COMPARISON OF SEVOFLURANE WITH PROPOFOL ON THE INCIDENCE OF EMERGENCE AGITATION AFTER GENERAL ANAESTHESIA IN PAEDIATRIC PATIENTS UNDERGOING LAPARATOMY SURGERY AT RSUP PROF. DR. I. G. N. G. NGOERAH

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ABSTRAK

Penelitian ini bertujuan untuk menunjukkan bahwa perbandingan antara penggunaan sevofluran dan propofol sebagai obat pemeliharaan anestesi dapat mengurangi insiden AK pada pasien pediatrik yang menjalani operasi laparotomi di RS PROF. Dr. I.G.N.G. Ngoerah. Penelitian ini adalah studi kohort prospektif yang dilakukan pada 84 pasien berusia 3-12 tahun dengan ASA I-II yang menjalani operasi laparotomi. Semua pasien dibagi menjadi dua kelompok, yaitu kelompok yang menerima pemeliharaan anestesi dengan sevofluran dan kelompok yang menerima pemeliharaan anestesi dengan propofol. Setelah anestesi dari awal ekstubasi hingga 1 jam di ruang pemulihan, pasien diperiksa dan dicatat apakah terjadi AK menggunakan Pediatric Anesthesia Emergence Delirium (PAED) dan tingkat keparahannya. Jika skornya > 12, pasien diindikasikan mengalami AK. Hasil penelitian menunjukan bahwa perbandingan penggunaan obat pemeliharaan anestesi menggunakan propofol dan sevofluran terhadap insiden AK dan ditemukan bahwa 21,4% dari kelompok yang menggunakan propofol mengalami AK, dan 59,5% dari kelompok yang menggunakan sevofluran mengalami AK, nilai p <0,001 dengan OR 5,392; 95% CI [2.06 - 14.09]. Dalam penelitian ini, ditemukan bahwa semakin muda usia meningkatkan risiko insiden AK dibandingkan dengan anak-anak yang lebih tua. Propofol secara signifikan mengurangi insiden Agitasi Kebangkitan (AK) dibandingkan dengan sevofluran pada pasien pediatrik yang menjalani operasi laparotomi di RS PROF. Dr. I. G. N. G. Ngoerah.

Kata kunci : agitasi kebangkitan, laparotomi, pediatrik, propofol, sevofluran

ABSTRACT

This study aims to demonstrate that the comparison between the use of sevoflurane and propofol as maintenance anesthesia drugs can reduce the incidence of Emergence Agitation (EA) in pediatric patients undergoing laparotomy surgery at Prof. Dr. I.G.N.G. Ngoerah Hospital. This research is a prospective cohort study conducted on 84 patients aged 3-12 years with ASA I-II who underwent laparotomy surgery. All patients were divided into two groups, the group receiving maintenance anesthesia with sevoflurane and the group receiving maintenance anesthesia with propofol. After anesthesia from the start of extubation to 1 hour in the recovery room, patients were examined and recorded whether EA occurred using Pediatric Anesthesia Emergence Delirium (PAED) and its severity. If the score was > 12, the patient was indicated to experience EA. The results of the study showed that the comparison of the use of anesthesia maintenance drugs using propofol and sevoflurane on the incidence of EA revealed that 21.4% of the propofol group experienced EA, while 59.5% of the sevoflurane group experienced EA, with a p-value <0.001 and OR 5.392; 95% CI [2.06 - 14.09]. In this study, it was found that younger age increases the risk of EA incidence compared to older children. Propofol significantly reduces the incidence of Emergence Agitation (EA) compared to sevoflurane in pediatric patients undergoing laparotomy surgery at Prof. Dr. I.G.N.G. Ngoerah Hospital.

Keywords *: emergence agitation, sevoflurane, propofol, pediatric, laparotomy*

INTRODUCTION

Pediatric patients undergoing laparotomy surgery at IBS RSUP Prof. Dr. I.G.N.G Ngoerah are increasingly supported by advancements in medical skills and technology. The rise in laparotomy surgery cases has led to an increase in general anesthesia for pediatric patients. General anesthesia for pediatric patients is commonly performed using inhalation techniques, mainly due to the need for pediatric patients to be sedated to avoid psychological stress and facilitate anesthesia procedures. General anesthesia using inhalation gases has the side effect of Emergence Agitation (EA). Despite efforts to reduce its occurrence, EA cases remain significant.

