, and RPSS score in both groups, the value was considered significant if $p < 0.05$. Flowchart research can be seen in figure 1.

RESULT

This study involves 40 patients who had met the inclusion and exclusion criteria, divided into two groups with 20 subject research for each group. Characteristics of the subjects are presented in Table 1.

Based on table 1, the age characteristics of the patients were found to be relatively homogeneous ($p > 0.05$). By gender, male subjects in the Thiopental group were 10 (50%) and in the group receiving Propofol is 8 (40%). While the female sex subjects receiving Thiopental numbered ten people (50%) and in the group receiving Propofol was 12 people (60%). From the results of the table can be concluded that patients in this study are relatively homogeneous ($p > 0.05$).

Based on ASA status, subjects with ASA 1 in the Thiopental group received eight people (40%) and in the group receiving Propofol amounted to 7 people (37.5%). While the subject of ASA 2 who received Thiopental amounted to 12 people (60%) and in the group who received Propofol amounted to 13 people (62.5%). From the results of the table can be concluded that patients in this study are relatively homogeneous ($p > 0.05$).

Comparisons of systolic and diastolic blood pressure between group A and group B were observed in the T0, T1, T2, and T3 time categories presented in Table 2.

The mean systolic before thiopental administration was 132.4 ± 6.5 mmHg, whereas in the Propofol group was 133.1 ± 8.5 mmHg. The mean diastolic blood pressure before thiopental administration was 74.8 ± 4.9 mmHg, whereas in the Propofol group was 75.8 ± 3.8 mmHg. The result of the analysis using independent sample t-test showed that blood pressure before drug administration in both groups had no significant difference ($p > 0.05$). (table 2)

In T1 observation, the mean systolic in the Thiopental group was 118.3 ± 10.6 mmHg while in the propofol group with mean 126.35 ± 7.6 mmHg.

Tabel 2 Comparison of systolic and diastolic blood pressure between Group A and Group B

Variable	Time	Group A (Thiopental 4.5 mg/kg) Mean ± SD	Group B (Propofol 2 mg/kg) Mean ± SD	p-value*
Systolic	T0	132.4 ± 6.5	133.1 ± 8.5	0.757
	T1	118.3 ± 10.6	126.35 ± 7.6	0.009*
	T2	106.8 ± 9.4	117.5 ± 5.6	0.000*
	T3	111.5 ± 8.9	119.3 ± 7.0	0.004*
Diastolic	T0	74.8 ± 4.9	75.8 ± 3.8	0.459
	T1	67.6 ± 6.9	76.1 ± 6.2	0.000*
	T2	59.5 ± 6.8	68.2 ± 6.3	0.000*
	T3	62.6 ± 6.4	70.2 ± 5.4	0.000*

*significant p <0.05

Table 3 Comparison of heart rate between group A and group B

Variable	Time	Group A (Thiopental 4.5 mg/kg) Mean ± SD	Group B (Propofol 2 mg/kg) Mean ± SD	p-value*
Heart rate	T0	80.2 ± 6.0	81.0 ± 7.4	0.694
	T1	70.6 ± 6.0	72.9 ± 6.2	0.233
	T2	66.9 ± 5.5	69 ± 7.2	0.466
	T3	70.9 ± 7.1	72.8 ± 8.6	0.322

*significant p <0.05

Table 4 Comparison of mean arterial pressure between group A and B

Variable	Time	Group A (Thiopental 4.5 mg/kg) Mean ± SD	Group B (Propofol 2 mg/kg) Mean ± SD	p-value*
Mean arterial pressure (MAP)	T0	94 ± 4.8	94.95 ± 4.0	0.504
	T1	83.97 ± 6.7	90.55 ± 5.4	0.002*
	T2	75.28 ± 6.1	84.3 ± 5.06	0.00*
	T3	78.95 ± 6.1	85.95 ± 4.3	0.00*

