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Effects of Propofol and Thiopental on Brain Relaxation and Hemodynamic Response to Craniotomy Supratentorial Tumors Removal

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Abstract

Surgical procedures for brain tumors, particularly supratentorial tumor removal via craniotomy, present challenges related to brain relaxation and maintaining hemodynamic stability. The choice of intravenous anesthetics, such as Propofol and Thiopental, is crucial due to their distinct effects on intracranial pressure (ICP), cerebral blood flow (CBF), and hemodynamic parameters. This study aimed to compare the effects of Propofol and Thiopental on brain relaxation and hemodynamic responses during supratentorial tumor removal. A randomized experimental study was conducted at Arifin Achmad General Hospital, Riau, Indonesia, from May to September 2024 involving patients undergoing elective craniotomy for supratentorial tumors. Patients were divided into two groups: the Propofol group (1–3 mg/kg body weight, with maintenance of 50-100 µg/kg/min) and the Thiopental group (4–6 mg/kg body weight, with maintenance of 100–200 µg/kg/min), both receiving continuous infusion until a bispectral index of 40–60 was achieved. Hemodynamic parameters, including systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), and heart rate, were measured at various stages: before induction, during surgery, and at multiple intervals. Brain relaxation was subjectively assessed by a neurosurgeon using a four-point scale. Results showed that 90% of subjects receiving Thiopental experienced good brain relaxation during duramater opening, compared to 70% in the Propofol group, though this difference was not statistically significant ($p=0.118$). Hemodynamically, the Thiopental group exhibited higher diastolic blood pressure and MAP at induction ($p<0.05$). In conclusion, Thiopental demonstrated superior hemodynamic stability, albeit both agents provided equally effective brain relaxation.

Keywords: Brain relaxation, craniotomy, hemodynamics, neuroanesthetics, supratentorial tumors

Introduction

Brain tumors represent a major neurological challenge due to their high morbidity, mortality, and complex management. Globally, the incidence of primary brain tumors is estimated at approximately 6–7 cases per 100,000 population per year, with a 5-year survival rate of around 30–35%, depending on tumor type and gradeIn high-income regions such as North America and Europe, the incidence has increased over recent decades, reaching approximately 20–22 per 100,000 populationa. Despite advances in neurosurgical and oncological care, mortality remains substantial, particularly for malignant tumors. In Indonesia, national health data indicate a higher proportion of brain tumor cases in women than in men, with the majority classified as benign lesions, underscoring the continued clinical burden of intracranial tumors.[1]

Craniotomy remains the primary treatment modality for many supratentorial brain tumors. In this setting, intraoperative brain relaxation is a critical factor influencing surgical exposure, operative time, and the risk of complications such as cerebral ischemia and brain injury. Poor brain relaxation is associated with increased intracranial pressure (ICP), impaired cerebral perfusion, and unfavorable neurological outcomes. Brain relaxation is commonly assessed through direct inspection and palpation by the

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surgeon after the skull bones and dura layer are opened. A four-point scale is often used to describe the degree of brain relaxation, ranging from perfect condition to severe swelling requiring intervention.[2]

Anesthetic management plays a central role in controlling intracranial dynamics during neurosurgical procedures. Intravenous anesthetic agents are widely favored in neuroanesthesia because of their effects on cerebral blood flow, cerebral metabolic rate, and intracranial pressure. Thiopental, a barbiturate introduced into clinical practice in the early twentieth century, has long been recognized for its ability to reduce cerebral metabolic demand and intracranial pressure, thereby offering a degree of neuroprotection against ischemic injury. The use of thiopental was controversial in the United States because this agent was also used as an injection agent for the Capital Punishment.[3] Although its use has declined in some regions, thiopental remains widely employed in many countries due to its favorable effects on intracranial physiology.[4] Propofol, introduced in the mid-1980s, has largely replaced thiopental in many settings because of its rapid onset, predictable anesthetic depth, and faster recovery profile, while also providing effective control of intracranial pressure and cerebral metabolism.[4,5]

Despite widespread use of both agents, controversy persists regarding their comparative effectiveness in achieving optimal brain relaxation while maintaining stable hemodynamic conditions during craniotomy. Previous studies have reported inconsistent findings, and many investigations focus primarily on pharmacokinetic or recovery profiles rather than direct intraoperative assessment of brain relaxation.

