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Perioperative Use of Dexmedetomidine in Pediatric Congenital Heart Surgery: Effects on Hemodynamics and Organ Protection

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Abstract

This study explored how dexmedetomidine (Dex) influences perioperative hemodynamics and provides organ protection in children with congenital heart disease (CHD) undergoing open-heart surgery with hypothermic cardiopulmonary bypass. Ninety pediatric patients were randomly divided into three groups (n = 30 each): group C received 0.9% saline at 0.2 μg/kg/hour, group D1 received Dex at 0.2 μg/kg/hour, and group D2 received Dex at 0.4 μg/kg/hour. Anesthesia induction was performed using fentanyl, propofol, and 1% sevoflurane. Hemodynamic variables were recorded from before induction (T0) to 30 minutes after extubation (T7). Cerebral oxygen extraction and arteriovenous oxygen differences in the internal jugular vein were calculated using the Fick principle. Serum biomarkers for cardiac, cerebral, and renal injury were measured with enzyme-linked immunosorbent assays. The incidence of acute kidney injury (AKI) was determined by serum creatinine levels. Tracheal extubation times, postoperative pain scores, and emergence agitation scores were also assessed. Both Dex groups (D1 and D2) demonstrated more stable hemodynamics, lower cardiac and cerebral injury markers, and shorter extubation times compared with the control group. No significant differences were found among the groups in blood urea nitrogen, neutrophil gelatinase-associated lipocalin levels, or AKI incidence. Dex administration also reduced the occurrence of tachycardia, nausea, vomiting, moderate agitation, and FLACC pain scores. Moreover, the higher Dex dose (0.4 μg/kg/hour) was associated with a further reduction in fentanyl and dopamine requirements relative to the lower dose (0.2 μg/kg/hour). Dexmedetomidine anesthesia effectively preserves hemodynamic stability and reduces organ injury in children with congenital heart disease.

Keywords: Organ injury, Congenital heart disease, Cardiopulmonary bypass, Hemodynamic parameter, Dexmedetomidine

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Introduction

Congenital heart disease (CHD) is among the most prevalent congenital malformations and is often associated with significant intraoperative stress and the need for extracorporeal circulation [1]. In recent years, the number of pediatric CHD surgeries in China has risen substantially, with most procedures performed under general anesthesia combined with hypothermic cardiopulmonary bypass (CPB) [2]. Postoperatively, CHD patients may be at risk of long QT syndrome due to pathological alterations in cardiac action potential duration caused by defective slow delayed rectifier potassium channels [3, 4].

CPB is a critical adjunct in open-heart surgery, ensuring organ perfusion and oxygenation during the procedure.

However, many CHD children present with compromised cardiac function, and CPB itself can trigger a pronounced stress response. During CPB, clamping of the ascending aorta significantly reduces normal organ perfusion, while direct exposure of blood to the extracorporeal circuit and oxygenator promotes the release of inflammatory cytokines, potentially leading to systemic inflammatory response syndrome [5]. Stress-induced hyperglycemia and hyperlactatemia, together with ischemia-reperfusion injury from hemodynamic fluctuations, can cause substantial functional damage to the heart, lungs, brain, and kidneys [6]. Although surgical outcomes in CHD have improved dramatically [7], optimizing anesthesia to protect vital organs and support long-term neurodevelopment remains a critical challenge. Hence, developing a safe and effective perioperative sedation strategy to mitigate stress responses and maintain oxygen supply-demand balance in pediatric patients is urgently needed.

Dexmedetomidine (Dex) is a highly selective α2-adrenergic receptor agonist that produces sedation and hypnosis by activating presynaptic and postsynaptic α2 receptors in the locus coeruleus, inducing a sleep-like state. Its widespread expression in organs such as the liver, lungs, kidneys, and brain allows Dex to exert systemic effects [8], Prior studies have demonstrated that Dex stabilizes hemodynamics [9], reduces opioid and sedative requirements [10], lowers the incidence of postoperative delirium [11], and provides neuroprotective benefits [12]. These properties have made Dex a valuable anesthetic adjunct in perioperative and ICU settings, particularly in cardiothoracic surgery. For example, Nazir *et al*. [13] showed that Dex effectively controls hypotension during lumbar spine surgery, while Goyal *et al*. [14] reported that Dex serves as a viable alternative to fentanyl in breast cancer surgery due to its superior hemodynamic stability, anesthetic-sparing effect, and recovery profile. Animal studies further suggest that Dex may attenuate renal inflammation and ischemia-reperfusion injury [15, 16]. A meta-analysis by Jiang *et al*. [17] concluded that Dex reduces inflammatory mediator release, dampens neuroendocrine stress responses, and mitigates ischemic brain injury.

Despite its widespread use in adults, Dex remains off-label in pediatric patients in China. Pharmacokinetic studies indicate that children over one year of age exhibit similar Dex pharmacokinetics to adults [18], and children older than one month respond similarly to adult patients [19]. While Dex is recognized for its clinical benefits in adult populations, its application in pediatric CHD surgery is still not well defined. Therefore, this study aimed to investigate the effects of different Dex dosages on perioperative hemodynamics and organ protection, including cardiac, cerebral, and renal function, in children with CHD.

Materials and Methods

Informed consent and ethics

Ethical approval for this study was granted by the Ethics Committee of Guangxi University of Chinese Medicine, Ruikang Hospital, and written informed consent was secured from all participants' guardians. The trial has been registered in the Chinese Clinical Trial Registry under the number ChiCTR18000171819.

Study design and participants

This study recruited children scheduled for elective atrioventricular septal defect (AVSD) repair under cardiopulmonary bypass (CPB) at Ruikang Hospital, Guangxi University of Traditional Chinese Medicine, between July 1, 2017, and February 28, 2018.