*significant p <0.05

Table 5 Comparison of RPP score between group A and group B

Variable	Time	Group A (Thiopental 4.5 mg/kg) Mean ± SD	Group B (Propofol 2 mg/kg) Mean ± SD	p*
RPP score	T0	10603.2 ± 748.9	10788.5 ± 1193	0.560
	T1	8376.6 ± 914.3	9218 ± 971.0	0.008*
	T2	7150.0 ± 816.6	8105.8 ± 935.9	0.001*
	T3	7905.9 ± 951.5	8300.8 ± 1498	0.326

*significant p <0.05

On the observation of T2, the mean systolic in the Thiopental group was 106.8 ± 9.4 mmHg while in the propofol group with mean of 117.5 ± 5.6 mmHg. On observation of T3 the mean systolic in the Thiopental group was 111.5 ± 8.9 mmHg while in the propofol group with mean of 119.3 ± 7.0 mmHg. The result of the analysis using independent sample t-test showed that there was significant difference mean of systolic blood pressure in two study groups at T1, T2, T3 ($p < 0.05$). (table 2)

In T1 observation, the mean diastolic level in the Thiopental group was 67.6 ± 6.9 mmHg while in the propofol group with mean of 76.1 ± 6.2 mmHg. On the observation of T2 the mean systolic in the Thiopental group was 66.9 ± 5.5 mmHg while in the propofol group with mean of 69 ± 7.2 mmHg. On observation of T3, the mean systolic in the Thiopental group was 70.9 ± 7.1 mmHg while in the propofol group with mean of 72.8 ± 8.6 mmHg. The results of the analysis using independent sample t-test showed that there was significant difference mean diastolic blood pressure in two study groups on T1, T2, T3 ($p <0.05$). (table 2)

The comparison of heart rates between groups A and group B observed in the T0, T1, T2, and T3 time categories are presented in Table 3.

The mean pulse rate before thiopental administration was 80.2 ± 6.0 times/minute, while in the Propofol group was 81.0 ± 7.4 times/minute. The result of the analysis using independent sample t-test showed that the average pulse rate before drug administration in both groups had no significant difference ($p > 0.05$). In T1 observation, the mean pulse rate in the Thiopental group was 70.6 ± 6.0 times/minute while in the propofol group with mean of 72.9 ± 6.2 times/minute. In T2 observation the mean pulse rate in the Thiopental group was 66.9 ± 5.5 times/minute while in the propofol group with mean of 69 ± 7.2 times/minute. In T3 observation the mean pulse rate in the Thiopental group was 70.9 ± 7.1 times/minute while in the propofol group with mean of 72.8 ± 8.6 times/minute. The result of the analysis using independent sample t-test showed that there was no significant difference of mean pulse rate in the two study groups in T1, T2, T3 ($p > 0.05$). (table 3)

Comparison of Mean Arterial Pressure (MAP) between groups A and group B observed in the time categories T0, T1, T2, and T3 are presented in Table 4.

The mean of MAP prior to Thiopental induction was 94 ± 4.8, whereas in the Propofol group was 94.9 ± 4.0. The result of the analysis using independent sample t-test showed that RPP before drug administration in both groups had no significant

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difference ($p > 0.05$). In T1 observations, the mean of MAP in the Thiopental group was 83.9 ± 6.77 while in the propofol group with mean of 90.5 ± 5.4. In T2 observation the mean of MAP in Thiopental group was 83.96 ± 6.77 while in propofol group with mean of 75.28 ± 6.1. In the T3 observation, the mean of MAP in the Thiopental group was 78.95 ± 6.1 while in the propofol group with the mean of 85.9 ± 4.3. The result of analysis using independent sample t-test showed that there was significant difference of MAP average in two study groups at T1, T2, T3 ($p < 0.05$). (table 4)

The comparison of the RPP score between groups A and group B observed in the time categories T0, T1, T2, and T3 is presented in Table 5.

