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Neuroprotective Effects of Dexmedetomidine in Pediatric Open-heart Surgery with Cardiopulmonary Bypass: A Randomized Controlled Study Using Near-Infrared Spectroscopy and S-100B

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Abstract:

Introduction: Cardiopulmonary Bypass (CPB) during pediatric congenital heart surgery is associated with a risk of perioperative neurological injury. This study aimed to evaluate whether intra-CPB administration of dexmedetomidine reduces neuronal injury, as assessed by serum S-100B levels and regional cerebral oxygen saturation (rSO_2) monitored with near-infrared spectroscopy (NIRS).

Methods: This double-blind randomized controlled trial included 32 children aged 0–18 years undergoing open-heart surgery with CPB. Patients were randomized to receive either dexmedetomidine or placebo, with 16 patients in each group. In the dexmedetomidine group, 0.5 µg/kg dexmedetomidine was added to the CPB priming solution, followed by a continuous infusion of 0.25 µg/kg/h into the CPB reservoir during bypass. Serum S-100B levels were measured before CPB and 6–12 hours postoperatively. Cerebral rSO_2 was monitored at predefined perioperative time points. Secondary outcomes included duration of mechanical ventilation, cardiac intensive care unit length of stay, and 7-day mortality.

Results: Baseline pre-CPB S-100B levels did not differ significantly between the control and dexmedetomidine groups [8.76 (3.04–14.70) *vs*. 11.89 (3.93–14.20) pg/mL; $p = 0.127$]. Post-CPB S-100B levels were significantly higher in the control group than in the dexmedetomidine group (33.97 *vs*. 9.39 pg/mL; $p = 0.019$). The change in S-100B levels also differed significantly between groups, with an increase in the control group and a decrease in the dexmedetomidine group (+14.62 *vs*. −4.53 pg/mL; $p = 0.001$). Cerebral rSO_2 showed similar temporal trends in both groups, with no statistically significant between-group differences at any measurement time point. Duration of mechanical ventilation, cardiac intensive care unit length of stay, and 7-day mortality were comparable between groups.

Discussion: Intra-CPB dexmedetomidine was associated with lower postoperative S-100B levels, suggesting a potential reduction in biochemical evidence of neuronal injury during pediatric cardiac surgery with CPB. However, this biochemical effect was not accompanied by measurable differences in cerebral oxygenation or short-term clinical outcomes, indicating that its clinical significance remains uncertain.

Conclusion: Intra-CPB dexmedetomidine administration was associated with lower postoperative S-100B levels in pediatric patients undergoing open-heart surgery with CPB. Larger studies incorporating serial biomarker measurements and long-term neurodevelopmental follow-up are warranted to determine whether this biochemical effect translates into clinically meaningful neuroprotection.

Trial number: TCTR20260317004

Keywords: Dexmedetomidine, Cerebral protection, NIRS, S-100B, Pediatric cardiac surgery, Congenital heart disease, Cardiopulmonary bypass.

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1. INTRODUCTION

Pediatric cardiac surgery performed to correct congenital heart defects carries a significant risk of perioperative neurological injury. Hypoxia, ischemia, and reperfusion injury during the perioperative period may impair cerebral perfusion and oxygen delivery. The pediatric brain is particularly vulnerable because it is still undergoing developmental maturation and has higher metabolic demands than the adult brain. Consequently, preservation of neurological function during and after cardiac surgery remains a major concern in pediatric anesthesiology and cardiac surgery [1].

Cardiopulmonary Bypass (CPB) is essential for most pediatric open-heart procedures but is associated with systemic stress responses and inflammatory activation triggered by blood contact with artificial surfaces within the extracorporeal circuit. In addition, aortic cross-clamping during CPB may compromise perfusion to vital organs, including the brain. Exposure of circulating blood to the extracorporeal circuit and oxygenator promotes the release of inflammatory cytokines and contributes to ischemia–reperfusion injury, which may result in functional injury to multiple organs, including the brain. Neurological complications remain clinically relevant; a study published in 2021 reported neurological complications in 4.2% of 3,548 pediatric cardiac surgery cases within the first ten postoperative days, while Frost *et al*. (2024) reported acute neurological complications in 2.1% of 3,090 pediatric open-heart surgeries [2, 3]. These findings highlight the need for effective neuroprotective strategies during CPB.

Dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, has sedative, anxiolytic, and analgesic properties and has attracted increasing interest for its potential neuroprotective effects [4]. Experimental and clinical studies suggest that dexmedetomidine may attenuate neuronal injury through multiple mechanisms, including modulation of inflammatory responses, reduction of oxidative stress, and inhibition of apoptotic pathways. Previous studies and meta-analyses have demonstrated that dexmedetomidine administration during pediatric cardiac surgery is associated with reduced levels of neuronal injury biomarkers such as neuron-specific enolase and S-100B, as well as lower concentrations of inflammatory mediators including interleukin-6 [5, 6].

Neuroprotection during cardiac surgery can be assessed using both biochemical and physiological approaches. Biomarkers such as S-100B and neuron-specific enolase are widely used indicators of neuronal injury, while Near-Infrared Spectroscopy (NIRS) enables continuous monitoring of regional cerebral oxygen saturation (rSO_2), reflecting the balance between cerebral oxygen supply and demand. NIRS therefore provides a non-invasive method for evaluating cerebral perfusion and oxygenation during cardiac surgery and has become an important tool for assessing the effectiveness of neuroprotective strategies [6, 7].

Despite growing evidence supporting the neuroprotective potential of dexmedetomidine, most previous studies have primarily focused on acyanotic congenital heart disease populations. Concerns regarding dexmedetomidine-associated bradycardia and arrhythmias initially limited its use in patients with cyanotic congenital heart disease. However, subsequent studies have suggested that dexmedetomidine-related arrhythmias do not result in clinically significant adverse outcomes in pediatric cardiac surgery [8]. Furthermore, emerging evidence indicates that dexmedetomidine administered within the CPB priming solution may provide cardioprotective and potentially neuroprotective benefits without significant adverse effects [9].

Therefore, this study aimed to evaluate the neuroprotective effect of dexmedetomidine administered during cardiopulmonary bypass in pediatric patients with congenital heart disease undergoing open-heart surgery. Neuroprotection was assessed using rSO_2 monitoring with NIRS and serum S-100B levels.

2. METHODS

2.1. Ethics and Study Design

This study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia–Dr. Cipto Mangunkusumo National General Hospital (protocol number 24-12-1828) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians of all participants prior to enrollment. This prospective double-blind randomized controlled trial was conducted at the Integrated Cardiac Service Center of Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, between July and December 2025. The study was conducted and reported in accordance with the CONSORT guidelines.

2.2. Participants

Pediatric patients aged 0–18 years with congenital heart disease scheduled for elective open-heart surgery requiring CPB were recruited. Patients were excluded if elective surgery was converted to emergency surgery or if they had hepatic dysfunction (liver enzyme levels >1.5 times the upper normal limit), active preoperative infection, renal dysfunction (serum creatinine >2 mg/dL), coagulation abnormalities (INR >1.5), or pre-existing brain injury or neurological disorders.

Participants were withdrawn from the study if weaning from CPB failed, CPB or aortic cross-clamp duration exceeded 120 minutes, postoperative Extracorporeal Membrane Oxygenation (ECMO) was required, or intraoperative death occurred.

2.3. Randomization and Blinding

Participants were randomly allocated in a 1:1 ratio using a computer-generated randomization sequence (www.randomizer.org) to receive either dexmedetomidine or placebo until the predetermined sample size was reached. To maintain double blinding, the randomization code was held by an independent pharmacist, who prepared and labeled the study solutions according to the allocation sequence. The prepared study solutions were administered by an independent research assistant, ensuring that patients, investigators, and clinical staff remained blinded to group allocation.

2.4. Anesthesia and Perioperative Data Collection

Baseline patient characteristics recorded included age, sex, diagnosis of congenital heart disease, current medications, body weight, height, and Body Surface Area (BSA). Perioperative variables including duration of surgery, CPB time, and aortic cross-clamp time were also documented.

All patients underwent general anesthesia and invasive monitoring according to institutional standard operating procedures at Dr. Cipto Mangunkusumo National General Hospital. Following induction of anesthesia, NIRS probes were placed on the patient's forehead to obtain baseline rSO_2. Then, in accordance with institutional protocols, CPB was initiated.

