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Research Article

Effect of Propofol TIVA Compared Sevoflurane Inhalation Anesthesia on Triglyceride Levels After Elective Craniotomy Surgery

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ABSTRACT

Background: Propofol TIVA has been shown to be more effective than sevoflurane in craniotomy surgery. Propofol TIVA offers the benefit of giving better brain relaxation during surgery while also being less expensive than sevoflurane. Nonetheless, it is important to highlight that propofol has side effects that should be considered. Large doses and prolonged anesthesia may result in increased triglycerides (lipids) as well as Propofol Infusion Syndrome (PRIS). As part of their investigation into the detrimental effects of propofol, researchers discovered the necessity for controls to avoid confusing the effects of the surgery itself. Therefore, sevoflurane was chosen as the control group to comprehend and analyze the effects of propofol more accurately. **Methods**: A prospective observational study analysis was conducted on elective craniotomy patients at RSUD Dr. Soetomo from November to December 2023. 52 subjects were divided into two groups, namely the TIVA Propofol and Sevoflurane Inhalation groups. Each group will be examined for preoperative triglyceride levels and postoperative triglyceride levels while already in the ICU. **Results**: Postoperative triglyceride levels in the Propofol TIVA group were significantly higher. In the comparison test between the two anesthesia methods on triglyceride levels, there was a significant effect in the Propofol TIVA group. In the test of the relationship between the duration of anesthesia in both groups, there was no significant relationship. In the test of the relationship between the total dose of propofol and triglyceride levels, it was found that the greater the dose of propofol used, the higher the increase in triglyceride levels. In the test of the relationship between the total amount of sevoflurane and triglyceride levels, it was found that the greater the dose of sevoflurane used, the greater the decrease in triglyceride levels, which was statistically not significant. **Conclusion**: TIVA Propofol increases triglyceride levels compared to sevoflurane inhalation in patients undergoing elective craniotomies.
Keywords: Craniotomy, Triglycerides, TIVA propofol, Sevoflurane.

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INTRODUCTION

The most common treatment for surgically removing brain tumors is a craniotomy. Also, craniotomy can be performed for two reasons: head trauma and non-head trauma. This procedure may also be used to remove hematomas, control bleeding from ruptured blood vessels (cerebral aneurysms), repair arteriovenous malformations (abnormal blood vessels), remove cerebral abscesses, lower intracranial pressure, perform a biopsy, and treat hydrocephalus. The majority of craniotomies are performed for non-traumatic reasons. Tumors or malignancies are the least stressful causes of craniotomy action.[1] Meningiomas are the most prevalent primary brain tumors in adults, accounting for approximately one-third of all intracranial tumors. Meningiomas make up roughly 37.6% of all primary CNS tumors and 53.3% of all benign CNS tumors, according to histological results.[2] The majority of meningiomas are histologically benign (WHO grade I), and surgical excision has traditionally been the primary treatment option. Operations are usually recommended for symptomatic meningiomas or when the growth is rapid and thought to produce symptoms or will result in more dangerous operations later. 22.0-35.5% of meningiomas are grade II/III (high-grade meningiomas), indicating aggressive clinical characteristics.[3]

General anesthesia has transformed the medical landscape, allowing surgeons to perform more intricate and extended surgical procedures. The evolution of neurosurgical practices has introduced new challenges for anesthesiologists. An anesthesiologist is expected not only to function as an anesthesia expert but also to think and operate akin to a neurosurgeon and neurologist. Fundamental principles in neuro-anesthesia involve optimizing a patient's operative condition, maintaining cerebral perfusion pressure (CPP), and ensuring adequate brain oxygenation.