The phenomenon of EA was first discovered and reported in the early 1960s, where pediatric patients undergoing tonsillectomy, thyroidectomy, and circumcision surgeries experienced EA after being anesthetized using a combination of drugs: Ether, scopolamine, and ketamine (Coté, 2017). According to research by (Whitman, 2018), the incidence of EA was 23.1% with sevoflurane compared to 3.7% with propofol. A study by Kanaya, et al. (2014) showed that propofol had a lower probability of agitation compared to sevoflurane, with a combined OR of 0.25 (95% CI 0.16-0.39, P = 0.000). The incidence of agitation was lower with total intravenous anesthesia (TIVA) compared to sevoflurane (14.9% vs. 38.3%, P = 0.018) (Chandler et al., 2013). With advances in pharmacology, inhalation gas usage that often leads to EA in pediatric patients has been reduced and combined with postoperative analgesic administration, which has been effective in reducing EA occurrences.

At IBS RSUP Prof. Dr. I.G.N.G Ngoerah, inhalation gases like sevoflurane are still more commonly used for maintenance anesthesia in pediatric patients compared to intravenous drugs like propofol. According to (Maldonado, 2013) the hypothesis regarding the pathophysiology of EA involves an imbalance between thalamus function and neurotransmitter availability, leading to disrupted thalamus function as an information filter to the cerebral cortex due to neurotransmitter imbalances such as acetylcholine, dopamine, glutamate, gamma-aminobutyric acid (GABA), norepinephrine, and serotonin. Physiologically, the brains of preschool-aged children (2-5 years old) exhibit characteristics related to normal age-related regression, where neurotransmitter functions such as acetylcholine, dopamine, and GABA are immature. Additionally, psychologically, preschool-aged children are not ready to face unfamiliar environments, leading to fear and confusion when in unfamiliar environments such as the operating room.

Sevoflurane has a relatively fast onset of action during induction and rapid recovery due to its low blood solubility. This allows for rapid elimination from the patient's body. Sevoflurane works in the postsynaptic channel to inhibit (GABA and glycine) and also inhibits excitatory synaptic channel activity (NMDA receptors, nicotinic acetylcholine, serotonin, and glutamate) in the central nervous system. This can result in difficulty for patients previously maintained on sevoflurane to adapt to their surroundings due to sudden cessation of NMDA receptor inhibition. On the other hand, propofol acts on the central nervous system by interacting with neurotransmitter receptors, particularly GABA-A receptors (gamma-aminobutyric acid A receptors) (Chidambaran et al., 2015). Thus, during patient recovery from anesthesia, there is no neurotransmitter imbalance with propofol, but adaptation disturbances may still lead to EA in pediatric patients who are unable to recognize sudden environmental changes. Propofol has been FDA-approved in the USA since 1989 as an induction agent for pediatric patients above 3 years old. Its use as an induction agent for pediatric patients under 3 years old is still debated. The advantage of using propofol compared to inhalation gases is fewer post-anesthesia side effects such as nausea and EA. Propofol is commonly used for anesthesia induction and maintenance, procedural sedation, and critical care sedation in pediatric patients (Angelini et al., 2001).

Most commonly used anesthesia drugs for general anesthesia maintenance in pediatric patients involve inhalation gases. One drawback of using inhalation gas sevoflurane is the occurrence of side effects when patients begin to recover from anesthesia. Patients may wake up in the recovery room agitated, which can endanger both the patient and those around them, such as dislodging the patient's IV access, surgical drain, or wound dressing. This problem arises due to the patient's agitation and purposeless movements. EA incidents can be managed by adding sedative or additional analgesic drugs. The administration of additional drugs during EA incidents prolongs patient care, as patients take longer to transfer to regular care units or to be discharged home. Family concerns also contribute to delayed discharge, as they fear recurrence of similar events or lingering anesthesia symptoms. Moreover, EA incidents result in increased treatment costs compared to patients who do not experience EA. An alternative for general anesthesia in pediatric patients is intravenous drugs such as propofol.

At IBS RSUP Prof. Dr. I.G.N.G Ngoerah, inhalation gases are still frequently used as the primary choice for maintenance anesthesia in pediatric patients compared to intravenous drugs like propofol. Based on this, the researcher aims to determine the comparison of sevoflurane with propofol on the incidence of Emergency Agitation (EA) in pediatric patients undergoing laparotomy surgery at IBS RSUP Prof. Dr. I.G.N.G Ngoerah.