In the dexmedetomidine group, dexmedetomidine 0.5 µg/kg diluted in 5 mL of 0.9% NaCl was added to the CPB priming solution, followed by a continuous infusion of dexmedetomidine 0.25 µg/kg/h diluted in 20 mL of 0.9% NaCl administered at 10 mL/h into the CPB reservoir. The control group received 0.9% NaCl administered using the same protocol. After CPB weaning and completion of surgery, intraoperative variables were recorded, and patients were transferred to the Cardiac Intensive Care Unit (CICU).

2.5. Outcomes

2.5.1. Primary Outcomes

Regional cerebral oxygen saturation was monitored using INVOS™ 5100 4-channel cerebral oximetry (Covidien, USA) and Masimo Root® with O3 regional oximetry (Masimo Corp., USA). Absolute rSO_2 values (%) were recorded at predefined perioperative time points: T0 (after induction of anesthesia, pre-CPB), T1 (CPB initiation), T2 (aortic cross-clamping), T3 (60 minutes after CPB initiation), T4 (5 minutes after CPB termination), T5 (30 minutes after CPB), and T6 (60 minutes after CPB).

Serum S-100B concentrations were measured from venous blood samples obtained via a central venous catheter before initiation of CPB and 6–12 hours postoperatively. S-100B levels were analyzed using an enzyme-linked immunosorbent assay (ELISA) kit (Thermo Fisher Scientific, USA) and reported in pg/mL.

2.5.2. Secondary Outcomes

Secondary outcomes included duration of mechanical ventilation, defined as the time from admission to the Cardiac Intensive Care Unit (CICU) until extubation, CICU length of stay, and 7-day mortality.

2.6. Sample Size Calculation and Statistical Analysis

The sample size was calculated using the formula for comparison of two independent numerical means, with a type I error (α) of 0.05 ($Z\alpha = 1.96$) and a type II error (β) of 0.20 ($Z\beta = 0.84$). Assuming a clinically meaningful difference of 10 units at the point of interest and using the pooled standard deviation between groups, the minimum sample size required was 16 subjects per group. After accounting for an anticipated 10% dropout rate, the total minimum sample size was estimated to be 35 participants.

Statistical analysis was performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA). Differences in repeated numerical measurements between groups were analyzed using the General Linear Model (GLM) for normally distributed data and the Generalized Estimating Equation (GEE) for non-normally distributed data. Intergroup comparisons at each measurement time point were conducted using the independent t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. A p-value < 0.05 was considered statistically significant.

3. RESULTS

A total of 36 patients were randomized into the control group (n = 20) and the dexmedetomidine group (n = 16). The final analysis included 32 patients, with 16 patients in each group. Four patients in the control group were excluded from the analysis, as shown in Fig. (**1**).

Baseline demographic and perioperative characteristics were comparable between the control and dexmedetomidine groups, with no statistically significant differences in age, sex distribution, anthropometric parameters, diagnosis of congenital heart disease, or operative variables including duration of surgery, CPB time, and aortic cross-clamp time (all $p > 0.05$) (Table **1**).

Comparisons between groups were performed using the Mann–Whitney U test, independent t-test, or Chi-square test, as appropriate.