Eligible participants were aged 1–6 years, diagnosed with CHD or AVSD, classified as ASA II–III, and preoperatively assigned NYHA class I or II. Patients were excluded if they had severe malnutrition, cyanosis, prematurity, low birth weight, prior cardiac surgery, hypersensitivity to narcotics, pulmonary hypertension, or comorbid conditions affecting brain, liver, or kidney function, including cerebral palsy, severe renal or hepatic disease, metabolic disorders, or congenital syndromes such as Trisomy 21.

A preliminary trial involving 20 children evaluated four regimens: medium-dose Dex (0.2 μg/kg/hour), low-dose Dex (0.1 μg/kg/hour), control (0.9% saline at 0.2 μg/kg/hour), and high-dose Dex (0.4 μg/kg/hour), with 5 patients per group. Continuous intravenous infusion of Dex or saline was maintained from anesthesia induction until the end of surgery. No significant differences were observed between the low-dose Dex group and control in hemodynamic stability, postoperative recovery, or organ function, likely due to limited dosing and sample size. Based on these findings, Dex doses of 0.2 and 0.4 μg/kg/hour were selected for the main study.

Of the 127 children initially screened, 9 failed to meet inclusion criteria, 5 withdrew, and 23 declined participation, leaving 90 patients for analysis. Participants were randomly assigned into three groups: group D2 (Dex 0.4 μg/kg/hour), group C (saline 0.2 μg/kg/hour), and group D1 (Dex 0.2 μg/kg/hour), with 30 children per group **(Figure 1)**. Randomization was conducted using SPSS software, with the initial seed set at 20161201.

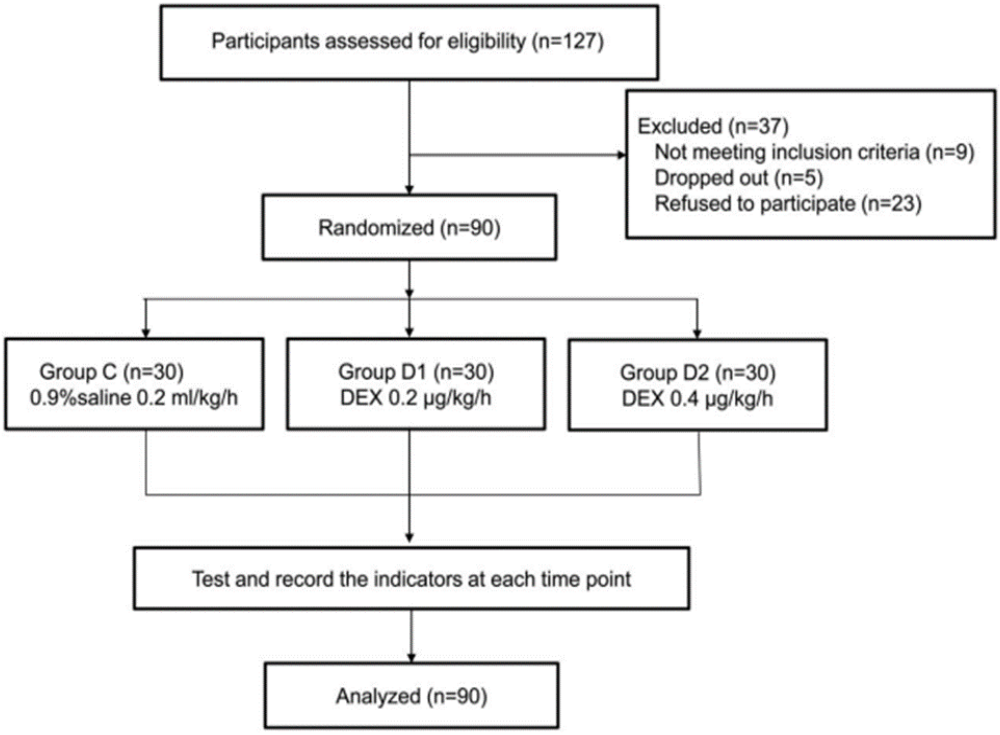


Figure 1. Participant Flow Diagram

Children assessed for eligibility for elective repair of congenital heart defects under cardiopulmonary bypass

Anesthetic process

All children were fasted for 6–8 hours and restricted from fluids for 2–4 hours prior to surgery. A preoperative skin test for cefazolin was performed, and in the absence of an allergic reaction, cefazolin was administered intravenously 30 minutes before surgery. Midazolam (0.1 mg/kg) was given intravenously for premedication. Once consciousness was lost, continuous monitoring of electrocardiogram, blood pressure, heart rate (HR), oxygen saturation, and Bispectral Index (BIS) was initiated.

Anesthesia induction was performed with intravenous vecuronium bromide (0.1 mg/kg), fentanyl (3–8 μg/kg), and propofol (1–3 mg/kg). When BIS values reached 45–60, oral tracheal intubation was performed, followed by connection to a mechanical ventilator. Ventilation parameters were set as follows: tidal volume 6–8 mL/kg, respiratory rate 15–32 breaths per minute, inspiratory-to-expiratory ratio 1:1.5, inspiratory oxygen concentration 50%, and end-tidal carbon dioxide maintained at 35–45 mmHg (1 mmHg = 0.133 kPa). Dexmedetomidine infusion was continued from induction until the end of surgery at rates of 0.2 μg/kg/hour for group D1, 0.4 μg/kg/hour for group D2, and normal saline for group C.

CPB management and surgical procedure and

CPB was performed using a Stockert SII heart-lung machine, Dideco hollow fiber oxygenator (Sorin, Italy), and pediatric extracorporeal circulation circuits. All procedures were conducted by the same team of cardiothoracic surgeons. A median sternotomy was performed, followed by intravenous heparin administration (3.0–3.5 mg/kg) and cannulation of the aorta, superior vena cava, and inferior vena cava to initiate CPB.

