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Nebulized Dexmedetomidine to Reduce Delirium after General Anesthesia Sevoflurane Inhalation in Preschool Children Undergoing Elective Surgery

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Abstract

Surgery in children remains a major challenge, particularly due to complications such as post-anesthetic delirium, with an incidence rate of up to 80%, especially in preschool-aged children when sevoflurane is the primary agent. Nebulized dexmedetomidine has been shown to reduce the incidence of post-anesthetic delirium with minimal risk of side effects. This study aims to evaluate the effectiveness of nebulized dexmedetomidine in reducing the incidence of post-anesthetic delirium in preschool-aged children undergoing elective surgery, as part of enhancing recovery after pediatric surgery (ERAPS). This research was a double-blind, randomized controlled trial, involving 72 pediatric patients aged 2–6 years undergoing elective surgery under general anesthesia with sevoflurane. Subjects were randomly divided into two groups; Treatment group receiving nebulized dexmedetomidine 2 mcg/kg (n=36) and Control group receiving nebulized normal saline (n=36). The primary outcome was the incidence of delirium during recovery at 15, 30, 60, and 120 minutes, assessed using the Pediatric Anesthesia Emergence Delirium (PAED) Scale. Statistical analysis revealed a significantly lower incidence of post-anesthetic delirium in the nebulized dexmedetomidine group (19.4%) compared to the control group (52.8%) at 15, 30, and 60 minutes ($p<0.05$), with a reduction in proportion by 33.4% ($p=0.003$). Relative risk analysis (RR = 0.427, 95% CI: 0.218–0.835; PF = 0.631) demonstrated that dexmedetomidine provides protective effects and significantly reduces the incidence of post-anesthetic delirium in preschool-aged children undergoing elective surgery with sevoflurane inhalational anesthesia. No side effects requiring intervention were observed during this study.

Introduction

Along with the development of medical science and technology, currently surgery on children is still a major challenge in the world of medicine, both in terms of surgical techniques, anesthesia and post-operative care aspects. Surgery on children not only requires high medical skills, but also involves special care to address physical and emotional needs that are clearly different from adult patients. The uniqueness of pediatric surgery and anesthesia lies in the anatomical and physiological conditions of children which are different from adults. The impact of surgery on children is quite significant, both for children, families, and the health system (Ulfah, 2021; Tumaji et al., 2020). Clinically, children have a higher risk of anesthetic and post-operative complications such as post-anesthetic delirium. In addition, from a psychological perspective, children tend to be more susceptible to emotional trauma due to

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surgery, from an economic perspective that burdens families and the health system, including the cost of surgery, post-operative care, and the potential for longer hospitalization.

Data from Prof. Dr. IGNG Ngoerah General Hospital in 2022-2024 there were more than 500 pediatric patients undergoing surgery with the largest age in the preschool group aged 2-7 years (Giovanni et al., 2024). Most of the surgeries performed were gastrointestinal operations with 95% facilitated by inhalation general anesthesia. Until now, inhalation anesthetic gas is still the means for induction and maintenance of anesthesia in children, especially sevoflurane. This is because sevoflurane has several advantages that make it the main choice in clinical practice, namely fast, easy and comfortable for induction, especially for patient populations who have difficulty cooperating such as children due to the low blood-gas partition coefficient (0.69), a non-irritating aroma that makes children more comfortable when inhaling it during the induction process and reduces the risk of coughing or laryngospasm compared to other agents such as desflurane or isoflurane. In addition, sevoflurane is also very good as an agent for maintaining anesthesia, by allowing easy adjustment of the depth of anesthesia during surgical procedures. This ensures better hemodynamic stability compared to other anesthesia agent techniques (Mohkamkar et al., 2014; Morris et al., 2009).