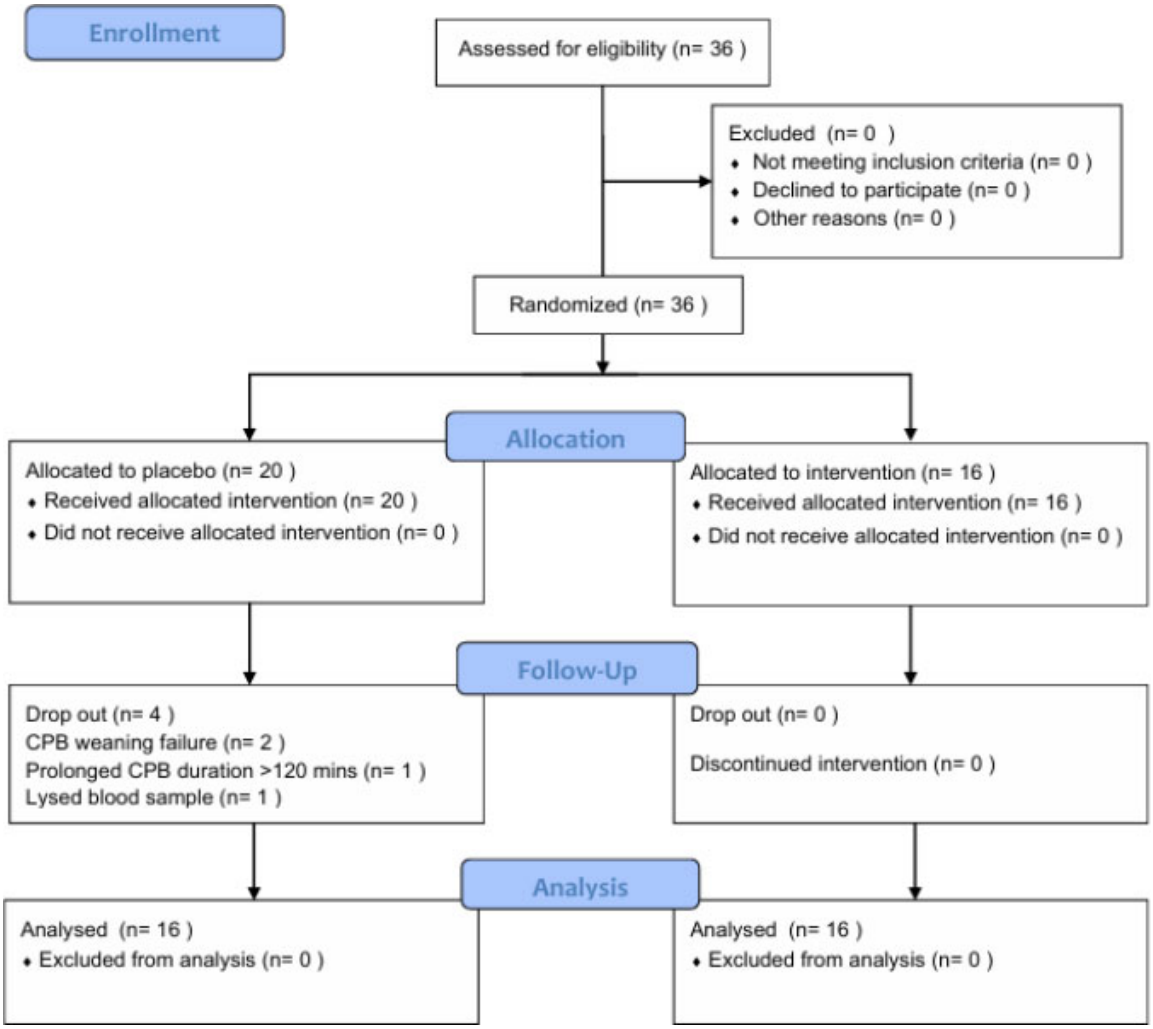

Fig. (1). Consort diagram of study flow algorithm.

Table 1. Baseline demographic and perioperative characteristics of the study participants.

Variable	Control (n = 16)	Dexmedetomidine (n = 16)	*p* value
Age (months)*	4.5 (2.92–7.71)	4.0 (3.33–7.67)	0.59
Sex†	-	-	0.457
Female	4 (36.4%)	9 (56.3%)	-
Male	12 (75.0%)	7 (43.7%)	-
Body weight (kg)*	13.0 (10.3–20.7)	13.5 (11.3–22.7)	0.696
Height (cm)*	97.0 (84.2–112.5)	99.0 (91.1–120.6)	0.564
Body surface area (m^2)*	0.59 (0.49–0.79)	0.61 (0.54–0.86)	0.616
Diagnosis†	-	-	0.472
Acyanotic CHD	11 (68.8%)	8 (50.0%)	-
Cyanotic CHD	5 (31.2%)	8 (50.0%)	-
Duration of surgery (min)‡	226.25 ± 45.44	208.75 ± 50.05	0.309
CPB duration (min)‡	75.31 ± 26.74	70.63 ± 24.81	0.611
Aortic cross-clamp time (min)‡	51.31 ± 23.58	46.13 ± 19.07	0.499

Note: * Data are presented as median (interquartile range).
† Data are presented as n (%).
‡ Data are presented as mean ± standard deviation.

Across the seven predefined perioperative time points (T0–T6), rSO_2 values showed comparable temporal trends in both groups, with a decline during CPB followed by gradual recovery after CPB termination. No significant between-group differences were detected at any time point (all $p > 0.05$). (Table 2).