In neurosurgical procedures utilizing inhalation anesthesia like Desflurane, Isoflurane, and Sevoflurane. Sevoflurane, specifically used in neurosurgery, has demonstrated shorter recovery and extubation times compared to isoflurane. The benefits of sevoflurane over other inhalation anesthetics include: 1) reduced blood gas solubility; 2) has a fast start and off-set; 3) steadiness and precision throughout the maintenance period of anesthesia; 4) little metabolism, low metabolites, possibility for low side effects; 5) reduced airway irritation; this is particularly advantageous in cases where the induction of anesthesia is smooth and easy.[4-5] On the other hand, Propofol remains the most frequently used intravenous anesthetic. On the other hand, Propofol is a prominent sedative

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medication recognized for its quick onset of action, short half-life, and acceptable recovery profile for anesthesia and remains the most widely used intravenous anesthetic.[6] Notably, in Dr. Soetomo Hospital, tumor craniotomy and brain surgical procedures have advantages such as 1) quick onset and offset; 2) Smooth Induction and Recovery; 3) Anti-emetic effects; 4) lower price than sevoflurane ; 5) Better brain relaxation.[7]

Elevated triglyceride levels were observed with the use of long-chain propofol (LCT) compared to medium and long-chain propofol (LCT/MCT), indicating an increase in triglyceride levels in both groups. The LCT propofol group exhibited initial triglyceride levels of 83.35 ± 27.99 mg/dL and postoperative triglyceride levels of 199.40 ± 30.68 mg/dL. Meanwhile, the LCT/MCT propofol group showed initial levels of 75.55 ± 43.93 mg/dL and postoperative levels of 175.70 ± 25.81 mg/dL[8]. Hyperlipidemia is a disorder characterized by excessive levels of low-density lipoprotein, cholesterol, and triglycerides in the blood. Low HDL levels can lead to atherosclerosis and coronary heart disease. Hyperlipidemia also increases the risk of coronary heart disease due to atherosclerosis. Clinically, CHD thickens blood vessel walls, narrows lumens, and hardens arteries as a result of an imbalance in cholesterol levels. As a result, hyperlipidemia should be treated with a statin medicine like simvastatin.[9] No data is available regarding the increase in triglyceride levels with the use of inhalation anesthesia sevoflurane, but studies in animal models using inhalation agent isoflurane showed initial triglyceride levels of 72.29 ± 7.83 mg/dL and levels at 2 hours post-operation of 88.36 ± 10.46 mg/dL.[5] This study aims to analyze the impact of TIVA Propofol compared to inhalation anesthesia with sevoflurane on postoperative triglyceride levels in craniotomy procedures.

METHODS

This study was designed as a prospective observational analysis. The research was conducted at the Integrated Surgical Center at Dr. Soetomo General Hospital, Surabaya, East Java, Indonesia, from November to December 2023. This study received approval from the Dr. Soetomo Hospital Health Research Ethics Committee under reference number 0829/KEPK/XI/2023.

Samples were collected through consecutive sampling. The sample was collected through sequential sampling, with a minimum sample size of 40 people divided into two groups. Inclusion criteria for patients encompassed individuals aged 18 to 65 years, with American Society of Anesthesiologists (ASA) physical status ranging from 1 to 3, and a Glasgow Coma Scale (GCS) score of 13-15. Exclusion criteria included patients with a history of dyslipidemia or those receiving dyslipidemia treatment using statins or non-statins, as well as patients contraindicated for propofol administration. There are certain situations where propofol administration might be contraindicated. Patients contraindicated for propofol may include those with: 1) Allergies or sensitivity. Patients who have a known allergy or hypersensitivity to propofol or its ingredients. Severe Egg or Soy Allergy, Some propofol formulations contain egg or soy lecithin, and patients with severe allergies to these components may be at risk; 2) Severe Cardiovascular Instability: In some cases, patients with severe cardiovascular instability or compromised cardiac function may not be suitable candidates for propofol due to its vasodilatory and myocardial depressant effects; 3) Hypertriglyceridemia: Propofol formulations containing intralipid may lead to increased triglyceride levels, and caution is advised in patients with pre-existing hypertriglyceridemia.