Despite having many advantages, there are some major weaknesses and shortcomings or impacts of the use of sevoflurane inhalation gas, namely the occurrence of post-anesthetic delirium. Several studies have reported that the incidence of post-anesthetic delirium is quite large, reaching 80% of the number of anesthesia in children with the highest incidence in younger children (preschoolers) and those undergoing invasive procedures (Andriyanto et al., 2019). Children who experience post-anesthesia delirium show clinical signs of restlessness, confusion, and aggressive behavior that can increase the risk of self-harm or injury during the post-operative period, which can affect delays in recovery and increase the length of hospitalization, so this is not in line with the development of enhanced recovery after pediatric surgery (ERAPS) (Klabusayová et al., 2022; Mahlangu, 2017).

In addition to inhalation anesthetic agents, important factors that correlate with the incidence of post-anesthetic delirium are preoperative pain and anxiety. Studies have shown that children who experience high anxiety before surgery have a greater risk of developing post-anesthetic delirium (Huan et al., 2023; Shi et al., 2019). This is due to an increased stress response that ultimately affects the child's neurological recovery when awakening from anesthesia. Postoperative pain also plays a major role in the occurrence of post-anesthetic delirium. Children who experience uncontrolled pain tend to show symptoms of delirium and confusion. Pain experienced by children after surgery causes increased activation of the sympathetic nervous system, which can trigger hyperactive behavior and confusion during the recovery phase and often requires rescue analgesia therapy in the form of opioids which have many side effects, especially causing nausea and vomiting (Shi et al., 2019).

Non-pharmacological therapy often does not provide the desired results because it cannot overcome triggers such as pain or anxiety, so one pharmacological effort that can be made to reduce the incidence of post-general anesthesia delirium is by administering Dexmedetomidine (Kanaya et al., 2014). Dexmedetomidine is a selective α2 adrenergic receptor agonist that can provide sedation, anxiolytic and analgesic effects by working on the locus coeruleus receptors in the pons (Tobias et al., 2007).

A more non-invasive, safe and comfortable route via intranasal or nebulizer jet dexmedetomidine 2 mcg/kgbb has been reported to reduce the incidence of post-anesthetic delirium in pediatric patients after general anesthesia (Yuen et al., 2008; Lin et al., 2022). This occurs because Dexmedetomidine via nebulization or intranasal causes slower absorption with good bioavailability reaching 65-83%, so the risk of hemodynamic instability is lower, and

sedation is lighter compared to intravenous administration (Anupriya et al., 2020; Ghai et al., 2018).

The use of Dexmedetomidine is now increasing, but research that focuses specifically on the effectiveness of nebulization in reducing delirium in preschool children undergoing elective surgery is still limited (Liu et al., 2021; Kocz et al., 2020). For this reason, researchers tried to provide nebulized Dexmedetomidine to reduce the incidence of delirium after inhalation general anesthesia in preschool children undergoing elective surgery. The aim of this study was to analyze the effectiveness of administering nebulized dexmedetomidine 2 mcg/kgbb in reducing the incidence of post-anesthesia delirium in preschool children undergoing elective surgery with sevoflurane inhalation general anesthesia.

Methods

This is a double-blind, randomized controlled trial. Participants are preschool pediatric patients aged 2–6 years undergoing elective surgery requiring general anesthesia. Participants will be randomly assigned to receive either nebulized dexmedetomidine 2 mcg/kg or 0.9% NaCl. The investigator, the healthcare providers (anesthesia team and operating room nurses) administering the medication, and the patients (and their guardians) will be blinded to the group assignment. The primary outcome measure is the incidence of delirium at recovery, assessed using a standardized pediatric delirium scale (PAED Score).

Subjects will be divided based on random allocation using computer-generated software, Allocation allocation is stored in a code number/Confidential envelope by an independent third party (pharmacist or reception room nurse) not directly involved in the study. The envelope will be opened when the subject is in the reception room by a third party assistant, while preparing a nebulizer containing dexmedetomidine or normal saline according to the group division by paying attention to the use of the same packaging, identical appearance (solution color), the same amount of solution dosage and the method of administration using the same tool for treatment and control subjects.