This study aims to compare the effects of propofol and thiopental on intraoperative brain relaxation and hemodynamic responses in patients undergoing craniotomy for supratentorial tumor removal at Arifin Achmad General Hosptal, Riau. By providing locally generated evidence, this study seeks to contribute to optimized anesthetic decision-making and improved perioperative management in neurosurgical practice.

Methods

This experimental study was designed to evaluate the effects of propofol and thiopental on intraoperative brain relaxation and hemodynamic parameters in patients undergoing elective craniotomy for supratentorial tumor resectionParticipants were allocated into two groups: Group A received propofol and Group B received thiopental, both administered as continuous infusions following anesthesia induction. The study was conducted at Arifin Achmad General Hospital, Riau Province, between May to September 2024, or until the predetermined sample size is achieved.

The study uses quantitative primary data, collected through direct measurements of systolic and diastolic blood pressure, mean arterial pressure (MAP), and heart rate. Brain relaxation is assessed subjectively by neurosurgeons based on a four-point scale. The study population comprised adult patients scheduled for elective supratentorial craniotomy. Consecutive sampling was applied, with a minimum sample size of 20 patients per group, including an additional 10% to account for potential dropouts). Eligible participants were aged 18–65 years, classified as American Society of Anesthesiologists (ASA) physical status I-II, and provided written informed consent. Patients with anticipated difficult airways or known hypersensitivity to propofol or thiopental were excluded. All participants fasted for at least six hours prior to-surgery and received balanced crystalloid fluids for preoperative hydration. Anesthesia induction was performed using either propofol at a dose of 1–3 mg/kg or thiopental 4–6 mg/kg, followed by continuous infusion of the assigned anesthetic agent. Infusion rates were adjusted to maintain a bispectral index (BIS) value between 40 and 60. Hemodynamic parameters and brain relaxation scores were recorded at predetermined intraoperative time points. Any adverse drug reactions were documented and managed according to standard clinical protocols.

Data were analyzed using descriptive. The Shapiro-Wilk tes was applied to assess the normality of numerical variables. Chi-square tests compare categorical variables, while t-tests or Mann-Whitney tests analyze numerical differences, depending on data distribution. Statistical significance was defined as a $p<0.05$ with a 95% confidence interval. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Riau. The study was conducted by a multidisciplinary team consisting of anesthesiology and neurosurgery specialists, and the findings will be reported to the Department of Anesthesiology and Critical Care of Universitas Riau.

Results

Table 1 presents the baseline characteristics of the study subjects. A total of 40 patients were included and evenly allocated to the thiopental (n=20) and propofol (n=20) groups. The median age was 47 years (range 22–64 years) in the thiopental group and 47.5 years (range 37–64

Table 1. Characteristic of Study Subject

Parameter	Thiopental (n=20)	Propofol (n=20)	p-value
Age (years), median (min–max)	47 (22–64)	47.5 (37–64)	0.549
Sex, n (%)			0.152
Male	7 (35.0)	3 (15.0)	
Female	13 (65.0)	17 (85.0)	
Weight (kg), mean±SD	63.7±8.9	62.0±10.8	0.251
Height (cm), mean±SD	157.4±7.2	155.9± 5.8	0.472
Tumor diameter (cm), median (min–max)	2.8 (1.7–5.4)	2.9 (0.8–6.4)	0.829
Tumor type, n (%)			
Meningioma	17 (85.0)	17 (85.0)	0.100
Hemangioma	0 (0.0)	2 (10.0)	0.154
Glioma	3 (15.0)	1 (5.0)	0.304
Midline shift, n (%)			
None	11 (55.0)	17 (85.0)	0.039*
< 5 mm	9 (45.0)	1 (5.0)	0.003*
≥ 5 mm	0 (0.0)	2 (10.0)	0.154
Brain relaxation after bone opening, n (%)			
Grade 1	14 (70.0)	9 (45.0)	0.731
Grade 2	4 (20.0)	7 (35.0)	0.300
Grade 3	2 (10.0)	4 (20.0)	0.389
Grade 4	0 (0.0)	0 (0.0)	
Brain relaxation after dural opening, n (%)			
Grade 1	15 (75.0)	8 (40.0)	0.025*
Grade 2	3 (15.0)	6 (30.0)	0.267
Grade 3	2 (10.0)	6 (30.0)	0.120
Grade 4	0 (0.0)	0 (0.0)	
Brain relaxation at dural closure, n (%)			
Grade 1	18 (90.0)	12 (60.0)	0.029*
Grade 2	2 (10.0)	8 (40.0)	0.030*
Grade 3	0 (0.0)	0 (0.0)	
Grade 4	0 (0.0)	0 (0.0)	
Duration (minutes), mean ± SD			
Surgery	216.0±77.4	206.5±52.5	0.652
Anesthesia	249.5±77.9	234.5±52.2	0.479