After aortic cross-clamping, 30 mL/kg of histidine-tryptophan-ketoglutarate solution was delivered into the aortic root, and cardiac malformations were corrected under full cardiac arrest. Moderate hypothermia (30–34°C) was maintained throughout CPB. Routine ultrafiltration with a Bellco blood ultrafilter was used to control blood dilution, keeping hematocrit between 0.25 and 0.35. After removal of the aortic cross-clamp, intravenous dopamine (3–6 μg/kg/min) and nitroglycerin (0.3 μg/kg/min) were administered and titrated according to blood pressure and central venous pressure. Heparin was neutralized with protamine in a 1:1 ratio following CPB.

Hemodynamic index

Hemodynamic parameters, including mean arterial pressure (MAP) and heart rate (HR), were monitored at eight specific time points: prior to anesthesia induction (T0), immediately before Dex or saline infusion (T1), following sternotomy (T3), 30 minutes after the start of infusion (T2), at the end of surgery (T5), at the conclusion of CPB (T4), and 30 minutes post-extubation (T7), during extubation (T6). Blood lactate (LA) concentrations were assessed at baseline, 30 minutes after CPB initiation, upon

completion of CPB, immediately postoperatively, and 24 hours after surgery. Levels of C-reactive protein (CRP) were measured preoperatively, at the end of surgery, and at 6, 24, and 48 hours following the procedure.

Detection of organ injury markers

Venous blood from the jugular bulb and arterial blood from the radial artery were drawn at five intervals: before surgery, 30 minutes after the initiation of CPB, at CPB termination, immediately post-surgery, and 24 hours after the operation. These samples were analyzed for arterial blood gases, and the arteriovenous oxygen difference (Ca–jvO_2) as well as the cerebral oxygen extraction ratio (O_2ER) were determined using the Fick equation.

$$Ca - jvO_2 = CaO_2 - CjvO_2 \quad (1)$$

$$O_2ER = (SaO_2 - SjvO_2)/SaO_2 \times 100\% \quad (2)$$

Peripheral venous blood (3–5 mL) was collected from participants at five intervals: preoperatively, immediately after surgery, and at 6, 24, and 48 hours postoperatively. Samples were centrifuged at 4,000 rpm for 10 minutes at room temperature, and the resulting serum was separated and stored at −80°C for subsequent analysis. Concentrations of cardiac injury markers (CK-MB, cTnI, H-FABP), cerebral injury markers (S100β, NSE), and the renal injury marker NGAL were measured using a double-antibody sandwich enzyme-linked immunosorbent assay in accordance with the manufacturers' instructions. Standard laboratory methods were employed to determine blood urea nitrogen (BUN) and serum creatinine (Scr) levels.

Acute kidney injury (AKI) was defined following the 2012 KDIGO guidelines: an increase in Scr by ≥26.5 μmol/L within 48 hours, a rise to more than 1.5 times the baseline, or urine output <0.5 mL/kg/h for over 6 hours.

Emergence agitation score

Emergence agitation was evaluated using a five-point scale: 0 = drowsy, 1 = awake and calm, 2 = crying and irritable, 3 = restless with inconsolable crying, and 4 = severe agitation [20]. Scores of 0–1 were classified as no agitation, 2 as mild, 3 as moderate, and 4 as severe agitation. All assessments were conducted in the ICU by a single physician who was blinded to the patient group assignments.

Postoperative pain score

Postoperative pain was assessed 10 minutes after tracheal extubation using the FLACC (Face, Legs, Activity, Cry, Consolability) scale [21]. Scores were interpreted as follows: 0 = relaxed, 1–3 = mild discomfort, 4–6 = moderate pain, and 7–10 = severe pain. Patients with a FLACC score of 4 or higher received intravenous tramadol (1 mg/kg) for analgesia.

Adverse reactions

Perioperative adverse events were monitored, including hypertension (systolic blood pressure >120 mmHg), hypotension (systolic blood pressure <60 mmHg), bradycardia (heart rate <70 beats/min), and tachycardia (heart rate >170 beats/min). In addition, the incidence of nausea and vomiting was tracked during the first three postoperative days.

Statistical analysis

Statistical analyses were conducted using SPSS version 23.0. Continuous variables were first assessed for normality using the Shapiro–Wilk test and for homogeneity of variance with Levene's test. Normally distributed data are presented as mean ± standard deviation ($\bar{x} \pm s$) and were compared between groups using one-way analysis of variance (ANOVA), while repeated measures ANOVA was applied for comparisons across multiple time points within groups. Non-normally distributed data are expressed as median with interquartile range and were analyzed between groups using the Kruskal–Wallis test. Categorical variables are reported as percentages, with between-group comparisons performed using the χ^2 test or Fisher's exact test as appropriate. A two-tailed P value < 0.05 was considered statistically significant.

Results and Discussion

Perioperative data and demographic

As presented in **Table 1**, the three groups were comparable with respect to baseline characteristics, including sex, age, height, weight, ASA classification, and type of surgery. No significant differences were observed among the groups for operative parameters such as duration of surgery, anesthesia, CPB, aortic cross-clamping, time to heart rate recovery, intraoperative blood loss, fluid infusion, or pre-bypass urine output.

Table 1. Demographic data in the study groups.