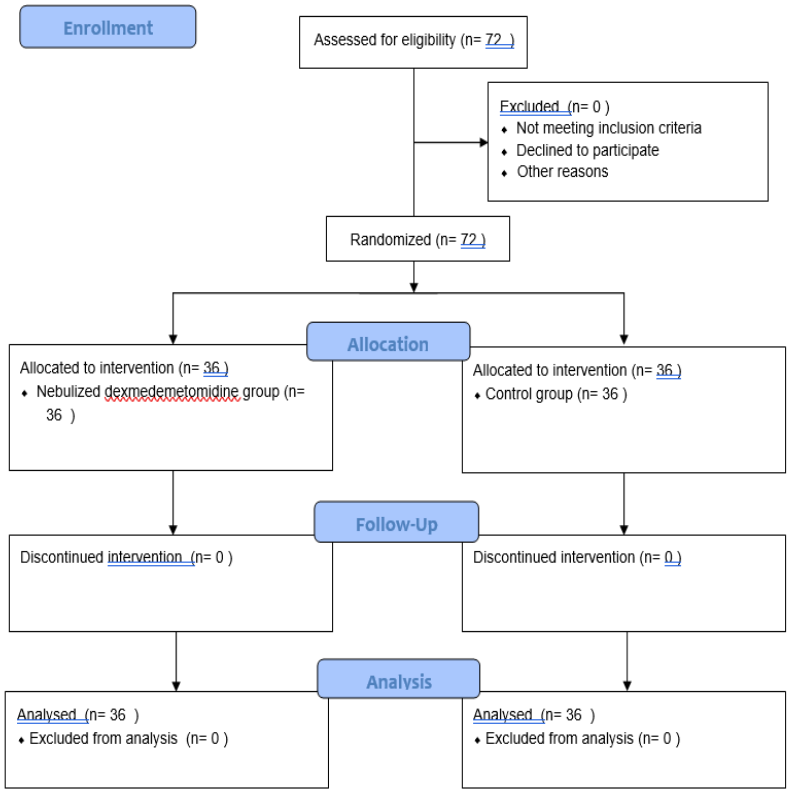

Figure 1. Consort Flow Chart

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The study was conducted at the Central Surgical Installation (IBS), and Wing Amerta, Prof. Dr. IGNG Ngoerah General Hospital, Denpasar from December 2024 to January 2025. The target population was all pre-school pediatric patients (2-6 years old) who would undergo scheduled surgery with general anesthesia. The accessible population was all hospitalized pediatric patients aged 2-6 years who would undergo surgery at Prof. Dr. IGNG Ngoerah General Hospital with general anesthesia techniques during October to November 2024.

Samples were drawn from a prospectively accessible population.using consecutive sampling, namely the population of hospitalized pediatric patients aged 2-6 years who will undergo surgery at Prof. Dr. IGNG Ngoerah General Hospital with general anesthesia techniques during November 2024 - January 2025 or until the number of samples is met. The subjects who are actually studied (actual study subjects) are samples who are truly willing to participate in the study by filling out the research informed consent form.

The study eligibility criteria included inclusion, exclusion, and dropout criteria. The inclusion criteria included pediatric patients aged 2–6 years who used sevoflurane general anesthesia with orotracheal tube technique at IBS Wing Amerta RSUP Prof. Dr. IGNG Ngoerah in the period November 2024 to January 2025. The exclusion criteria included patients with status >ASA II, difficult airway management, emergency surgery, congenital abnormalities of vital organs, malnutrition (BMI >95 or <5th percentile WHO), mental/cognitive disorders, upper respiratory tract infections in the last 2 weeks, allergy to dexmedetomidine, or surgery lasting >180 minutes. The dropout criteria included patients who experienced laryngospasm, were not extubated, or required reintubation so that the post-anesthesia delirium score could not be assessed.