Table 2 Comparison of Propofol and Thiopental in Brain Relaxation

Groups	Adequate Relaxation (n) (%)	Inadequate Relaxation (n) (%)	p-value	PR	95% CI
Bone Opening					
Thiopental	18 (90.0)	2 (10.0)	0.331	1.1	(0.9–1.5)
Propofol	16 (80.0)	4 (20.0)			
Duramater Opening					
Thiopental	18 (90.0)	2 (10.0)	0.118	1.3	(0.,9–1.8)
Propofol	14 (70.0)	6 (30.0)			
Duramater Closing					
Thiopental	20 (100.0)	0 (0.0)	-	-	-
Propofol	20 (100.0)	0 (0.0)			

Note: PR, prevalence ratio; CI, confidence interval. p-values were calculated using the Chi-square or Fisher's exact test as appropriate

years) in the propofol group, with no significant difference between groups (p=0.5). Females predominated in both groups, accounting for 65.0% of subjects in the thiopental group and 85.0% in the propofol group, without a statistically significant difference in sex distribution.

Mean body weight and height were comparable between groups. The mean body weight was 63.7±8.9 kg in the thiopental group and 62.0±10.8 kg in the propofol group (p=0.251), while mean height was 157.4±7.2 cm

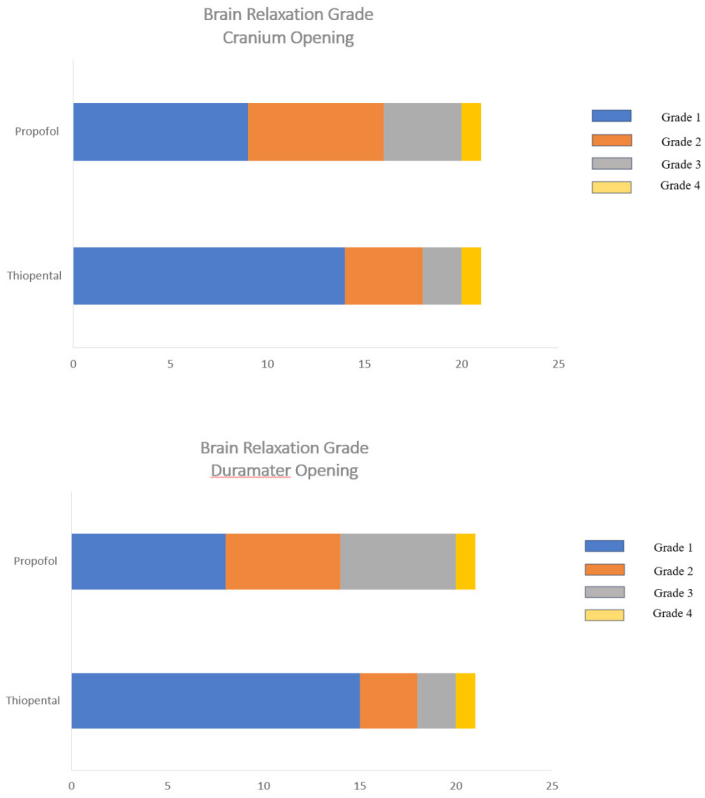

Figure 1 Brain Relaxation Grade in Cranium Opening and Duramater Opening

Table 3 Comparison of Propofol and Thiopental in Hemodynamics

Hemodynamic Parameter	Propofol (mean ± SD)	Thiopental (mean ± SD)	p-value
Systolic Blood Pressure (mmHg)			
Pre-operation	133.9±18.1	137.5±18.2	0.528
Induction	124.9±20.7	135.3±20.6	0.122
Post-induction	110.7±22.3	118.3±16.2	0.225
Intubation	107.8±24.2	115.9±18.6	0.243
Post-intubation	112.2±26.1	118.8±18.0	0.354
Incision	107.6±19.1	108.0±15.9	0.943
Dural closure	104.3±11.5	106.3±10.7	0.572
