# Assessment the Effect of Dexmedetomidine on Incidence of Paradoxical Hypertension After Surgical Repair of Aortic Coarctation in Pediatric Patients

### Abstract

Objective: The aim of the study was to assess the effect of dexmedetomidine on the incidence of paradoxical hypertension in patients undergoing aortic coarctation repair. Design: Randomized observational study. Setting: University hospital and cardiac center. Patients: The study included 108 pediatric patients with isolated aortic coarctation. Methods: The patients were classified into two groups (each = 54): Group D: the patients received dexmedetomidine as a loading dose of 0.5 µg/kg over 10 min followed by infusion 0.3 µg/kg/h during surgery and continued for the first 48 postoperative hours. Group C: The patients received an equal amount of normal saline. The medication was prepared by the nursing staff and given to anesthetist blindly. The collected data included the heart rate, systolic and diastolic arterial blood pressure, incidence, onset, severity and treatment of paradoxical hypertension, fentanyl dose and end-tidal sevoflurane concentration, amount of blood loss and urine output. Main Results: The heart rate, systolic and diastolic blood pressure decreased significantly with dexmedetomidine than Group C (P < 0.05). The incidence and severity of the paradoxical hypertension was lower with dexmedetomidine than Group C (P = 0.011, P = 0.017, respectively). The onset the paradoxical hypertension was earlier in Group C than dexmedetomidine (P = 0.026). The dose of fentanyl and sevoflurane concentration decreased significantly with dexmedetomidine (P = 0.034, P = 0.026, respectively). The blood loss decreased with dexmedetomidine (P = 0.020) and the urine output increased with dexmedetomidine (P = 0.024). The incidence of hypotension and bradycardia was more with dexmedetomidine (P < 0.05). Conclusion: Dexmedetomidine is safe in pediatric patients undergoing aortic coarctation repair. It minimized the incidence and severity of paradoxical hypertension. It decreased the required antihypertensive medications.

Keywords: Aortic coarctation, dexmedetomidine, paradoxical hypertension

# Introduction

Surgical repair of aortic coarctation is frequently associated with paradoxical hypertension. The incidence of hypertension is 56%–100% of cases.<sup>[1,2]</sup> The pathogenesis of paradoxical hypertension is not known well and may be related to the anatomical changes in the aorta,<sup>[3]</sup> and the increased activity of the sympathetic nervous system.<sup>[4]</sup> Surgical repair of coarctation is associated with a marked increase in plasma renin activity,<sup>[5,6]</sup> and elevated plasma norepinephrine concentration during the early phase of systolic hypertension and maintained elevated through the first 24–48 postoperative hours.<sup>[4,7,8]</sup>

Dexmedetomidine is a highly selective alpha-2 agonist; it decreases the central sympathetic output and the release of epinephrine and norepinephrine<sup>[9-12]</sup> and also it decreases the release of renin and therefore it decreases the arterial blood pressure.<sup>[13,14]</sup>

The aim of the study was to assess the effect of dexmedetomidine on the incidence of paradoxical hypertension in pediatric patients undergoing aortic coarctation repair.

### Methods

After approval from the local Ethics Committee and obtaining written informed parental consent a randomized study included 108 children scheduled for elective repair of aortic coarctation. The inclusion criteria included patients with isolated aortic coarctation (diagnosed by echocardiography) without other congenital cardiac defects. Exclusion criteria were known allergy to

**How to cite this article:** Soliman R, Saad D. Assessment the effect of dexmedetomidine on incidence of paradoxical hypertension after surgical repair of aortic coarctation in pediatric patients. Ann Card Anaesth 2018;21:26-33.