Division of treatment and control subjects using the technique*permuted random sampling*using a computer-generated randomization sequence. Participants will be selected from the population that meets the inclusion criteria and thenrandomly assigned to either the intervention (dexmedetomidine) or control group. This randomization ensures that each group is similar in terms of baseline characteristics, so that any differences in outcomes can be more strongly attributed to the intervention.

Data analysis techniques used descriptive analysis to describe the characteristics of the subjects and research variables. Normally distributed numerical data were analyzed using the Independent t-test, while non-normal data used the Mann-Whitney U Test. Categorical data were presented as relative frequencies. Hypothesis analysis used a one-way test with a comparison of proportions through the chi-square test or Fisher's exact test, with conclusions based on the 95% Confidence Interval (CI) and P value <0.05. The relationship between dexmedetomidine administration and the incidence of postoperative delirium was analyzed using Relative Risk (RR) and Preventive Fraction (PF). All analyses were performed with the help of SPSS version 30 software.

Result and Discussion

In this study, there were 72 subjects divided into two groups, namely the Dexmedetomidine Nebulization group (n = 36) and the Control group (n = 36) which were randomly allocated. Demographic data showed no difference between the two groups in terms of age, weight, height, ASA physical status, duration of surgery, and duration of anesthesia. The normality of categorical variables was analyzed using cross tabulation with the Chi-Square test (because the requirements for the chi-square test were met expected value > 5), and the results were normally distributed (p> 0.05). Normality in numeric variables was analyzed using the Shapiro-Wilk test, and the results were normally distributed (p> 0.05) so that it was continued with the independent t-test, while those that were not normally distributed were continued with the Mann-Whitney U test to determine whether there was a significant difference in the variables between the two intervention groups.

Table 1. Hemodynamics before and after dexmedetomidine nebulization

	Dexmedetomidine Nebulization (n = 36)	Control (n = 36)	p value
HR pre-nebulization	114.0 (18.75)	104.5 (21.0)	0.426*
Post-nebulization HR	102.5 (24.5)	106.5 (20.0)	0.093*
RR pre-nebulization	22.0 (3.0)	22.0 (4.0)	0.685*
RR post-nebulization	22.0 (3.0)	22.0 (4.0)	0.781*
Pre-nebulization SpO2	99.0 (0.75)	98.5 (1.0)	0.105*
SpO2 post-nebulization	99.0 (1.0)	98.5 (1.0)	0.065*
Pre-nebulization systolic	94.5 (8.0)	92.5 (10.0)	0.320*
Post-nebulization systolic	89.0 (2.75)	93.0 (12.0)	0.036
Pre-nebulization diastolic	58.0 (8.25)	58.0 (9.0)	0.991*
Post-nebulization diastolic	56.0 (8.75)	57.0 (10.0)	0.704*

Data were not normally distributed and are presented in median (interquartile range). Normality test was performed using Shapiro-Wilk test (n < 50). *Mann-WhitneyU test, if P > 0.05 there is no significant difference between groups.

Datahemodynamics in 72 subjects showed that overall there was no significant difference between the hemodynamics of the dexmedetomidine nebulization group and the control group (p>0.05). There was a significant difference where the post-nebulization systolic was seen to be lower, but this decrease in systolic was not clinically significant (<20%) and did not require further intervention. There were no side effects of bradycardia, desaturation or severe hypotension in all subjects in this study.

Table 2. Comparison of post-anesthesia pain assessment between groups (FLACC Score)

	Dexmedetomidine Nebulization (n = 36)	Control (n = 36)	p value
FLACC 15th Minute	4 (2)	3 (3)	0.121
FLACC 30th Minute	2 (2)	2 (1)	0.211
FLACC 60th Minute	2 (1)	2 (1.75)	0.954
FLACC 120th Minute	1 (2)	1 (1.75)	0.528

There was no significant difference in FLACC scores between the dexmedetomidine nebulization and control groups. Data were not normally distributed and are presented in median (interquartile range). Normality test was performed using the Shapiro-Wilk test.