METHOD

This research is a prospective cohort study that was conducted single-centeredly and examined whether or not the patient became agitated after being extubated in the operating room until he was permitted to leave the recovery area. The study was carried out under the direction of IBS RSUP Prof. Dr. I.G.N.G. Ngoerah, with consent from the Hospital Ethics Committee. Using a computer-generated random number table, patients were divided into both intervention groups at random in a 1:1 ratio. While group P2 was given anaesthesia with maintenance Propofol, group P1 was given anaesthesia with Sevoflurane. Sequential opaque envelopes with sequential seals were filled with random numbers. Both the surgeon and the patient's parents were informed about the surgery that was carried out (Figure 1)

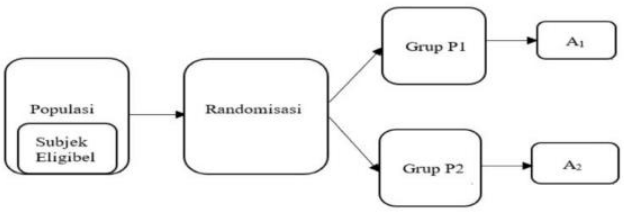

Figure 1. Research Design

Group P1 : Group receiving maintenance anaesthesia with Sevoflurane.
Group P2 : Group receiving maintenance anaesthesia with Propofol
A1 : incidence of agitation after receiving P1
A2 : Incidence of agitation after receiving P2

This study aimed to study pediatric patients who underwent laparotomy surgery at IBS RSUP Prof. Dr. I.G.N.G Ngoerah under general anesthesia. The accessible population included all pediatric patients who met the inclusion criteria and underwent laparotomy surgery during the study period until the minimum number of samples was met. The research sample was part of an accessible population selected based on eligibility criteria. The study included patients with ASA physical status I-III, aged 3-12 years, and ideal body weight according to CDC 2000. Exclusion criteria included impaired consciousness, respiratory disorders, impaired kidney function, and impaired liver function. Drop-out criteria included hemodynamic disturbances,

allergic reactions, complications, or death during the research process. The study aimed to provide valuable insights into the effectiveness of laparotomy surgery in pediatric patients.

This study used consecutive sampling to select subjects based on arrival order until 84 samples were collected. A simple randomized sampling technique was used, with patients randomly allocated into both intervention groups using a sevoflurane maintenance random number table, while group P2 received anesthesia with propofol maintenance. This study investigates the use of general anesthesia techniques with sevoflurane maintenance or Propofol maintenance in pediatric patients undergoing laparotomy surgery. The dependent variable is a PAED value > 12, indicating that EA occurs after extubation until the patient leaves the recovery room. The control variables are age, BMI, and physical status (ASA). Confounding variables include patients with impaired consciousness, respiratory function, kidney function, liver function, or complications.

Laparotomy surgery involves a skin incision in the abdominal area, and the degree of agitation is determined using the Pediatic Anesthesia Emergence Delerium (PAED) score. Anesthesia costs are calculated based on the type of drug given, and age is based on the patient's medical record. Body mass index (BMI) is measured using a microtoise and a needle weight scale. ASA physical status is assessed based on the American Society of Anesthesiologists' classification. Research materials and instruments include a questionnaire, anesthesia machine, anesthesia circuit, Abocath 20G and 22G, syringe, facemask, syring pump, infusion pump, intubation set, and PAED score table. The research procedure involves submitting an ethical clearance to the Faculty of Medicine, Udayana University, and applying for a research permit. Patients are selected and randomly allocated into two groups: those who received Sevoflurane maintenance and those who received Propofol maintenance. Patients' parents are informed about the research procedures, benefits, and results.

The data analysis was conducted using the intention to treat method, using the Statistical Package for Social Sciences application. Categorical and continuous variables were presented as mean and standard deviation, with statistical testing using the independent samples t test and Chi-square test of independence. Normality and equality of variances were tested before statistical testing. Results were displayed in table format for clarity. A P value of less than 0.05 was considered statistically significant. Descriptive analysis described subject characteristics and research variables based on treatment groups. Normality tests were conducted to determine the normal distribution of sample distribution and EA incidence parameters after general anesthesia. The mean comparison test was used to compare data distributions, using the independent t test if normal and the Mann-Whitney test if not normal. The entire data analysis process was conducted using SPSS 25 statistical software.

RESULTS

An observational analytic study with a hospital-based, single-centered prospective cohort study design was conducted by taking data from patients at the IBS of Prof. Dr. I.G.N.G. Ngoerah Hospital. This study aimed to compare the incidence of Emergency Agitation (EA) in paediatric patients undergoing laparatomy surgery under general anaesthesia between those using propofol and those using sevoflurane. Information extracted included demographic data, propofol and sevoflurane use, ASA status, length of surgery, length of anaesthesia, and EA response assessed post extubation. The study had a total of 84 patients, with 42 patients belonging to the propofol-treated group and 42 patients belonging to the sevoflurane-treated group. After obtaining the data, descriptive analyses were performed on each study variable.