Parameter	Group C (n=30)	Group D1 (n=30)	Group D2 (n=30)	P-value	F/χ^2 value
Age (years)	2.5 ± 1.80	2.55 ± 1.61	3.15 ± 1.79	0.727	0.638
Gender (Male/Female)	16/14	19/11	17/13	0.422	0.875
Height (cm)	84.45 ± 16.79	85.50 ± 19.14	94.75 ± 17.89	0.146	1.922

Weight (kg)	12.25 ± 4.08	12.40 ± 4.99	13.46 ± 4.59	0.656	0.424
ASA physical status (II/III)	21/9	23/7	20/10	0.685	0.757
Type of congenital heart defect				0.833	1.461
• ASD	9	7	6		
• VSD	16	15	17		
• ASD + VSD	5	8	7		
Duration of surgery (min)	182.85 ± 24.00	185.65 ± 19.96	184.65 ± 21.57	0.920	0.084
Duration of anesthesia (min)	250.40 ± 31.91	256.95 ± 23.77	253.05 ± 24.65	0.744	0.297
Cardiopulmonary bypass (CPB) time (min)	75.90 ± 21.43	76.40 ± 14.55	71.55 ± 15.63	0.626	0.472
Aortic cross-clamp time (min)	37.75 ± 16.15	37.75 ± 13.86	36.50 ± 13.04	0.951	0.050
Heart automatic recovery time (min)	2.20 ± 0.83	1.65 ± 0.88	1.75 ± 1.07	0.148	1.977
Intraoperative blood loss (mL)	63.40 ± 19.73	52.80 ± 19.71	58.00 ± 13.90	0.185	1.737
Intraoperative infusion volume (mL)	113.50 ± 51.33	101.50 ± 28.89	103.00 ± 34.84	0.608	0.501
Deleukocyted red blood cells (units)	1.23 ± 0.43	1.30 ± 0.47	1.27 ± 0.45	0.848	0.067
Intraoperative fentanyl dose (μg/kg)	404.33 ± 50.36	364.00 ± 32.01	333.33 ± 45.66	<0.001	20.214
Intraoperative propofol dose (mg/kg)	206.67 ± 39.42	180.00 ± 37.32	176.00 ± 35.29	0.004	5.966
Adverse reactions					
• Hypotension, n (%)	4 (13.3%)	5 (16.7%)	8 (26.7%)	0.493	1.794
• Tachycardia, n (%)	7 (23.3%)	1 (3.3%)	0 (0%)	0.003	11.799
• Bradycardia, n (%)	2 (6.7%)	3 (10.0%)	3 (10.0%)	0.872	0.274
• Nausea and vomiting, n (%)	8 (26.7%)	2 (6.7%)	2 (6.7%)	0.047	5.958

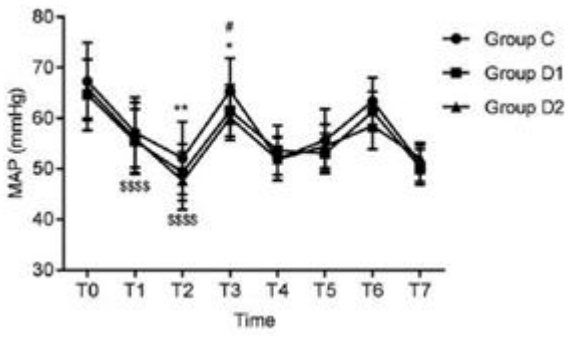
The Bispectral Index (BIS) was maintained between 45 and 60 in all three groups, and anesthetic dosages were titrated based on BIS, mean arterial pressure, and heart rate. Compared with group C, intraoperative administration of fentanyl and propofol was significantly reduced in groups D1 and D2 ($P < .05$). Moreover, fentanyl requirements were lower in group D2 than in D1, whereas propofol usage did not differ significantly between these two Dex groups **(Table 1)**.

Regarding adverse events, no cases of hypertension occurred in any group. Blood pressure and heart rate decreased slightly 30 minutes after dexmedetomidine infusion, with the effect appearing dose-dependent. There were no significant differences in the incidence of hypotension or bradycardia among the groups. In contrast, the experimental groups showed a significant reduction in tachycardia, nausea, and vomiting compared with group C ($P < .003$ and $P = .047$, respectively).

All surgeries were completed successfully, and intracardiac defects in AVSD patients were fully corrected across all groups. No serious adverse events were reported during the 1-year follow-up.

Hemodynamic data

Figures 2a and 2b show that Dex administration led to a marked decrease in mean arterial pressure (MAP) and heart rate (HR) (MAP: $P < .01$; HR: $P < .001$), which then gradually increased by T3 compared with T1. In groups D1 and D2, significant differences from baseline (T0) were observed only for MAP at T1 and T2 and for HR at T1, T2, and T3 (all $P < .001$). By T3, MAP in group D2 and HR in both D1 and D2 remained significantly lower than those in the control group (MAP: $P < .05$; HR: $P < .001$).



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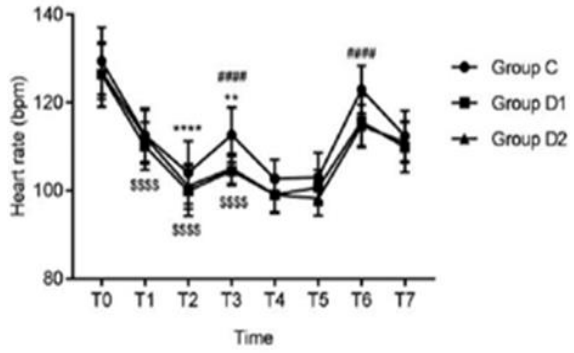