## Rabie Soliman, Dalia Saad

Department of Anesthesia, Cairo University, Cairo, Egypt

Address for correspondence: Dr. Rabie Soliman, Department of Anesthesia, Cairo University, Egypt. E-mail: rabiesoliman@hotmail. com



This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

the study medication, liver, renal, respiratory diseases, mental retardation, or psychological diseases. The patients received phenergan orally 0.5 mg/kg 2 h before surgery in the wards. The patients were transferred to the operative room and after attaching the monitors to patients, intravenous anesthetic induction by thiopental (3-5 mg/kg) or inhalational induction by sevoflurane, fentanyl (2 µg/kg), and rocuronium (0.6 mg/kg) and after tracheal intubation, the patients were ventilated mechanically. Two arterial lines were inserted (one in the right radial artery and another in the femoral artery), and then the central line was inserted in the right internal jugular vein. The anesthesia was maintained with an oxygen/air mixture (50:50), sevoflurane (1%-3%), fentanyl 1-3 µg/kg/min, and cisatracurium 1-2 µg/kg/min. The patients were randomly allocated (using simple randomization through a process of coin-tossing) into two equal groups (n = 54 each), and the study medications were prepared in 50 ml syringe by nursing staff and given to the anesthetist:

- Group D (dexmedetomidine group): The patients received a loading dose of dexmedetomidine 0.5  $\mu$ g/kg (started after insertion of the central line) over 10 min, followed by intravenous infusion 0.3  $\mu$ g/kg/h by a computer-controlled infusion pump during the surgery and continued for the first 48 postoperative hours.
- Group C (control group): The patients received an equal amount of normal saline.

The surgery was done in the right lateral position. All patients received mannitol (20%) 0.25 g/kg before aortic cross-clamping. The repair was done by the resection of coarctation segment and end-to-end anastomosis of the proximal-to-distal aorta.

During aortic cross-clamping, the elevated blood pressure was controlled by the study medications, increased concentration of sevoflurane (1%-5%), and the addition of bolus doses of fentanyl (1–2  $\mu$ g/kg). If the paradoxical hypertension after aortic declamping was not controlled well by sevoflurane (1%-5%), and bolus doses of fentanyl, nitroglycerine (0.5-10 µg/kg/min), sodium nitroprusside infusion (0.5-10 µg/kg/min), or esmolol infusion (0.50-200 µg/kg/min) was added and at the end of surgery, the patients were transferred to the pediatric cardiac surgical intensive care unit (ICU). The hypotension was treated with fluid administration and a bolus dose of ephedrine. Bradycardia was treated with a bolus dose of atropine (0.02 mg/kg). The patients were extubated according to the hemodynamic stability and parameters of extubation.

In ICU, oral antihypertensive medications (through a nasogastric tube), metoprolol 2 mg and enalapril 0.5 mg twice daily were started after confirmation of bowel sounds. After the first 48 postoperative hours, the study medications were stopped, while other medications such

as nitroglycerine, nitroprusside, and esmolol were weaned gradually.

### **Monitoring of patients**

The monitors included the heart rate, arterial blood pressure (right radial artery and femoral artery), incidence, onset, severity and treatment of paradoxical hypertension, central venous pressure, arterial oxygen saturation, end-tidal carbon dioxide, and body temperature. The data were recorded before anesthesia induction and every 5 min during surgery. Arterial blood gases were checked every 30 min. End-tidal concentrations of sevoflurane were recorded every 5 min during the procedure (Dräger, Fabius GS, Premium Germany). In the pediatric cardiac surgical ICU, the same parameters were monitored every 5 min.

### Outcomes

The primary outcome was the incidence of paradoxical hypertension and the requirement for antihypertensive medications. The secondary outcome was the safety of the study medications. The safety was assessed by the occurrence of any adverse events to the patients.

### Sample size calculation

Power analysis was performed using the Chi-square test for independent samples on the incidence of paradoxical hypertension in patients undergoing repair of aortic coarctation because it was the main outcome variable in the present study. A pilot study was conducted before starting this study because there are no available data in the literature for the incidence of paradoxical hypertension in patients undergoing repair of aortic coarctation with dexmedetomidine administration. The results of the pilot study showed the incidence of paradoxical hypertension was 20% in dexmedetomidine group and 45% in control group. Taking power 0.8 and alpha error 0.05, beta 0.2, a minimum sample size of 54 patients was calculated for each group.