Kolmogorov-Smirnov normality test was performed on numerical variables. Age, BMI, duration of surgery and duration of anaesthesia were not normally distributed ($p<0.05$), so Mann-Whitney test was performed on these variables (Table 1).

Table 1. Kolmogorov-Smirnov Normality Test Results

Variable	Statistic	df	Sig.
Age			
EA	0,293	34	0,000
No EA	0,136	50	0,021
IMT			
EA	0,251	34	0,000
No EA	0,129	50	0,036
Duration of Surgery			
EA	0,201	34	0,001
No EA	0,174	50	0,001
Duration of Anesthesia			
EA	0,183	34	0,005
No EA	0,162	50	0,002

Table 2. Distribution Of Study Subjects Based On Demographic Data

Variable	EA (n=34)	No EA (n=50)	P value
Age	4 [3 – 12]	10 [3 – 12]	0,000
Gender			0,503
Male	20 (58,8%)	33 (66%)	
Female	14 (41,2%)	17 (34%)	
IMT	18,5 [16,4 – 24,5]	22,4 [16,6 – 24,8]	0,036
ASA Physical Status			
I	31 (91,2%)	40 (80%)	0,164
II	3 (8,8%)	10 (20%)	
Duration of Surgery (Minutes)	86 [67 – 134]	105,5 [65 – 135]	0,014
Duration of Anesthesia (Minutes)	91,5 [15 – 145]	113 [78 – 145]	0,001

Based on table 2, the median age of the study subjects who experienced EA was 4 years with the youngest age of 3 years and the oldest 12 years, and in the group that did not experience EA 10 years with the youngest age of 3 years and the oldest 12 years, p value <0.001. both groups were dominated by male gender, 58.8% in the group that experienced EA and 66% in the group that did not experience EA, p value of 0.503. The body mass index of both groups varied with a median of 18.5 kg/m2 in the group that experienced EA with the smallest value of 16.4 kg/m2 and the largest of 24.5 kg/m2, while in the group that did not experience EA the median body mass index was 22.4 kg/m2 with the smallest value of 16.6 kg/m2 and the largest of 24.8 kg/m2, p value <0.036. The ASA physical status of both groups was dominated by ASA I, which was 91.2% in the group that experienced EA and 80% in the group that did not experience EA, p value of 0.164. The duration of surgery in the group that experienced EA had a median of 86 minutes, with a minimum value of 67 minutes, and a maximum of 134 minutes and in the group that did not experience EA had a median of 105.5 minutes with a minimum value of 65 minutes and a maximum of 135 minutes, p value of 0.014. The length of anaesthesia in the group that experienced EA had a median of 91.5 minutes with the smallest number being 15 minutes and the largest being 145 minutes, while in the group that did not experience EA had a median of 113 minutes with the smallest number being 78 minutes with the largest number being 145 minutes (Table 2).

Table 3. Comparison Of Research Groups

Variabel	EA (n=34)	No EA (n=50)	P value	OR [CI 95%]
Propofol	9 (21,4%)	33 (78,6%)	<0,001	5,392 [2,06 – 14,09]
Sevofluran	25 (59,5%)	17 (40,5%)		

A chi-square correlation test was performed on the variable of propofol and sevoflurane use on the incidence of EA and found that 21.4% of the group using propofol experienced EA, and 59.5% of the group using sevoflurane experienced EA, p value <0.001 with OR 5.392; 95% CI [2.06 - 14.09] (Table 3, Figure 3).

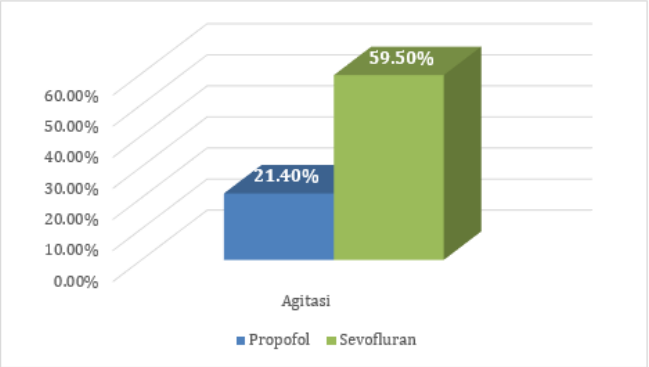

Figure 3. Incidence Of EA Between Propofol And Sevoflurane Groups Assessed Using The PAED Scale

DISCUSSION

Based on demographic data, it has been found that younger age significantly correlates with the occurrence of EA. A study by (López Segura & Busto-Aguirreurreta, 2023) stated that one of the risk factors for postoperative agitation and delirium in pediatric patients is age under 5 years. (Urits et al., 2020) found similar results, indicating that EA is most common and more prevalent in preschool-aged children compared to adults, with an overall incidence rate of 12-13% in pediatric patients.