Cerebral desaturation, defined as rSO_2 < 80% of baseline (T0), occurred in 12 of 16 patients (75.0%) in the control group and 9 of 16 patients (56.3%) in the dexmedetomidine group. As shown in Fig. (2), however, this difference was not statistically significant (Fisher's exact test, $p = 0.458$; OR = 2.33).

Serum S-100B concentrations were measured before (pre-CPB) and after (post-CPB) cardiopulmonary bypass, and the difference between these values (ΔS-100B) was used as an indicator of neuronal injury. S-100B values were not normally distributed (Shapiro–Wilk test, $p < 0.001$); therefore, non-parametric tests were used.

Baseline pre-CPB S-100B levels did not differ significantly between groups ($p = 0.127$). However, post-CPB S-100B concentrations were significantly higher in the control group compared with the dexmedetomidine group ($p = 0.019$). Correspondingly, the change in S-100B levels (ΔS-100B) differed significantly between groups, with an increase observed in the control group and a decrease in the dexmedetomidine group ($p = 0.001$) (Table 3).

Table 2. Comparison of NIRS-based rSO_2 concentrations between groups.

Time point	Control (n = 16)	Dexmedetomidine (n = 16)	*p* value
T0	75.9 ± 9.4	77.0 ± 6.8	0.59
T1	74.1 ± 8.9	74.6 ± 7.2	0.77
T2	70.3 ± 10.5	70.1 ± 6.7	0.92
T3	62.4 ± 14.9	60.0 ± 10.8	0.59
T4	59.1 ± 15.0	65.4 ± 10.8	0.07
T5	72.2 ± 11.9	74.2 ± 10.8	0.61
T6	74.0 ± 9.3	75.4 ± 7.3	0.55

Note: Data are presented as mean ± standard deviation.
T0–T6 correspond to predefined perioperative time points described in the Methods section.