Patients were divided into two groups: TIVA Propofol anesthesia or Inhalation Sevoflurane anesthesia. Changes in patients triglyceride levels before and after surgery were observed. Statistical analysis was conducted using the paired t-test for normally distributed data and the Wilcoxon signed-rank test for non-normally distributed data. A comparison between the changes in triglyceride levels under TIVA Propofol and Inhalation Sevoflurane anesthesia was performed using the independent t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Statistical analysis was carried out using IBM SPSS Statistics 26.

RESULTS

The population for this study was obtained from patients who underwent elective craniotomy procedures in the Dr. Soetomo Hospital in Surabaya, East Java, Indonesia. There were 52 individuals, divided into two groups: 26 subjects for the inhalation anesthesia group using sevoflurane and another 26 subjects for the TIVA (Total Intravenous Anesthesia) group using propofol. Patients' characteristics are presented in Table 1. Overall, there were no differences in sex, ethnicity, age, BMI, systolic and diastolic BP, MAP, heart rate and body temperature between both groups.

Comparison of pre- vs. post-levels of Triglycerides in the TIVA Propofol anesthesia group showed pre-values with a Mean ± SD of 103.73 ± 39.20, while post-values with a Mean ± SD of 527.38 ± 38.08. The Wilcoxon test yielded a p-value of <0.001, indicating a significant difference (< 0.05) between Triglyceride levels pre- and post-anesthesia in the TIVA Propofol group. Post-anesthesia Triglyceride levels were notably higher than pre-anesthesia levels, signifying that the administration of TIVA Propofol significantly increased Triglyceride levels in patients. (Table 2). Furthermore, in Table 2, the comparison of pre- and post-levels of Triglycerides in the Sevoflurane anesthesia group revealed pre-values with a Mean ± SD of 117.54 ± 31.42, whereas post-values ranged with a Mean ± SD of 98.96 ± 26.49. The Wilcoxon test indicated a p-value of <0.001, denoting a significant difference (<0.05) between Triglyceride levels pre- and post-anesthesia in the Sevoflurane group. Post-anesthesia Triglyceride levels were notably lower than pre-anesthesia levels, demonstrating that the administration of Sevoflurane anesthesia significantly decreased Triglyceride levels in patients.

Comparison of TIVA Propofol anesthesia and Sevoflurane anesthesia on pre-operative Triglyceride levels revealed that the TIVA Propofol group with a Mean ± SD of 103.73 ± 39.20, while the Sevoflurane group with a Mean ± SD of 117.54 ± 31.42 (Table 3). The Mann-Whitney test yielded a p-value of 0.146, signifying that there was no significant difference in Triglyceride levels between the TIVA Propofol and Sevoflurane anesthesia groups in the pre-operative stage, suggesting equivalency in the baseline Triglyceride levels between these two anesthesia groups. Additionally, post-operative Triglyceride levels revealed that the TIVA Propofol group with a Mean ± SD of 527.38 ± 38.08, while the Sevoflurane group with a Mean ± SD of 98.96 ± 26.49. The Mann-Whitney test resulted in a p-value of <0.001, signifying a significant difference in Triglyceride levels between the TIVA Propofol and Sevoflurane anesthesia groups post-treatment.

Table 4 describes the comparation between total dose and anesthetic time to triglyceride level. There was a significantly difference in total propofol dose and delta triglyceride level with p value 0.007 (p<0.05). However, there was no significantly difference between anesthetic duration in both propofol and sevoflurane group, so is the total sevoflurane dose.

DISCUSSION

Triglycerides are tri-esters composed of glycerol bound to three molecules of fatty acids and a primary cause of vascular disease and are commonly compared to cholesterol using a lipoprotein electrophoresis test. An increase in triglyceride concentration will result in hyperlipoproteinemia.[10] They constitute a primary component of plant fats and body fats in humans and animals. [11] Elevated triglyceride

Table 1. Characteristics of patients.