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Table 3. Comparison of PAED Scores, Wake Time, and Extubation Time between Dexmedetomidine Nebulization and Control Groups

	Dexmedetomidine Nebulization (n = 36)	Control (n = 36)	p value
PAED Minute 15	8 (4)	12 (2.5)	<0.001*
PAED Minute 30	7 (3)	10 (3)	<0.001*
PAED 60th Minute	5.5 (5.75)	8 (2)	<0.013*
PAED 120th Minute	4 (7.5)	5 (5)	0.175
Wake Up Time (minutes)	10 (9)	10 (5)	0.05
Extubation Time (minutes)	10 (4.75)	6 (5)	0.05

The table data above is not normally distributed and is displayed in median (interquartile range). Normality test was performed using Shapiro-Wilk test (n < 50). *Mann Whitney test, if p < 0.05, there is a significant difference between the two groups.

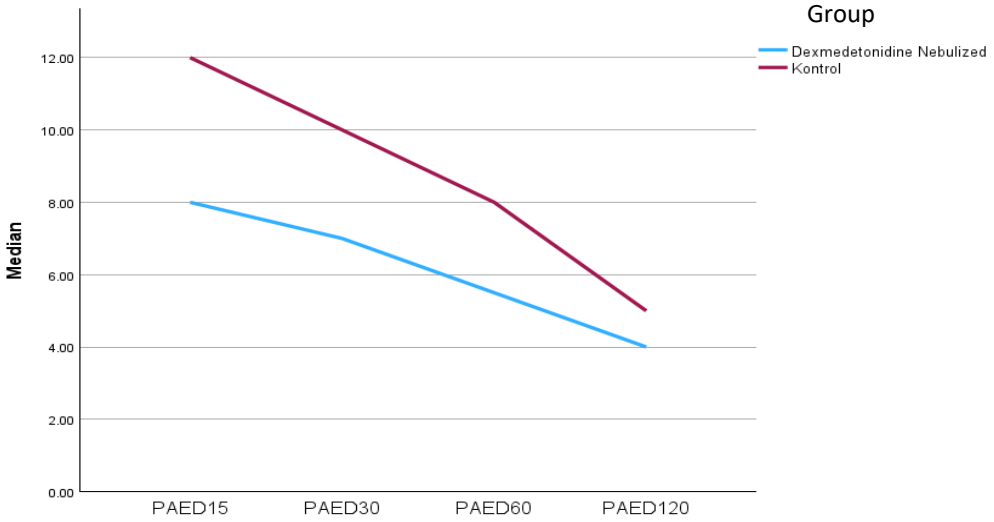

Figure 2. Median comparison graph of PAED scores

Figure 2. Median graph of comparison of PAED Score, between Dexmedetomidine Nebulization Group and Control. PAED score data and emergence time in 72 subjects showed a significant difference between PAED values at 15, 30, and 60 minutes of dexmedetomidine nebulization group and control (p <0.05) while at 120 minutes PAED there was no difference (p>0.05). There was no significant difference in the awakening time in this study. Extubation time was also not statistically significant, but quantitatively there was a difference in extubation time between the dexmedetomidine nebul group (10) and control (6).

Table 4. Comparison of Delirium Incidence Rates between Dexmedetomidine and Control Groups

	Group		***p value***
	Dexmedetomidine	**Control**	
Delirium	7 (19.4%)	19 (52.8%)	0.003
No delirium	29 (80.6%)	17 (47.2%)	

In this study, the incidence of delirium after inhalation general anesthesia was measured using the PAED scale (value >10) in the PAED minute group which showed a significant difference (p <0.05). The proportion of delirium incidence in the dexmedetomidine group (19.4%) was lower than the control group (52.8%) absolute risk reduction was (33.4%).