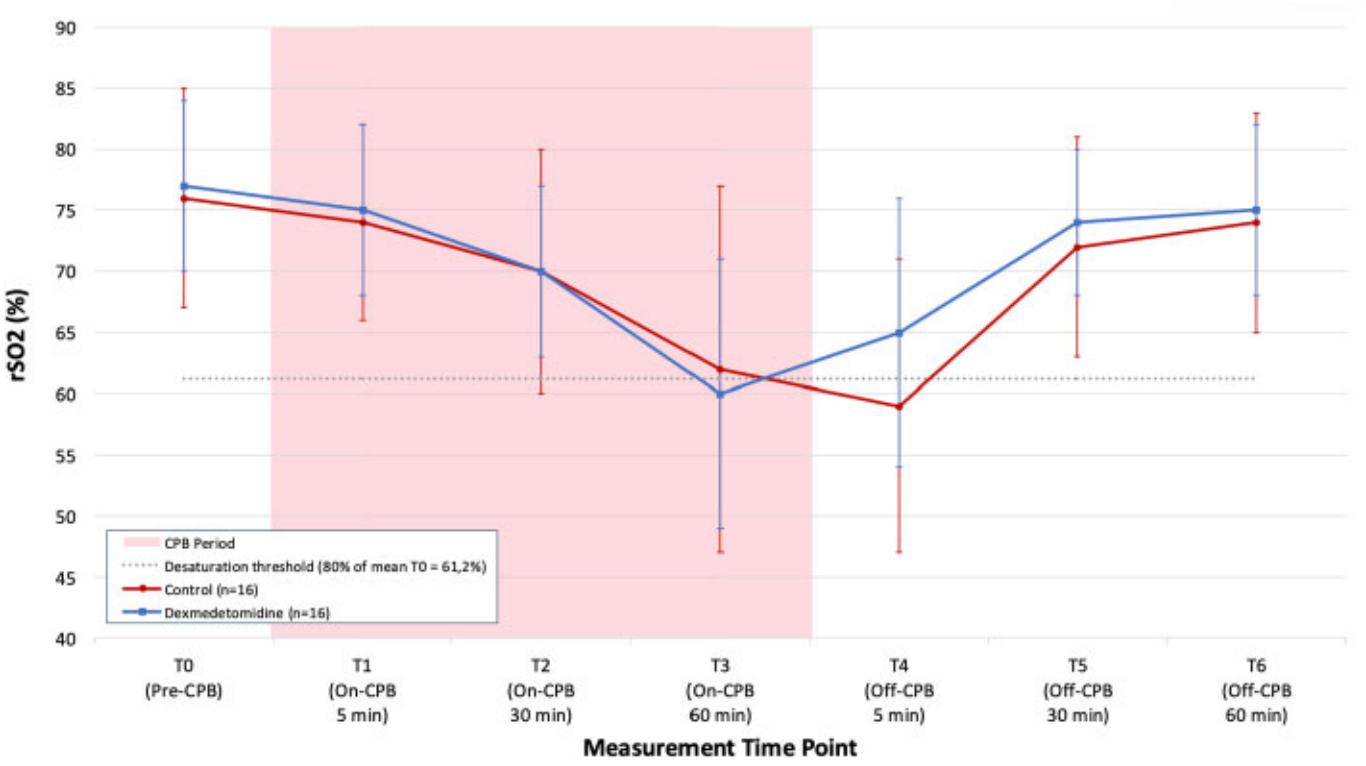

Fig. (2). Trend of rSO2 values (%) in control and dexmedetomidine groups at each measurement time point.

Table 3. Comparison of serum S-100B concentrations between groups before and after CBP.

Parameter	Control (n = 16)	Dexmedetomidine (n = 16)	*p* value
S-100B pre-CPB (pg/mL)	8.76	11.89	0.127
S-100B post-CPB (pg/mL)	33.97 $	9.39	0.019
ΔS-100B (pg/mL)	+14.62	−4.53	0.001

Note: Data are presented as median. Comparisons between groups were performed using the Mann–Whitney U test.

Table 4. Comparison of clinical outcomes between the control and dexmedetomidine groups.

Variable	Control (n = 16)	Dexmedetomidine (n = 16)	*p* value
Duration of mechanical ventilation (days)*	1.00 (0.76–2.86)	1.00 (0.84–4.91)	0.780
CICU length of stay (days)*	2.00 (1.52–4.11)	2.00 (1.45–5.80)	0.985
7-day clinical status, n	-	-	-
Discharged to ward	14	13	—
Still on ventilator	1	2	—
Death	1	1	1.000

Note: Data are presented as median (IQR). Between-group comparisons were performed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables.

Within-group analysis showed a significant increase in S-100B levels after CPB in the control group and a significant decrease in the dexmedetomidine group.

No significant differences were observed between the dexmedetomidine and control groups in duration of mechanical ventilation, CICU length of stay, or 7-day mortality (all $p > 0.05$). At postoperative day 7, most patients in both groups had been transferred to the general ward (Table **4**).

4. DISCUSSION

Baseline demographic and perioperative characteristics were comparable between the control and dexmedetomidine groups, including age, sex, body weight, height, body surface area, type of congenital heart disease (cyanotic *vs*. acyanotic), duration of surgery, CPB time, and aortic cross-clamp time. The absence of significant differences between groups is methodologically important, as younger age, cyanotic heart disease, and prolonged CPB or cross-clamp duration are known risk factors for perioperative neurological injury in pediatric cardiac surgery [1-3].

The absence of significant differences in CPB duration and aortic cross-clamp time between groups is methodologically important, as these variables are well-recognized contributors to cerebral hypoperfusion, microembolization, and systemic inflammatory activation that may result in neurological injury [1, 10].

4.1. Effect of Dexmedetomidine on Regional Cerebral Oxygen Saturation

No significant differences in rSO_2 were observed between the dexmedetomidine and control groups at any of the seven measurement time points. Despite this, a clear difference was observed in S-100B concentrations between groups. This dissociation suggests that the neuroprotective effect of dexmedetomidine in this population may not be mediated by improvements in the balance between cerebral oxygen supply and demand, but rather through direct cellular and molecular mechanisms.

Dexmedetomidine is known to exert anti-inflammatory, anti-excitotoxic, and anti-apoptotic effects through intracellular signaling pathways that promote neuronal survival [11, 12]. These mechanisms may confer neuroprotection without necessarily altering global cerebral oxygen extraction as measured by NIRS.