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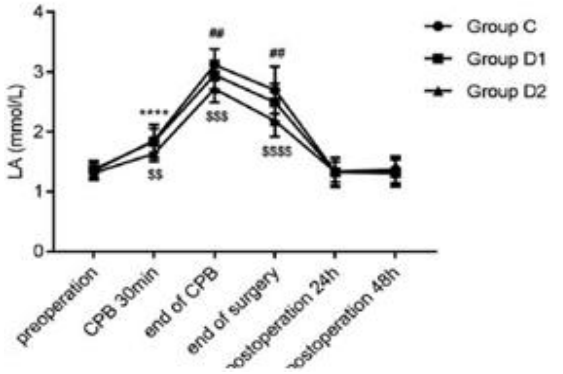

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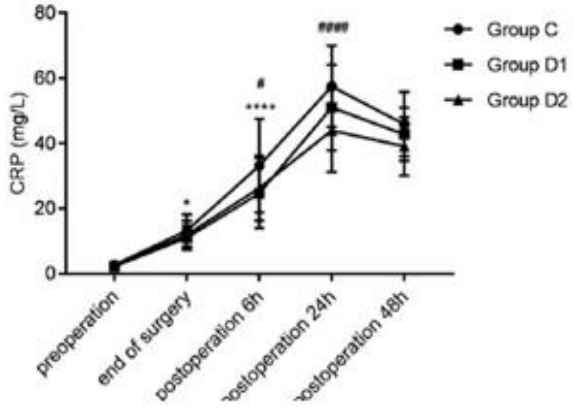


d)

Figure 2. Impact of dexmedetomidine on hemodynamic parameters and inflammatory markers. Comparison of (a) mean arterial pressure (MAP), (b) heart rate (HR), (c) serum lactate (LA), and (d) C-reactive protein (CRP) across three study groups at various time points.

Statistical significance markers: ∗P < .05, ∗∗∗∗P < .0001, ∗∗P < .01 compared with T1 $P < .0001 compared with T0 #P < .05, ####P < .0001 compared with Group C ∗∗∗∗P < .0001 compared with preoperative baseline ##P < .01, ####P < .0001 compared with Group C P < .01, $$P < .0001, $$$P < .001 compared with Group D1

Time points: T7: 30 minutes after extubation, T6: at tracheal extubation, T0: before anesthesia induction, T5: at the end of surgery, T4: at the end of cardiopulmonary bypass (CPB), T1: immediately before dexmedetomidine administration, T3: after sternotomy, T2: 30 minutes after starting the infusion of dexmedetomidine (0.2 or 0.4 μg/kg/h) or placebo (saline)

Abbreviations: MAP = mean arterial pressure LA = lactate CRP = C-reactive protein

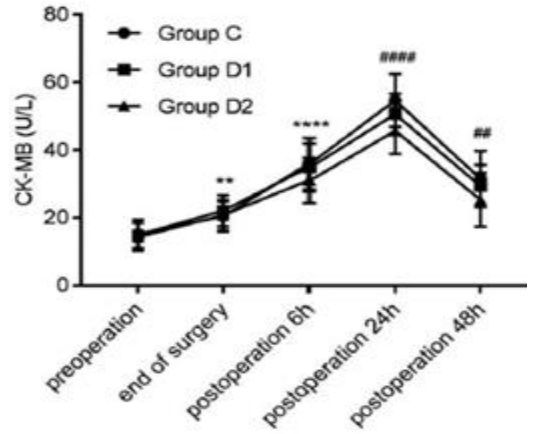
Lactic acid, reflecting tissue perfusion and oxygen delivery, increased significantly 30 minutes after CPB initiation and reached its highest level at CPB completion in all groups (P < .001), returning to baseline by 24 hours postoperatively. Compared with the control group, group D1 showed lower LA at the end of surgery, while group D2 exhibited significantly reduced LA at both the end of CPB and surgery (both P < .01). Additionally, LA levels in group D2 were consistently lower than those in group D1 at 30 minutes after CPB, CPB termination, and surgery completion **(Figure 2c)**.

CRP levels rose from the end of surgery to 24 hours postoperatively in all groups, gradually declining by 48 hours but remaining elevated relative to baseline. Notably, CRP concentrations

were significantly lower in group D1 than group C at 6 hours after surgery (P < .05) and in group D2 compared with group C at 24 hours postoperatively (P < .001) **(Figure 2d)**.

Concentration changes of H-FABP, cTnI and, CK-MB

CK-MB, cTnI, and H-FABP are widely used markers for assessing perioperative myocardial injury. In the present study, CK-MB and cTnI exhibited similar trends across all three groups. Postoperatively, CK-MB and cTnI levels rose continuously from baseline up to 24 hours after surgery, whereas H-FABP levels began to decrease at 6 hours postoperatively. No significant differences in CK-MB were observed between group D1 and either group C or D2 at any time point **(Figure 3a)**. In contrast, CK-MB in group D2 was significantly lower than in group C at 24 and 48 hours post-surgery. Similarly, cTnI levels in group D2 were reduced at 6, 24, and 48 hours postoperatively, and H-FABP levels were lower at the end of surgery and at 6 hours post-operation compared with group C. Additionally, significant differences between groups D1 and D2 were noted at 6 hours postoperatively for both cTnI (P < .001) and H-FABP (P < .01) **(Figures 3b and 3c)**.