Table 5. Multivariable analysis of PAED values

Variables	**B (Coefficient)**	**SE (Standard Error)**	**Wald**	**df**	**Sig (P-Value)**	**Odds Ratio**
Intervention Group	**-1.315**	0.576	5.209	1	**0.022**	0.268
Gender	1.189	0.667	3.173	1	0.075	3.284
Type of Operation	-0.201	0.182	1.226	1	0.268	0.818
FLACC >= 4 (pain)	**0.569**	0.628	0.821	1	**0.365**	1,766
Constant	0.733	1,931	0.144	1	0.704	2,082

Comparison Test of Dexmedetomidine and Control Proportions

To measure the strength of the association between dexmedetomidine administration and the incidence of postoperative delirium (table 5.5) using Relative Risk, RR = (Incidence of

dexmedetomidine group) / (Incidence of control group).Measurement of the proportion of risk prevented by treatment compared to control. Using Preventive Fraction.$\mathrm{PF} = 1 - \mathrm{RR}$

Relative Risk (RR) Formula;

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

Where :

a : delirium with dexmedetomidine

b : no delirium with dexmedetomidine

c : delirium in the control group

d: no delirium in the control group

Relative Risk = 0.367 (95% CI: 0.218-0.835; p = 0.003)

Preventive Factor (PF) Formula

$$PF = \frac{(c/(c+d)) - (a/(a+b))}{c/(c+d)} \times 100\%$$

Preventive Factor = 0.631 or 63.1% (protection factor against delirium events).

From the data obtained a comparison of the frequency and percentage of delirium and non-delirium cases between the two groups, a statistically significant difference was obtained in the incidence of delirium between the two groups (p value <0.05). Participants in the dexmedetomidine group had a 0.367 or 36.7% risk of experiencing delirium compared to the Control group. Because the RR is less than 1, this indicates that the dexmedetomidine group has a protective effect against delirium. Preventive Factor = 0.633 which means that intervention with dexmedetomidine nebulization prevents the potential for delirium compared to the control group by 63.1%. The p-value of 0.003 indicates that this difference is very unlikely to occur by chance, so this relationship is statistically strong.

The results showed that in demographic data, there were no significant differences in age characteristics (p = 0.081), body weight (BW) (p = 0.980), height (TB) (p = 0.078), gender (p = 0.448), type of surgery (p = 0.588), and ASA classification (p = 0.237) between the dexmedetomidine nebulization group and the Control group. These results indicate that both groups in this study have the same demographic characteristics, the absence of significant differences in demographic characteristics between these groups indicates that the treatment and control groups can be compared validly.

The results showed a significant difference in the use of additional sedation (p = 0.014) in the control group, which had a higher proportion (77.8%) compared to the Dexmedetomidine group (50%). These results indicate that Dexmedetomidine, which is known to have a sedative effect through activation of alpha-2 adrenergic receptors, can reduce the need for additional sedation drugs during the procedure, as reported by Mason et al. (2021).Previous research by(Bonagua et al, 2020)showed that the use of nebulized dexmedetomidine in pediatric patients successfully reduced the need for other anesthetic drugs in preschool patients who required intravenous access procedures, thus supporting the findings in this study that nebulized dexmedetomidine can be used as a primary or additional agent in anesthetic procedures, especially in patients with minimal sedation requirements.