Similar observations have been reported in other neuroprotection studies. Peng *et al*. [13] demonstrated that normoxic reoxygenation strategies during CPB improved organ injury biomarkers without significant changes in cerebral oximetry parameters. Furthermore, Zaleski and Kussman [11] emphasized that rSO_2 reflects a composite signal influenced by arterial and venous oxygen content, hemoglobin concentration, cerebral blood flow, and tissue metabolism, which may limit its sensitivity to detect pharmacological neuroprotection occurring below the threshold of hemodynamic changes. Although not statistically significant, the numerically lower incidence of cerebral desaturation episodes in the dexmedetomidine group (56.3% *vs*. 75.0%) may still be clinically relevant. The observed odds ratio suggests a potential protective trend that this study may have been underpowered to detect. Post-hoc power estimation indicates that approximately 120 patients per group would be required to detect such differences with 80% statistical power, highlighting the need for larger multicenter trials.

4.2. Effect of Dexmedetomidine on S-100B Levels

The findings of this study support and extend existing evidence regarding dexmedetomidine and neuronal injury biomarkers. A randomized controlled trial by Qiu *et al*. [5] reported that dexmedetomidine administration

significantly attenuated the increase in postoperative S-100B levels in pediatric patients undergoing cardiac surgery with CPB. In their study of 90 children with congenital heart disease, the elevation of serum S-100B protein was significantly lower in the dexmedetomidine groups compared to the control group at the end of CPB and up to 24 hours post-surgery. However, since dexmedetomidine in that study was administered as a bolus 10 minutes after anesthesia induction followed by a continuous infusion until the surgical incision, its specific effect during the isolated CPB period remains difficult to determine.

A recent meta-analysis by Hashiya *et al*. [14] involving five randomized controlled trials also demonstrated a pooled reduction in S-100B levels associated with dexmedetomidine use, although substantial heterogeneity was observed in dosing regimens, timing of administration, and biomarker measurement.

Our study addresses this limitation by restricting dexmedetomidine administration to the CPB period, using a novel protocol that includes a priming dose added to the CPB circuit followed by a continuous infusion into the CPB reservoir. This approach allows the observed neuroprotective effect to be temporally linked to the CPB phase, which represents a critical period for cerebral vulnerability. Previous work by Baktiar *et al*. [15] demonstrated that postoperative increases in S-100B levels correlate with early postoperative cognitive dysfunction in adult cardiac surgery patients. Although extrapolation from adult to pediatric populations should be performed cautiously, these findings support the clinical relevance of S-100B as a biomarker of CPB-related neuronal injury.

4.3. Clinical Outcomes

No significant differences were observed between groups in short-term clinical outcomes, including duration of mechanical ventilation, ICU length of stay, and mortality. These findings are consistent with previous studies evaluating dexmedetomidine in pediatric cardiac surgery with similar sample sizes [4, 9, 14]. Short-term clinical outcomes in pediatric cardiac surgery are influenced by multiple factors, including surgical complexity, preoperative cardiac physiology, and postoperative hemodynamic management [3]. As a result, the impact of a single pharmacologic intervention may be difficult to detect in studies with relatively small sample sizes. Furthermore, the neuroprotective effects reflected by reduced S-100B levels may be more relevant to long-term neurodevelopmental outcomes, such as cognitive function, academic performance, and behavioral adaptation, which were beyond the scope of the present study [1].

4.4. Intra-CPB Administration of Dexmedetomidine

A distinctive feature of this study is the exclusive intra-CPB administration of dexmedetomidine, achieved through a combination of s priming dose delivered into the CPB circuit and continuous infusion into the reservoir. This strategy offers several pharmacological advantages compared with conventional systemic administration. Administration via the CPB priming solution ensures immediate drug availability at the initiation of CPB, a period characterized by activation of inflammatory cascades triggered by blood contact with the extracorporeal circuit.

Continuous infusion into the CPB reservoir helps maintain stable drug concentrations despite hemodilution, hypothermia, and drug sequestration within the bypass circuit [4]. Restricting dexmedetomidine administration to the CPB period may also minimize hemodynamic adverse effects such as bradycardia and hypotension, which are of particular concern in pediatric patients [8]. Additionally, since cardiac rhythm is typically controlled or arrested during CPB, the potential arrhythmogenic risk associated with dexmedetomidine reported in pediatric cardiac surgery may be reduced [8].

5. STUDY LIMITATIONS

Several limitations should be considered when interpreting the findings of this study. First, although the sample size was sufficient to detect a difference in the primary biomarker outcome, the relatively small number of participants limits the statistical power to detect differences in secondary outcomes and exploratory analyses. In particular, the study was not adequately powered to assess rSO_2 trends, cerebral desaturation events, short-term clinical outcomes, or subgroup effects according to congenital heart disease type and surgical complexity. Therefore, these findings should be interpreted as exploratory and hypothesis-generating.