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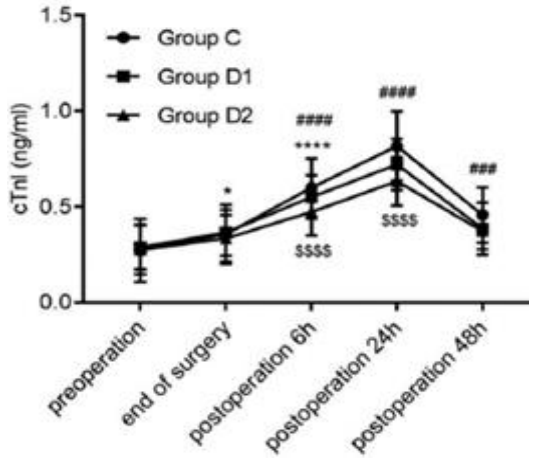

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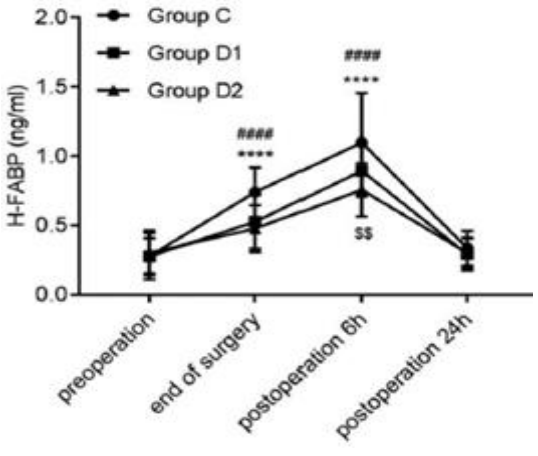
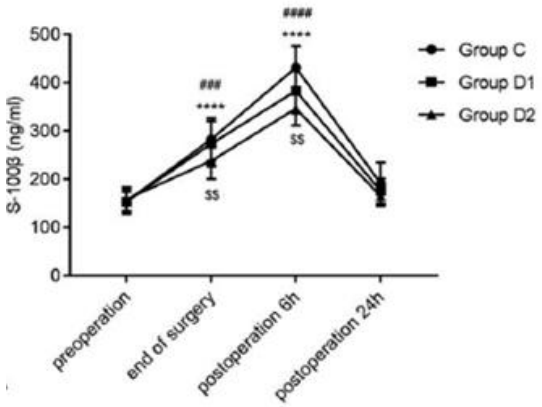


c)

Figure 3. Dexmedetomidine effects on markers of myocardial injury. Comparison of CK-MB (a), cTnI (b), and H-FABP (c) among the three groups at various perioperative time points. Statistical significance: ∗∗P < .01, ∗P < .05, ∗∗∗∗P < .0001 vs preoperative baseline; ###P < .001, ##P < .01, ####P < .0001 vs Group C; $$P < .01, $$$$P < .0001 vs Group D1. Abbreviations: CK-MB, creatine kinase-MB; cardiac troponin I, cTnI; H-FABP, heart-type fatty acid-binding protein.

Figures 4a and 4b show that, relative to baseline, all groups experienced marked elevations in S100β at surgery completion and 6 hours afterward, while NSE levels rose significantly at 6, 24, and 48 hours postoperatively (all P < .001). At the end of surgery and 6 hours postoperatively, S100β concentrations in group D2 were lower than those observed in groups C and D1. Measurements taken 30 minutes into CPB revealed significant increases in the arteriovenous oxygen difference ($Ca–jvO_2$) and cerebral oxygen extraction ratio (O_2ER) in every group (P < .001), with group D2 showing higher values than group C **(Figures 4c and 4d)**.



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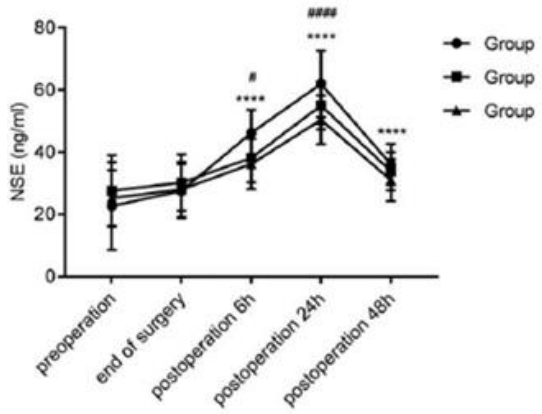

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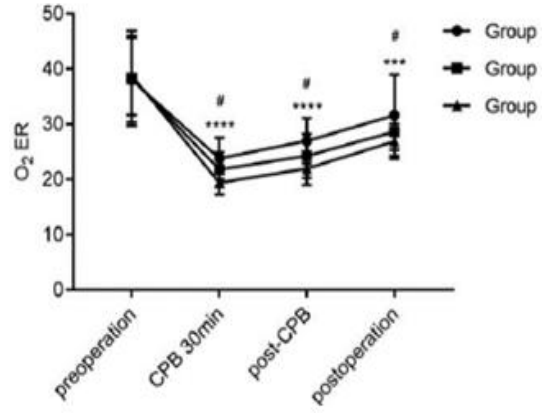

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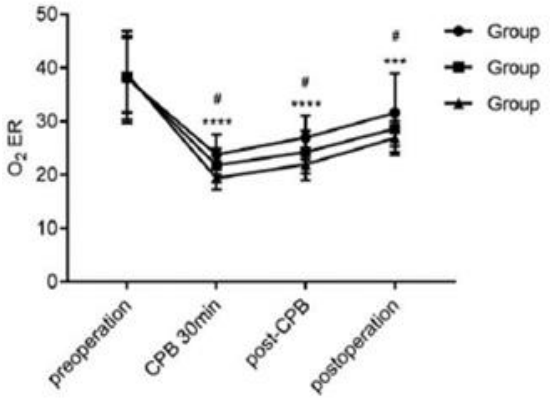