From the results of the hemodynamic profile, the results of the study showed that physiological parameters such as heart rate (HR), respiratory rate (RR), oxygen saturation (SpO2), and

diastolic blood pressure did not show significant differences between the dexmedetomidine nebulization group and the control, both before and after nebulization. However, there was a significant difference in systolic blood pressure after nebulization ($p = 0.036$), with the dexmedetomidine group having a lower value (median 89.0 mmHg) than the control group (median 93.0 mmHg). This effect is in accordance with the mechanism of action of dexmedetomidine which is known to lower blood pressure through activation of central alpha-2 adrenergic receptors, which reduces the release of norepinephrine and decreases peripheral vascular resistance (Castillo et al., 2020; Seyrek et al., 2011; Giovannitti et al., 2015). However, the effects of Dexmedetomidine on respiration, and SpO2 were not statistically significant, consistent with previous reports that Dexmedetomidine affects cardiovascular regulation more than respiratory function (Bonagua et al., 2020; Mason, 2021).The pharmacokinetic and dynamic effects of dexmedetomidine using the nebulization route provide the effect of reaching peak plasma levels more slowly compared to the intravenous route so that the effects of hypotension and bradycardia can be avoided (Wang et al., 2019; Castillo et al., 2020). However, the absence of significant differences in the duration of surgery and duration of anesthesia suggests that the effects of dexmedetomidine are more focused on hemodynamic stabilization and reducing the need for additional sedation, rather than affecting the overall duration of the procedure (Lin et al., 2020; Thamrin, 2011).

The results of the study further showed a comparison of PAED scores, wake-up time, and extubation time between the groups given dexmedetomidine nebulization and the control, that the administration of dexmedetomidine nebulization had a significant impact on the Pediatric Anesthesia Emergency Delirium (PAED) score at the 15th minute ($p < 0.001$), 30th minute ($p < 0.001$), and 60th minute ($p = 0.013$) compared to the control group.

The dexmedetomidine nebulization group showed lower PAED scores compared to the non-dexmedetomidine group consistently at all measurement times except for the 120th minute PAED ($p=0.175$). This is in line with the study of post-anesthesia delirium incidence by Eva et al. (2022) that the duration of post-anesthetic delirium generally varies depending on the patient population, type of anesthesia, and measurement method. However, in general, post-anesthetic delirium in preschool pediatric patients often occurs within 15 to 30 minutes after extubation, especially in the early phase of post-anesthetic recovery. This condition is usually transient and resolves within > 45 minutes, but in some cases, it can last longer depending on individual factors. Although the pathophysiological basis of post-anesthetic delirium is not fully understood, disturbances in the homeostatic process in the brain are considered an important factor. There are many risk factors that can trigger it but some of the most frequently described include younger age, male gender, use of benzodiazepines, or rapid recovery of consciousness after general anesthesia, for example the use of sevoflurane inhalation, and environmental factors such as waking up in an unfamiliar environment. Dexmedetomidine here can reduce the PAED score above because the dexmedetomidine profile can directly overcome several factors that cause post-anesthetic delirium, such as lack of cognitive development and fear of the environment, which are overcome by the sedation effect, while sensitivity to pain and discomfort are overcome by the analgesic effect (Huang et al., 2024).

The results of this study also showed that the use of dexmedetomidine can shorten the duration and reduce the severity (Figure 2) of delirium after sevoflurane inhalation anesthesia with a stable sedative effect without significantly prolonging the recovery time, namely the time to wake up ($p = 0.05$) and the time to extubation ($p = 0.05$) although the difference did not reach statistical significance. This finding is also in line with research (Lin et al., 2020),which showed that nebulized dexmedetomidine was effective in reducing the incidence of post-anesthetic delirium in pediatric patients without prolonging recovery time.

The relationship between multivariables with the results of increasing PAED values was also analyzed using the Logistic Regression test analysis (table 5) to find out the correlation between

the variables that most influenced the results of PAED values. At the beginning of the assessment, it was found that the variable of dexmedetomidine administration was the most significant factor influencing the results (minus) B value indicating that there was a negative effect of dexmedetomidine administration on the incidence of delirium. While the relationship between FLACC and the incidence of delirium had a positive correlation but did not reach a significant value in influencing PAED, this was because in this research protocol, pain control was carried out using standard post-op analgesics.