Diastolic Blood Pressure (mmHg)			
Pre-operation	77.1 ±8.0	80.0±8.6	0.277
Induction	70.3±9.7	78.2±7.2	0.006*
Post-induction	62.5±13.4	69.0±12.3	0.115
Intubation	61.7±8.9	65.6±9.8	0.191
Post-intubation	64.7±12.3	68.0±11.0	0.378
Incision	60.7±12.4	61.1±8.6	0.906
Dural closure	57.3±9.4	59.2±9.8	0.537
Mean Arterial Pressure (mmHg)			
Pre-operation	94.0±12.4	99.2±9.7	0.152
Induction	86.8±12.5	97.2±9.2	0.005*
Post-induction	77.4±13.2	85.4±12.2	0.054
Intubation	76.2±12.9	82.4±11.4	0.116
Post-intubation	76.0 ± 11.8	84.9±12.1	0.023*
Incision	76.4±12.8	75.4±12.1	0.814
Dural closure	72.0±8.3	74.9±9.2	0.309
Heart Rate (beats/min)			
Pre-operation	81.9±15.4	81.6±13.1	0.956
Induction	79.1±12.3	79.4±13.0	0.941
Post-induction	70.8±9.8	75.6±10.3	0.141
Intubation	75.9 ±12.8	75.4±10.6	0.883
Post-intubation	76.9±13.1	79.8±13.2	0.491
Incision	70.5±12.4	73.6±7.5	0.352

and 155.9±5.8 cm, respectively (p=0.47). Tumor diameter did not differ significantly between groups, with a median of 2.8 cm (range 1.7–5.4 cm) in the thiopental group and 2.9 cm (range 0.8–6.4 cm) in the propofol group (p=0.83).

Meningioma was the most common tumor type in both groups (85.0%), followed by glioma and hemangioma, with no statistically significant differences in tumor distribution. Midline shift differed between groups: absence of midline shift was more frequent in the propofol group (85.0%) compared with the thiopental group (55.0%), while a midline shift <5 mm was more common in the thiopental group (45.0%) (p<0.05).

The distribution of brain relaxation grades after bone opening, duramater opening, and duramater closing was comparable between