Subject characteristics	Anesthetic agent		Total (n=52)	p value
	TIVA Propofol (n=26)	Sevoflurane (n=26)		
Sex				
Male	7 (26.9%)	5 (19.2%)	12 (23.1%)	0.742
Female	19 (73.1%)	21 (80.8%)	40 (76.9%)	
Ethnicity				
Javanese	21 (80.8%)	19 (73.1%)	40 (76.9%)	
Maduranese	3 (11.5%)	5 (19.2%)	8 (15.4%)	0.741
Others	2 (7.7%)	2 (7.7%)	4 (7.7%)	
Age	46.00 ± 9.81	48.65 ± 11.07	47.33 ± 10.44	0.365
BMI	24.50 ± 4.58	25.00 ± 5.68	24.75 ± 5.12	0.971
Systolic BP	125.62 ± 20.37	123.12 ± 12.27	124.37 ± 16.70	0.594
Diastolic BP	78.27 ± 11.87	79.54 ± 7.46	78.90 ± 9.84	0.646
MAP	94.08 ± 13.87	94.00 ± 8.26	94.04 ± 11.30	0.981
Heart rate	88.46 ± 12.83	83.46 ± 12.12	85.96 ± 12.61	0.155
Body temperature	36.65 ± 0.11	36.67 ± 0.12	36.66 ± 0.11	0.454

Table 2. Pre and post-surgery triglycerides profile.

Triglycerides	Pre (mg/dL)	Post (mg/dL)	p value*
TIVA Propofol	103.73 ± 39.20	527.38 ± 38.08	<0.001
Sevoflurane	117.54 ± 31.42	98.96 ± 26.49	<0.001

Table 3. Comparation of triglyceride level in pre- and post-surgery between Tiva Propofol and sevoflurane.

Triglycerides	TIVA Propofol	Sevoflurane	p value*
Pre	103.73 ± 39.20	117.54 ± 31.42	0.146
Post	527.38 ± 38.08	98.96 ± 26.49	<0.001
Delta	423.65 ± 54.52	-18.58 ± 17.86	<0.001

Table 4. Delta triglyceride level related with anesthetic agents' administration.

Variable	Delta triglyceride level	P value
Propofol		
Total dose (ml)* 710.63 ± 97.8	423.65 ± 54.5	0.007
Anesthetic duration (minutes)** 390 (194-908)		0.142
Sevoflurane		
Total dose (ml)** 68.4 (45.8-189.5)	-12.5 (-60 – 3)	0.897
Anesthetic duration* 489 ± 154.9		0.324

*data is in mean (SD), **data is in median (min-max)

levels may result from increased availability of free fatty acids, glycerophosphate, reduced triglyceride lipase activity, or decreased lipid oxidation. [12] In this study, it was observed that post-anesthesia triglyceride levels were higher compared to pre-anesthesia levels, indicating that the administration of TIVA Propofol anesthesia was capable of increasing triglyceride levels in patients. Canatay & Baykan's study (2000) found that lipid profile levels in patients undergoing craniotomy with TIVA showed an increase after 2 hours of continuous intravenous propofol administration compared to the control group.[13] Furthermore, these levels decreased to an equivalent level as the control group after discontinuation of continuous propofol administration.

On the other side, this study found that with the administration of sevoflurane, post-anesthesia Triglyceride levels were lower compared to pre-anesthesia levels. This suggests that the administration of sevoflurane anesthesia led to a decrease in Triglyceride levels in patients. In a study by Mao et al. conducted on marmosets, a species of small New World monkeys, exposed to 1.5-2.5% sevoflurane for 6 hours, a decrease in triglyceride levels was observed compared to the control group[13]. However, in Chan et al.'s study, an increase in triglyceride levels was noted in the group exposed to 3% sevoflurane for 6 hours compared to the control group.[4] It can be concluded that the effects of sevoflurane on lipid metabolism may vary among different species.