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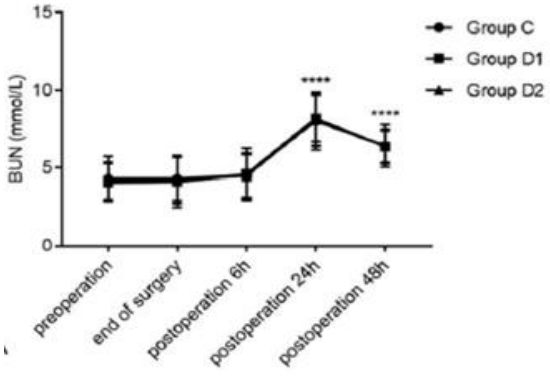
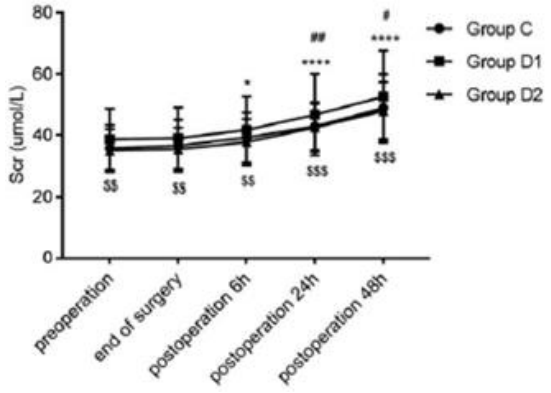
Figure 4. Dexmedetomidine effects on cerebral injury indicators. Comparison among the three groups for (a) S-100β, (b) NSE, (c) arterial–jugular venous oxygen difference (Ca–jvO_2), and (d) cerebral oxygen extraction ratio (O_2ER) at various perioperative time points. Statistical annotations: **P < .01, *P < .05, ****P < .0001, ***P < .001 compared with preoperative values; ##P < .01, #P < .05, ###P < .001, ####P < .0001 compared with Group C; $$P < .01 compared with Group D1. Abbreviations: NSE, neuron-specific enolase; Ca–jvO_2, arterial-internal jugular venous oxygen difference; O_2ER, oxygen extraction ratio.

Kidney injury parameters

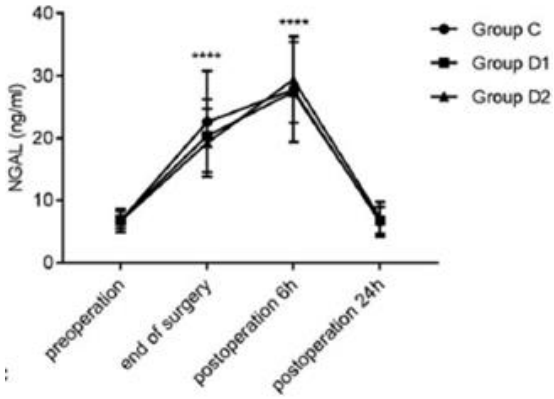
As shown in **Figure 5**, levels of NGAL, serum creatinine (Scr), and blood urea nitrogen (BUN) increased at the end of surgery and at 6 and 24 hours postoperatively compared with preoperative values. No significant differences were observed in NGAL or BUN among the three groups at any time point. However, Scr concentrations in group D2 were significantly lower than those in groups C and D1. Regarding acute kidney injury (AKI), 6 patients (20.0%) in group C and 4 patients (13.3%) in each of groups D1 and D2 developed AKI. The overall incidence of AKI did not differ significantly among the groups (F = 0.677, P = .713).



a)



b)



c)

Figure 5. Dexmedetomidine effects on renal function markers. Comparison of (a) blood urea nitrogen (BUN), (b) serum creatinine (Scr), and (c) neutrophil gelatinase-associated lipocalin (NGAL) among the three groups at various perioperative time points. Statistical significance: ****P < .0001, *P < .05vs preoperative values; ##P < .01, #P < .05vs Group C; $$P < .01, $$$P < .001 vs Group D1. Abbreviations: BUN, blood urea nitrogen; Scr, serum creatinine; NGAL, neutrophil gelatinase-associated lipocalin.

Results of emergence agitation score and postoperative pain score

As presented in **Table 2**, there were no significant differences among the three groups regarding mild agitation, severe agitation, or the overall incidence of emergence agitation. Notably, the frequency of moderate agitation was significantly lower in group D2 compared with group C (P = .002).

Postoperative pain score and emergence agitation score.

Table 2.

Postoperative Parameter	Group C (n=30)	Group D1 (n=30)	Group D2 (n=30)	F/χ^2/H value	P-value
Emergence Agitation (EA)					
Mild agitation, n (%)	6 (20.0%)	12 (40.0%)	11 (36.7%)	3.154	0.207
Moderate agitation, n (%)	12 (40.0%)	5 (16.7%)	1 (3.3%)	12.917	0.002
Severe agitation, n (%)	2 (6.7%)	0 (0%)	0 (0%)	4.091	0.129
Total EA incidence, n (%)	20 (66.7%)	17 (56.7%)	12 (40.0%)	4.390	0.111
Time to tracheal extubation (min)	167.17 ± 32.86	150.20 ± 24.70	152.30 ± 31.33	6.693	0.002
FLACC pain score at arrival in PACU [median (IQR)]	4 (3–6)	3 (2–5)	3 (2–3)	9.298	0.010
Rescue tramadol administration, n (%)	18 (60.0%)	13 (43.3%)	10 (33.3%)	4.390	0.039

Patients in groups D1 and D2 experienced faster tracheal extubation, with mean times of 150.20 ± 24.70 minutes and 152.30 ± 31.33 minutes, respectively, compared with 167.17 ± 32.86 minutes in group C (P = .002). Correspondingly, postoperative FLACC scores were lower in the Dex-treated groups than in the control group (P = .01), indicating reduced pain. Analgesic intervention with intravenous tramadol was required in 18 children from group C, whereas 13 children in D1 and 10 in D2 needed additional pain relief.