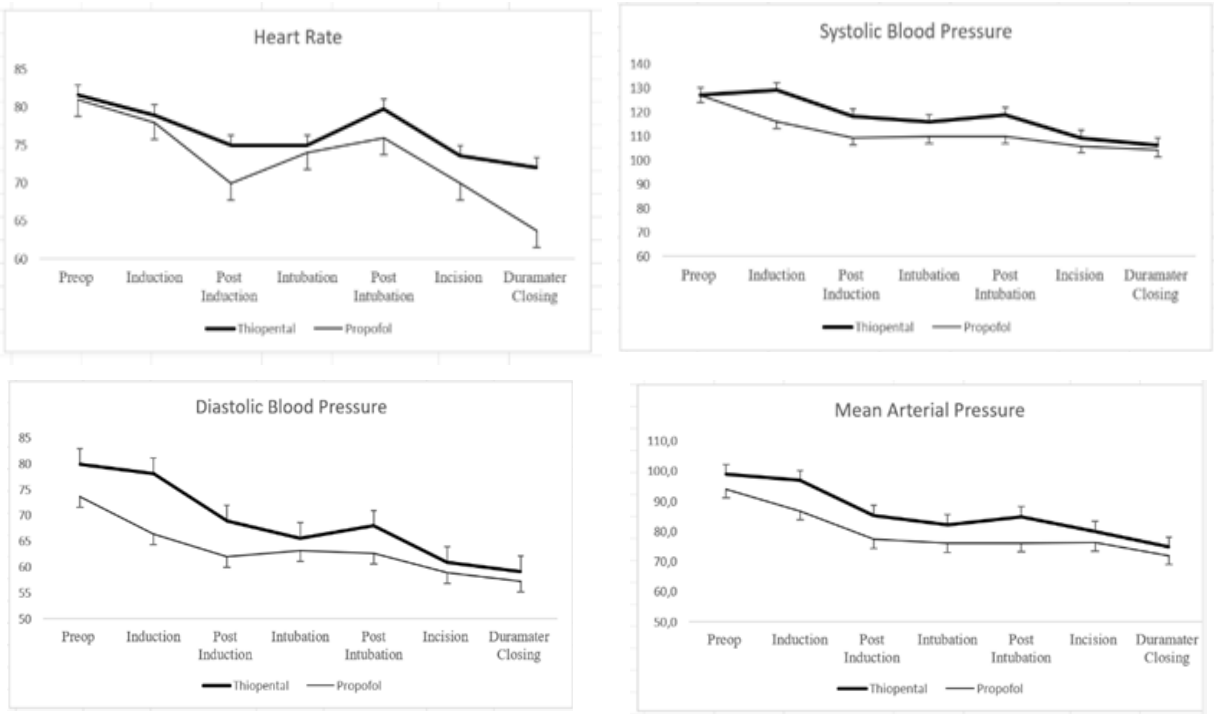

Figure 2 Intraoperative Cardiovascular Responses in Two Groups

groups, although statistically significant differences were observed for certain grades during duramater opening and closing. The mean duration of surgery and anesthesia did not differ significantly between groups.

The proportion of adequate brain relaxation at different surgical stages is shown in Table 2 and Figure 1. During bone opening, adequate brain relaxation was observed in 90.0% of subjects in the thiopental group and 80.0% in the propofol group, with no statistically significant difference between groups (p=0.331; PR 1.1). During duramater opening, adequate brain relaxation occurred in 90.0% of subjects receiving thiopental and 70.0% of those receiving propofol, and this difference was not statistically significant (p=0.12; PR 1.3). At the duramater closing stage, all subjects in both groups achieved adequate brain relaxation (100%), and no comparative statistical analysis was performed. Overall, no statistically significant differences in brain relaxation were observed between the two anesthetic agents at any surgical stage (Figure 1).

Hemodynamic parameters during surgery are presented in Table 3 and depicted in Figure 2. Systolic blood pressure values were consistently lower in the propofol group than in the thiopental group across all perioperative stages; however, none of these differences reached statistical significance (all p>0.05). During induction, mean systolic blood pressure was 124.9±20.7 mmHg in the propofol group and 135.3±20.6 mmHg in the thiopental group.

Diastolic blood differed significantly between groups during induction, higher values observed in the thiopental group compared with the Propofol group (78.2±7.2 vs 70.3±9.7 mmHg; p =0.006). No statistically significant differences in diastolic blood pressure were observed at the other perioperative stages.

Mean Arterial Pressure (MAP), showed significant differences during induction and post-intubation. During induction MAP was lower in the propofol group than in the Thiopental group, (86.8±12.5 vs 97.2±9.2 mmHg; p=0.005). At the post-intubation stage, MAP remained lower in the lower in the Propofol group compared with the Thiopental group (76.0±11.8 vs 84.9±12.1 mmHg; p=0.02). No significant differences were observed at the remaining stages.

Heart rate values were comparable between groups throughout most perioperative stages. A statistically significant difference was identified at duramater closing, where heart rate was lower in the propofol group than in the thiopental group (63.7±11.0 vs 72.1±8.3 beats/min; p=0.01).

Discussion

This study evaluates the comparative effects of thiopental and propofol on brain relaxation and hemodynamic stability during craniotomy for supratentorial tumor removal. Adequate brain relaxation is a fundamental goal in neuroanesthesia, as it reduces of the need for excessive brain retraction, minimizes the risk of secondary brain injury, and improves the surgical field. Brain relaxation was assessed at critical intraoperative stages, including post-bone opening, post-duramater opening, and post-duramater closure, allowing a comprehensive evaluation of anesthetic performance throughout the procedure.