This study revealed that the comparison test between TIVA Propofol anesthesia and sevoflurane anesthesia on pre-operative triglyceride levels in the TIVA Propofol anesthesia group showed no significant difference. However, for post-operative triglyceride levels in the TIVA Propofol anesthesia group, a significant difference was observed, indicating that the post-operative triglyceride levels in the TIVA Propofol anesthesia group were higher compared to those in the sevoflurane anesthesia group. This difference can be attributed to the triglyceride delta/change, where the change in triglyceride levels in the TIVA Propofol anesthesia group was larger, showing an increase compared to the sevoflurane anesthesia group, where the change in triglyceride levels decreased. Theoretically, propofol is believed to have a tendency to elevate triglyceride levels due to the emulsion components of propofol and its impact on the liver. [4,5,8,11-14] However,

the precise mechanism of sevoflurane's effect on triglyceride levels remains uncertain. A study by Chan et al. (2013b) conducted on the crested serpent eagle (*Spilornis cheela hoya*), evaluating physiological effects, hematocrit, plasma chemistry, and post-anesthesia behavioral effects following inhalation anesthesia with sevoflurane, revealed a decrease in triglyceride levels concurrent with the anesthesia duration. [4] The decrease in other blood components such as hematocrit, uric acid, and triglyceride in eagles undergoing anesthesia might suggest relative hemodilution.[15-16] It aligns with changes in regional blood flow that might occur in response to inhalation anesthesia. [17] The reduction in hydrostatic pressure due to anesthesia, primarily resulting from decreased blood vessel resistance, is likely the main cause of fluid accumulation in blood vessels and the compromised cellular element absorption function. [18]

Due to its formulation, propofol has been associated with an increased risk of hypertriglyceridemia. [19] Propofol is highly lipophilic and formulated in a 10% oil-in-water lipid emulsion. The lipid component is primarily composed of soybean oil and contains triglycerides, phospholipids, glycerol, vitamins, and minerals. Its main lipid is linoleic acid, a long-chain polyunsaturated omega-6 fatty acid. Therefore, increasing the dose of propofol may elevate triglyceride levels. Elevated triglyceride levels are associated with acute pancreatitis, which can be severe. The risk of acute pancreatitis increases when triglyceride levels exceed 500 mg/dL, and significantly higher risks are observed when triglyceride levels exceed 1000 mg/dL.[20] However, some case reports depict the development of propofol-induced acute pancreatitis without hypertriglyceridemia.[21]

After all, this is one of the profound studies comparing the effect of TIVA propofol and sevoflurane on triglyceride levels in patients undergoing surgery. However, this study possessed several limitations. Firstly, the researchers excluded patients with a history of dyslipidemia or undergoing dyslipidemia treatment or those with hypertriglyceridemia conditions. Therefore, these data might not be directly applicable to populations inclusive of hypertriglyceridemia risk groups. Secondly, this study was limited to measuring triglyceride levels as a biomarker indicating lipid elevation. This does not comprehensively represent the markers for lipid elevation. HDL, LDL, and total cholesterol are all important markers to monitor. According to the most recent World Health Organization (WHO) data, approximately half of all heart attacks occur in those who have excessive cholesterol. A high cholesterol level, also known as hypercholesterolemia, increases the risk of cardiovascular disease progression.[22] There's a need to observe markers like HDL, LDL, and total cholesterol. Additionally, the sampling was confined to only two collection times. Researchers did not observe over a longer period to determine the extent of anesthesia's effects on triglyceride or lipid level changes.

CONCLUSION

Finally, from the findings in this study, we can conclude that patients anesthetized with TIVA Propofol may experience higher change in triglyceride levels compared to Sevoflurane. Therefore, utilization of anesthetic agents other than TIVA propofol for patients with dyslipidemia or hypertriglyceridemia may be considered.

ETHICAL CONSIDERATIONS

The research was conducted in accordance with several ethical principles, namely anonymity and confidentiality. This study has met the ethical eligibility requirements of the Dr. Soetomo Hospital Health Research Ethics Committee.

CONFLICTS OF INTEREST

There is no conflict of interest in writing this research report.

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AUTHORS' CONTRIBUTION

All authors have the same contribution in writing this research report from the proposal preparation stage, data search, and data analysis, to the interpretation of research data, and the presentation of the final report.

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