Open-heart surgery under cardiopulmonary bypass (CPB) remains the primary treatment for congenital heart disease (CHD) [2]. Because the anatomy and physiology of children differ from adults, their responses to surgical and anesthetic stress are not identical, and organ protection strategies effective in adults may not be suitable for infants. In this study, both MAP and HR increased significantly at T3 (after sternotomy) and T6 (extubation), indicating that these surgical stages exert considerable physiological stress and can lead to hemodynamic instability in children. Nonetheless, MAP and HR in groups D1 and D2 were lower than in group C, suggesting that Dex attenuated the stress responses induced by sternotomy and extubation during CHD surgery, with more pronounced effects observed at a dosage of 0.4 μg/kg/hour. A dual-center trial by Petroz *et al.* [22] similarly reported dose-dependent stabilization of hemodynamic responses in children receiving Dex, consistent with our findings.

Dex, as a safe adjunct to general anesthesia, is commonly administered with a loading dose of 0.5–1.0 μg/kg followed by continuous infusion at 0.2–2.0 μg/kg/hour [23]. Pharmacokinetic studies by Su *et al.* indicated that continuous Dex infusion at 0.75 μg/kg/hour was well tolerated in pediatric patients after open-heart surgery [24]. In this study, infusion rates of 0.2 μg/kg/hour (D1) and 0.4 μg/kg/hour (D2) were applied, with no cases of hypertension observed, confirming the safety of these doses. Some hypotensive episodes occurred during CPB establishment—4 in group C, 5 in D1, and 8 in D2—likely due to cardiac traction or compression by the surgeon. Immediate relief of compression restored blood pressure in most children within one minute, while persistent hypotension was treated with phenylephrine. Additionally, tachycardia, nausea, and vomiting were less frequent in Dex-treated groups, indicating that Dex effectively mitigated complications such as arrhythmia-induced cardiac stress.

Elevated lactic acid (LA) is associated with postoperative cognitive dysfunction [25], and C-reactive protein (CRP) levels reflect the magnitude and activity of systemic inflammation [26]. Following CPB, both LA and CRP increased over time, but Dex infusion significantly blunted these elevations. Although high-dose opioids are standard for pediatric perioperative analgesia, they can cause respiratory depression, constipation, cognitive impairment, and other adverse effects [27, 28]. Previous studies, such as that by Dang *et al.* on 142 children undergoing bronchoscopy, demonstrated that Dex reduced midazolam requirements [29]. Our results showed that Dex lowered fentanyl and propofol dosages in a dose-dependent manner.

Emergence agitation is a common postoperative complication in children, occurring in 10–50% of cases [30]. Cohen *et al*. reported that Dex reduces the incidence of agitation during anesthesia maintenance or preoperatively [31]. In our study, moderate agitation was significantly less frequent in group D2 than in group C. Moreover, tracheal extubation times were shorter in the Dex groups, and fewer children required postoperative tramadol, indicating that Dex facilitates faster recovery and reduces pain. This effect may be mediated by activation of α2 receptors in the spinal dorsal horn, which produces analgesia and reduces pain-induced agitation [32, 33].

Markers of myocardial injury, including CK-MB, cTnI, and H-FABP, provide insights into cardiac damage. CK-MB trends reflect ongoing injury [34], while cTnI is a sensitive predictor of neonatal mortality and early myocardial damage in children [35], and H-FABP is involved in fatty acid metabolism in cardiomyocytes [36]. In our study, all three markers increased postoperatively,

but the rises were significantly smaller in Dex-treated groups than in controls, indicating myocardial protection with continuous Dex infusion at 0.2 μg/kg/hour.

Brain tissue is highly vulnerable to ischemia and hypoxia, which can trigger neuronal apoptosis and necrosis, leading to neurological deficits [37]. Cerebral oxygen metabolism, assessed via Ca–jvO_2 and O_2ER calculated from jugular bulb and arterial blood gas measurements, improved with Dex, showing increased oxygen delivery and reduced extraction, suggesting neuroprotective effects. Neuronal damage allows S100β and NSE to enter the circulation through the blood-brain barrier [38], and their serum levels correlate with the extent of brain injury [39, 40], making them reliable indicators. In this study, S100β and NSE increased postoperatively but remained significantly lower in the high-dose Dex group, indicating that continuous Dex at 0.4 μg/kg/hour promotes cerebral oxygen balance, reduces neuronal hyperactivity, and mitigates neurotoxicity [41].

Renal markers, including BUN, Scr, and NGAL, were elevated at different postoperative time points. However, no significant differences were observed in BUN, NGAL, or AKI incidence among the groups. This may be attributed to universal renal protection measures, such as strict fluid management and ultrafiltration during CPB, short CPB duration in children over 1 year, and the relatively moderate Dex dose of 0.4 μg/kg/hour, which is lower than doses used in many other studies.

This study has several limitations. First, postoperative agitation was monitored, but long-term organ function was not assessed. Second, Dex has not been widely studied in pediatric CHD surgery, so we focused only on children aged 1–6 years with AVSD, leaving its effects on neonates under 1 year unexplored, which warrants further investigation.

Conclusion

In children with CHD undergoing CPB, dexmedetomidine reduces the requirements for other anesthetic agents, attenuates inflammatory and stress responses, and helps maintain hemodynamic stability throughout the perioperative period. It also lowers levels of myocardial and brain injury markers, decreases the incidence of tachycardia, nausea, vomiting, and moderate agitation, and shortens tracheal extubation time. Furthermore, an infusion of 0.4 μg/kg/hour provides additional reductions in fentanyl and dopamine use compared with 0.2 μg/kg/hour. Overall, dexmedetomidine at 0.4 μg/kg/hour appears to be a safe and effective adjunct for anesthesia in pediatric open-heart surgery for CHD.

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Conflict of interest: None

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Ethics statement: None

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