The mean RPP before thiopental administration was 10603.2 ± 748.9, whereas in the Propofol group was 10788.5 ± 1193. The result of the analysis using independent sample t-test showed that RPP before drug administration in both groups had no significant difference ($p > 0.05$). In T1 observation, the mean RPP in the Thiopental group was 8376.6 ± 914.3 while in the propofol group with mean 9218 ± 971.0. In the observation of T2, the mean RPP in the Thiopental group was 7150.0 ± 816.6 while in the propofol group with the mean of 8105.8 ± 935.9. At T3 the mean RPP in the Thiopental group was 7905.9 ± 951.5 while in the propofol group with the mean of 8300.8 ± 1498. The result of the analysis using the independent sample t-test showed that there was significant difference of RPP in the two study groups at T1, T2 ($p > 0.05$). (table 5)

DISCUSSION

This study assessed the effect of propofol and thiopental on hemodynamic response including RPP (Rate Pressure Product) in craniotomy patients. This study was conducted because there is a difference between propofol and thiopental to hemodynamics and RPP in patients undergoing brain surgery. Research and guidance for the use of both drugs that have been done previously limited to just assessing hemodynamics alone without evaluating the RPP and no similar studies that assess the RPP conducted in Indonesia.

Prior research has shown that between the propofol and thiopental groups in suppressing the hemodynamic response after induction of general anesthesia there was a significant difference ($p < 0.05$) only at first minute in diastolic blood pressure. As for diastolic blood pressure, mean arterial pressure and heart rate were not found to be a significant difference.[12]

Research conducted by Yazici et al. (2013) shows the effects of propofol and thiopental administration evaluating different after induction of general anesthesia. From the available data it can be seen that in both groups both propofol and thiopental there is a decrease in systolic and diastolic blood pressure. However, in the thiopental group the reduction was greater than the propofol group from the previous blood pressure. The statistical results showed that propofol had a significant reduction ($p < 0.05$) in the fifth and tenth minutes. While in thiopental showed a significant decrease ($p < 0.05$) starting at the first minute, fifth and tenth.[7]

Based on the theory presented by Fairfield et al. (2010), that the induced hemodynamic effect of propofol with 2.5 mg / kgBW is decreased at all time points in systolic, mean arterial and diastolic pressures, there is an increase in baseline heart rate and cardiac output, after less than baseline.[11]

Study by Winarno et al. (2010), there was no significant differences obtained for systolic blood pressure, mean arterial pressure, and heart rate variables ($p > 0.05$) between the propofol and thiopental groups in the first, fifth and tenth minutes. While for diastolic blood pressure variables there was a significant difference ($p < 0.05$) between the propofol and thiopental groups in the first minute.[6]

In current study, induction was performed with 2mg/kg propofol injection and a thiopental injection of 4.5 mg/kg depleted within 1 minute. The results of the analysis using independent sample t-test showed that there was significant difference mean in systolic blood pressure in two study groups in T1, T2, T3 ($p < 0.05$).The result of analysis using independent sample t-test showed that there was a significant difference in mean diastolic blood pressure in two study groups in T1, T2, T3 ($p < 0.05$).The results of the analysis using independent sample t-test showed that there was no significant difference of mean pulse rate in the two study groups in T1, T2, T3 ($p > 0.05$).The result of the analysis using independent sample t-test showed that there was a significant difference of mean arterial pressure in the two study groups at T1, T2, T3 ($p > 0.05$). The result of the analysis using independent sample t-test showed that there was a significant difference of RPP score in the two study groups at T1 and T2 ($p > 0.05$).

The current study assessed how hemodynamic changes and RPP values were used in propofol and thiopental use in patients undergoing brain surgery. The results of this research show there was a significant difference in the presence of hemodynamic changes (blood pressure, pulse, and RPP values) during induction patients with propofol and thiopental drugs. Increased doses of use of propofol and thiopental induction drugs may increase the risk of greater hemodynamic changes during surgery.

CONCLUSION

Significant hemodynamic changes were lower after thiopental administration compared with propofol, the difference in RPP score was significantly higher after administration of propofol compared with thiopental.

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