The findings indicate that both thiopental and propofol were effective in achieving satisfactory brain including post-bone opening, post-duramater opening, and post-duramater closure, allowing a comprehensive evaluation of anesthetic performance throughout the procedure. At bone opening stage, a slightly higher proportion of patients receiving thiopental achieved adequate brain relaxation compared with those receiving propofol; however, this difference was not statistically significant. Similarly, at duramater opening, thiopental demonstrated a numerically higher prevalence of brain relaxation, yet without reaching statistical significance. By the duramater closure stage, all patients in both groups achieved optimal brain relaxation, suggesting that both anesthetic agents can reliably maintain favorable intracranial conditions until the end of surgery.

The observed tendency toward better brain relaxation with thiopental may be explained by its pharmacological effects. Thiopental reduces cerebral metabolic rate of oxygen ($CMRO_2$) and cerebral blood flow (CBF), resulting in decreased intracranial pressure (ICP) and improved brain compliance.[5,7,9] These effects have long supported its use in neuroanesthesia. Propofol also reduces ICP and $CMRO_2$; however, its more pronounced systemic vasodilatory effects may influence cerebral perfusion pressure (CPP), particularly in susceptible patients.[5,9] Although the prevalence ratios in this study suggest a possible clinical advantage of thiopental at certain stages, the absence of statistical significance indicates that both agents are comparably effective for brain relaxation when used appropriately.

Further, at the duramater opening stage, similar results were found, with 90% of subjects in the thiopental group experiencing brain relaxation, compared to 70% in the propofol group. This difference was also not significant (p=0.118), and the Prevalence Risk at the duramater opening stage was 1.286 (95% CI: 0.932–1.774), indicating that thiopental could achieve brain relaxation 1.286 times better than propofol. This shows that both drugs continue to provide similar relaxation effects during the duramater opening stage, which is more critical due to direct exposure to brain tissue.

At the duramater closure stage, both groups, whether thiopental or propofol, achieved brain relaxation in all subjects (100%), indicating that both anesthetic agents are equally effective in achieving optimal relaxation conditions at the end of the procedure. This suggests that both anesthetic agents can be relied upon to maintain brain relaxation until the end of the surgical procedure.

Some literature suggests that thiopental is effective in maintaining ICP and CPP (cerebral perfusion pressure) stability due to its measurable effects on hemodynamics. Thiopental is known to provide brain protection by reducing metabolism ($CMRO_2$) and cerebral blood flow (CBF), which effectively lowers intracranial pressure (ICP).[8] The reduction in CBF with thiopental tends to be more stable, maintaining a balance between the brain's oxygen demands and blood supply, which is beneficial for maintaining brain perfusion and preventing unwanted increases in ICP during anesthesia induction and surgical procedures. On the other hand, propofol is known to significantly lower ICP but also decrease MAP, which can potentially reduce CPP drastically in some patients.[5] This is supported by a study by Santra and Das, which found that propofol reduces cerebrospinal fluid pressure (CSFP) by up to 35.26%, but also causes a significant decrease in MAP. Therefore, the use of propofol during this stage requires close monitoring to ensure that CPP remains within safe limits to prevent ischemia in vital brain tissue.[9]

Although the statistical analysis shows that the difference between thiopental and propofol in terms of brain relaxation is not statistically significant, the data indicate that thiopental tends to be more clinically effective than propofol at some stages of surgery (Prevalence Rate 1.125 and 1.286). Thiopental's effectiveness in achieving brain relaxation can be observed at almost all stages of the surgery. While this difference is not statistically significant, the results reflect that thiopental provides a more consistent relaxation effect throughout the procedure. Thiopental's effectiveness in maintaining brain relaxation

until duramater closure may provide an additional advantage, particularly in minimizing the risk of post-operative complications related to brain pressure. This consideration can serve as a basis for preferring thiopental, especially in cases requiring optimal control of intracranial pressure.

The comparison between propofol and thiopental regarding hemodynamic parameters shows varied results at each stage of surgery. In this study, several parameters were observed, including systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), and heart rate, all of which are essential for monitoring cardiovascular stability during surgery.