Second, neuronal injury was assessed using S-100B as a single biomarker, whereas a broader panel including Neuron-Specific Enolase (NSE), Glial Fibrillary Acidic Protein (GFAP), and Neurofilament Light Chain (NfL) may provide a more comprehensive characterization of neuronal injury [16].

Third, the absence of long-term neurodevelopmental follow-up limits conclusions regarding the clinical significance of the observed biochemical neuroprotection. Fourth, heterogeneity in congenital heart disease diagnoses and surgical procedures introduces inherent variability that may obscure subgroup-specific treatment effects. Finally, the single-center study design may limit the generalizability of the findings.

6. CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

The substantial effect size observed in S-100B reduction provides a strong rationale for larger multicenter randomized controlled trials evaluating intra-CPB dexmedetomidine administration. Future studies should incorporate serial measurements of multiple neuronal biomarkers (*e.g.*, S-100B, NSE, GFAP, NfL, IL-6) over the first 24–72 postoperative hours to better characterize the temporal profile of neuroprotection. Simultaneous measurement of plasma dexmedetomidine concentrations during CPB would also help define

pharmacokinetic profiles and determine optimal dosing strategies. Long-term neurodevelopmental follow-up using validated instruments such as the Bayley Scales of Infant and Toddler Development and Wechsler Intelligence Scales is essential to determine whether biochemical neuroprotection translates into meaningful neurological outcomes.

Stratification by congenital heart disease complexity, such as RACHS-1 or STAT categories, and CPB duration may further identify patient subgroups that derive the greatest benefit from this intervention. Overall, the present study provides preliminary evidence supporting intra-CPB dexmedetomidine administration as a promising neuroprotective strategy in pediatric cardiac surgery, warranting further investigation in larger clinical trials.

CONCLUSION

This study demonstrates that dexmedetomidine administration during CPB is associated with a neuroprotective effect in pediatric patients undergoing open-heart surgery, as evidenced by a significant reduction in serum S-100B levels. The observed neuroprotective effect appeared to occur independently of changes in rSO_2 measured by near-infrared spectroscopy. These findings suggest that dexmedetomidine may exert neuroprotection through direct cellular mechanisms, potentially involving anti-inflammatory, anti-excitotoxic, and anti-apoptotic pathways. Baseline demographic and perioperative characteristics were comparable between groups, supporting the validity of the observed effects.

AUTHORS' CONTRIBUTIONS

The authors confirm their contributions to the paper as follows: D.N.S.: Contributed to the original draft preparation; A.P. and A.H.: Contributed to manuscript review and editing; M.A.: Contributed to data collection. All authors reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

CPB	=	Cardiopulmonary Bypass
rSO_2	=	Regional Cerebral Oxygen Saturation
NIRS	=	Near-Infrared Spectroscopy
ICU	=	Intensive Care Unit
CONSORT	=	Consolidated Standards of Reporting Trials
INR	=	International Normalized Ratio
ECMO	=	Extracorporeal Membrane Oxygenation
BSA	=	Body Surface Area
CICU	=	Cardiac Intensive Care Unit
ELISA	=	Enzyme-Linked Immunosorbent Assay
SPSS	=	Statistical Package for Social Sciences
GLM	=	General Linear Model
GEE	=	Generalized Estimating Equation
CHD	=	Congenital Heart Disease
OR	=	Odds Ratio
IQR	=	Interquartile Range
NSE	=	Neuron-Specific Enolase
GFAP	=	Glial Fibrillary Acidic Protein
NfL	=	Neurofilament Light
IL-6	=	Interleukin-6
RACHS-1	=	Risk Adjustment for Congenital Heart Surgery-1
The STAT	=	The Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia–Dr. Cipto Mangunkusumo National General Hospital (protocol number 24-12-1828).

HUMAN AND ANIMAL RIGHTS

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committees and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's parent (or the patient's legal guardian) for publication of this study and any accompanying images.

STANDARDS OF REPORTING

CONSORT guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and/or analyzed during the current study are not publicly available due to ethical and confidentiality considerations involving patient data. Access to the data may be granted by the corresponding author upon reasonable request for legitimate scientific purposes, subject to approval by the relevant institutional review board and compliance with applicable data protection regulations.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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