This study found that propofol can reduce the occurrence of EA in pediatric patients undergoing laparotomy surgery. This is consistent with a study by (Haile et al., 2021), which examined 90 pediatric patients undergoing surgery and compared the outcomes of PAED scores in groups using propofol and those using anesthesia other than propofol. The study found that out of a total of 90 research participants, 64% of the non-propofol group and 31% of the propofol group experienced EA, which was statistically significant with p = 0.002. Administering 1 mg/kg of propofol before the end of surgery in pediatric patients undergoing general anesthesia is effective in reducing the incidence and severity of EA. Based on these findings, the study recommends the use of 1 mg/kg of propofol at the end of surgery to reduce the occurrence of EA (Haile et al., 2021).

EA can occur in all age groups but is more common in pediatric patients, with an incidence ranging from 20 to 80%. This mostly occurs within 30 minutes after the end of surgery and anesthesia administration during the recovery period. Children become uncooperative, restless, easily irritable, inconsolable, writhing, crying, and groaning during recovery from anesthesia (Nasr & Hannallah, 2011). Various contributing factors to agitation include the type of surgery, especially ENT and eye surgeries, the type of anesthesia, particularly inhalation agents, pain, and pediatric age groups (Costi et al., 2015). There are several methods that can be used to reduce agitation in pediatric patients, and one safe method is the prophylactic use of sub-hypnotic doses of propofol at the end of surgery to reduce agitation as patients begin to regain consciousness and facilitate smooth recovery from general anesthesia (Huett et al., 2017).

Propofol is an intravenous agent commonly used for anesthesia induction and maintenance, procedural sedation, and critical care in pediatric patients. Its mechanism of action in the central nervous system involves interaction with various neurotransmitter receptors, especially GABA-A receptors. Sevoflurane is an inhalation anesthesia widely used for pediatric anesthesia or brief procedures due to its excellent hemodynamic stability and low

blood solubility, allowing for rapid induction and recovery from anesthesia, as well as control over the depth of anesthesia. However, when used alone, sevoflurane is associated with a higher incidence of EA in pediatric patients. The occurrence of EA is believed to be due to the low solubility of sevoflurane and desflurane in blood, resulting in rapid recovery from general anesthesia. The rapid recovery process from general anesthesia, combined with the immature psychological state of children, leads to post-anesthesia EA (Aarts et al., 2012). Moreover, the intrinsic characteristics of modern anesthesia gases lead to disruptions in the balance of synaptic inhibition and excitation. Anesthesia gases, especially sevoflurane, can increase noradrenaline in adrenergic areas of the brain (Shung, 2011).

Literature suggests that anesthesia agents such as sevoflurane and desflurane have a higher incidence of EA compared to midazolam, remifentanil, propofol, ketamine, and barbiturates (Dahmani et al., 2014). Sevoflurane indeed has higher incidence rates of side effects such as nausea, vomiting, and laryngeal spasm (Driscoll et al., 2017). Additionally, when sevoflurane is compared to isoflurane, no significant difference in agitation occurrence is found (Costi et al., 2015). Administering propofol during sevoflurane anesthesia has been shown to reduce the incidence of EA, but there is some debate regarding the timing of administration (Van Hoff et al., 2015). Some studies have shown that a bolus of 1 mg/kg of propofol at the end of sevoflurane anesthesia maintenance has beneficial effects in reducing EA incidence, but newer data show varied results (Ozturk et al., 2016). Continuous propofol infusion during anesthesia has been shown to be more effective than single propofol administration. Some studies have shown that transitioning to propofol during a 3-minute period at the end of sevoflurane anesthesia reduces EA incidence (Van Hoff et al., 2015).

The significant use of propofol can reduce the incidence of post-extubation EA compared to sevoflurane in pediatric patients undergoing laparotomy surgery at IBS RSUP Prof. Dr. I.G.N.G Ngoerah. Significant differences were found in age and duration of anesthesia regarding the occurrence of post-extubation EA compared to sevoflurane in pediatric patients undergoing laparotomy surgery at IBS RSUP Prof. Dr. I.G.N.G Ngoerah.

CONCLUSSION

The study found that propofol significantly reduces Emergency Agitation (EA) in pediatric patients undergoing laparotomy surgery compared to sevoflurane. Younger age also increased the risk of EA. Future research should use more time, cover more data, and involve more confounding variables in analyzing correlations. The research aims to serve as a reference and information for other researchers, ensuring that the findings are useful and relevant.

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