For systolic blood pressure, the analysis also showed no significant differences between the two groups at all stages of surgery, including pre-operation, induction, post-induction, and duramater closure. The average systolic blood pressure in both groups was within a similar range, and the p-value was always above 0.05. At the pre-operative stage, the average systolic blood pressure for the propofol group was 133.9±18.06 mmHg and for the thiopental group was 137.5±18.18 mmHg, with a p-value of 0.528, indicating no significant difference between the two groups. Although some conditions, such as post-intubation and post-incision, showed slight differences between the propofol and thiopental groups, these differences were not large enough to be considered statistically significant. Thiopental is known to provide better stability in systolic blood pressure compared to propofol, particularly during the critical induction phase.[8]

Diastolic blood pressure showed slightly different results. At the pre-induction stage, there was a significant difference between the propofol and thiopental groups, with the thiopental group showing significantly higher diastolic blood pressure. This suggests that thiopental tends to maintain diastolic blood pressure more stable compared to propofol at the beginning of the surgery. The decrease in diastolic blood pressure could increase the risk of hypotension, potentially lowering cerebral perfusion. This sharper decrease is likely due to the more potent vasodilation effects of propofol compared to thiopental, as explained in a study.[9] However, at other stages such as post-induction, intubation, and duramater closure, there was no significant difference between the two groups, indicating that after induction, both anesthetic agents provide similar effects on diastolic blood pressure.

Mean arterial pressure (MAP) differed significantly between groups at the induction and post-intubation stages, with thiopental demonstrating higher MAP values. MAP is an important indicator of good organ perfusion during anesthesia, and better MAP stability in the thiopental group can provide a clinical advantage. However, at other stages such as post-induction, incision, and duramater closure, there were no significant differences between the two groups. The significant decrease in MAP is consistent with findings in the literature, where propofol is known to have a stronger hypotensive effect than thiopental. This is largely due to propofol's depressant effects on myocardial contractility and peripheral vascular resistance.[5,9]

Heart rate remained largely similar between the two groups throughout most stages of surgery. At the pre-operative, induction, post-induction, incision, and duramater closure stages, the average and median heart rates in both groups were relatively similar, with p-values above 0.05. This suggests that both drugs have similar effects in maintaining the stability of the patient's heart rate during surgery. However, at the final stage of the surgery, namely duramater closure, the heart rate difference between propofol and thiopental approached significance,with the thiopental group showing slightly higher heart rates compared to propofol. This may indicate that thiopental tends to provide better heart rate stability at the end of the procedure. The stability of heart rate suggests that neither anesthetic agent triggers significant sympathetic responses during induction and intubation stages, which could lead to increased blood pressure and heart rate.[8] Therefore, both propofol and thiopental can be considered safe in this regard for maintaining cardiovascular stability in patients undergoing craniotomy.

Although most comparisons did not reach statistical significance, thiopental showed a consistent tendency toward better hemodynamic preservations, particularly during induction and post-intubation. This may be an important consideration in choosing an anesthetic agent, particularly in the context of neuroanesthesia, where the selection of the anesthetic agent should consider the patient's initial hemodynamic condition and the risk of hypotension, which requires optimal hemodynamic stability during the surgical procedure. Propofol, although producing similar effects, appears to have a slight tendency to cause a decrease in diastolic blood pressure and MAP at the beginning of the procedure, which may require more attention in

patients with cardiovascular issues.[2,5,810]

Several limitations should be considered when interpreting these findings. The study was conducted by a single center with a limited sample size, which may restrict the generalizability of the results. In addition, data collection was performed by a single investigator, potentially introducing observer bias. Other confounding factors, such as variations in surgical technique, anesthetic depth, and adjunctive medications, were not fully explored. Future studies with larger, multicenter cohorts and more comprehensive roles of thiopental and propofol in neuroanesthesia.

In conclusion, both thiopental and propofol are equally effective in achieving adequate brain relaxation during craniotomy for supratentorial tumor removal. While no statistically differences were observed in brain relaxation outcomes, thiopental demonstrated a tendency toward better hemodynamic stability at certain critical stages of surgery. The hemodynamic response is better in patients receiving thiopental compared to those receiving intravenous propofol at Arifin Achmad General Hospital, Riau Province. This research is expected to serve as a reference for future studies and contribute valuable information to the field.

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