Analysis Results In (table 4), namely the comparison of the incidence of delirium between the dexmedetomidine and control groups, showed that the proportion of incidents in the dexmedetomidine group was 7 cases (19.4%), lower than in the control group, namely 19 cases (52.8%). This difference was statistically significant with a p value = 0.003, indicating that absolute dexmedetomidine nebulization in reducing the proportion of delirium incidence after sevoflurane inhalation general anesthesia, namely in this study (33.4%). This is in line with previous research and literature that the administration of dexmedetomidine can reduce the incidence of delirium after anesthesia. Dexmedemetomidine research (Shi et al., 2019) intravenously, a dose of 0.5 mcg/kgbb before the end of surgery reduced the incidence of delirium after general anesthesia with sevoflurane by 53.3% to 24.4%, the proportion reduced was 28.9%. Research by (Shen et al., 2022) using intranasal dexmedetomidine 2 mcg/kgbb showed a decrease in the proportion of post-general anesthesia delirium incidence by 11.9% compared to the control group. Although the proportion decreased was smaller in the study (Shen et al., 2022). This may be due to the fact that the main general anesthesia procedures still use total intravenous administration and not entirely use inhalation agents as in this study.

In this study, the relative risk analysis (RR) data, the RR value was 0.367 (95% CI: 0.218–0.835; p value 0.003). This means that patients receiving nebulized dexmedetomidine have a 63.1% lower risk of experiencing delirium compared to the control group (protection factor [PF] = 0.631). This is in line with the systematic review and meta-analysis by Huang et al. (2024) showing three studies involving 240 subjects with nebulized dexmedetomidine and controls, reporting a significantly lower incidence of delirium in the nebulized dexmedetomidine group than the control group (RR: 0.30; 95% CI: 0.18–0.49; P <0.01), with no heterogeneity (I^2 = 0%). So the results of this research analysis connect the efficacy of previous studies on the administration of dexmedetomidine for post-anesthesia delirium that: 1) Effectiveness of Dexmedetomidine: Nebulization of dexmedetomidine has been shown to provide a reduction and protection effect against the incidence of delirium in preschool children after general anesthesia with sevoflurane inhalation. In this study, an absolute risk reduction/decrease in the proportion of delirium incidence was obtained by 33.4%; 2) Statistical Value (p-value): With a p-value < 0.05 (p = 0.003), these results strengthen the evidence that the difference in delirium incidence between the two groups did not occur by chance, but was a real effect of the dexmedetomidine intervention; 3) Confidence Interval (CI): The CI range (0.218–0.835) does not include or is less than 1, indicating that these results are valid and statistically significant in providing a preventive and protective effect against the occurrence of delirium after sevoflurane inhalation anesthesia in preschool children; 4) Clinical Practicality: With Preventive Factor (PF) = 0.631 or 63.1% as a protective value against delirium events, the use of dexmedetomidine can be considered as part of the anesthesia protocol, especially to prevent delirium after sevoflurane inhalation general anesthesia in vulnerable populations such as preschool children undergoing elective surgery.

Conclusion

Administration of dexmedetomidine nebulization 2 mcg/kgbb was proven to significantly reduce the incidence of delirium after general anesthesia sevoflurane inhalation by 33.4% and provide a protective effect of 63.1% in preschool pediatric patients undergoing elective surgery. These findings indicate the potential use of dexmedetomidine as an effective

preventive intervention in reducing the risk of post-anesthesia delirium in this population. Further studies with multicenter designs are recommended to strengthen the validity of the results and ensure generalization to a wider population. In addition, holistic measurements need to be carried out involving evaluation of parental comfort and perception of the anesthesia procedure to understand the clinical benefits more thoroughly. Multivariate analysis is also recommended to control for confounding variables, thus providing a more comprehensive picture of the effectiveness of dexmedetomidine. The results of this study can be the basis for the preparation of clinical guidelines for the use of dexmedetomidine nebulization in preventing post-anesthesia delirium in pediatric patients.

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