Data were statistically described in terms of mean  $\pm$  standard deviation or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using paired *t*-test. Within the group, comparison of numerical variables was done using repeated measures analysis of variance test using general linear model regression analysis. For comparing categorical data, Chi-square test was performed. The exact test was used instead when the expected frequency is <5. *P* < 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

# Results

Figure 1 shows the CONSORT diagram for the flow of participants through each stage of the present study. All

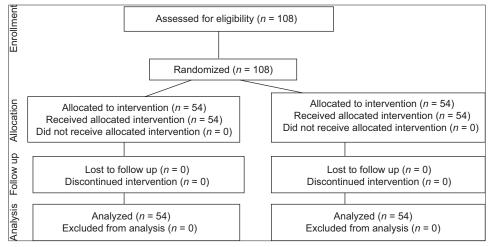


Figure 1: CONSORT diagram for the flow of participants through each stage of the present study

patients completed the study and all patients were analyzed for the study.

Table 1 shows no significant differences regarding the demographic data, preoperative medications, and the type of aortic coarctation (P > 0.05). There was no difference regarding the baseline systolic and diastolic blood pressure measured in the upper and lower limbs before anesthesia (P > 0.05).

There was no significant difference in the systolic and diastolic arterial blood pressure before the surgery and decreased after anesthesia in the patients of both groups, but the difference between the two groups was insignificant (P > 0.05). After aortic cross-clamping, the blood pressure increased in patients of both groups, but the increase in Group C was higher than Group D (P < 0.05), and controlled well by the study medication, increased concentration of sevoflurane, bolus doses of fentanyl, and addition of nitroglycerine and/or nitroprusside and the difference between the two groups was significant (P < 0.05). The blood pressure decreased nearly to the level before aortic cross-clamping, but the comparison between the groups was significant (P = 0.039) [Tables 2 and 3]. After aortic declamping, 9 patients in Group D and 20 patients in Group C suffered from paradoxical hypertension (P = 0.011), and managed by sevoflurane (1%– 5%), and bolus doses of fentanyl in addition to the infusion of nitroglycerine (0.5-10 µg/kg/min), sodium nitroprusside infusion (0.5-10 µg/kg/min), or esmolol infusion (0.50-200 µg/kg/min). The onset of paradoxical hypertension was earlier in Group C than Group D (P = 0.026). The degree of elevation (severity) in the paradoxical hypertension was higher in patients of Group C than patients of Group D (P = 0.017). The number of patients required for nitroglycerine was 4 patients in Group D and 20 patients in Group C (P = 0.001). The requirement for nitroprusside was 2 patients in Group D and 8 patients in Group C (P = 0.046). The esmolol was required for 6 patients in Group C and no patient in Group D required

Variables	Group D	of patients Group C	Р
variables	( <i>n</i> =54)	( <i>n</i> =54)	1
Age (year)	1.837±1.17	2.05±1.24	0.362
Weight (kg)	12.15±4.83	11.931±4.87	0.808
Sex			
Male	29	25	0.441
Female	31	23	0.123
Prostaglandin E1	2	3	0.647
Captopril	37	31	0.231
Metoprolol	7	10	0.428
Captopril and metoprolol	10	13	0.480
Aortic coarctation			
Fresh	48	50	0.506
Redo	6	4	0.506
Blood pressure (mmHg)			
Upper limb			
Systolic	124.44±6.87	125.29±6.95	0.523
Diastolic	93.81±8.23	94.55±7.64	0.628
Lower limb			
Systolic	63.74±5.08	64.50±4.34	0.406
Diastolic	40.50±2.35	41.09±3.71	0.324

Data are presented as mean±SD, *n*. Group D: Dexmedetomidine group, Group C: Control group, SD: Standard deviation

for esmolol (P = 0.011) [Figure 2a, 2b and Table 4]. The incidence of hypotension (hypotension as a side effect to dexmedetomidine or anesthetic medications and not to antihypertensive medications) was higher in Group D than Group C (P = 0.038) and treated by fluid administration and a bolus of ephedrine (2–5 mg).

Table 5 shows the changes in the heart rate of the patients of both groups. There was no significant difference before surgery (P > 0.05), but the heart rate decreased after anesthesia in the patients of both groups, and the decrease was more in the patients of Group D than Group C (P < 0.05) [Figure 2c]. The incidence of bradycardia was higher in Group D

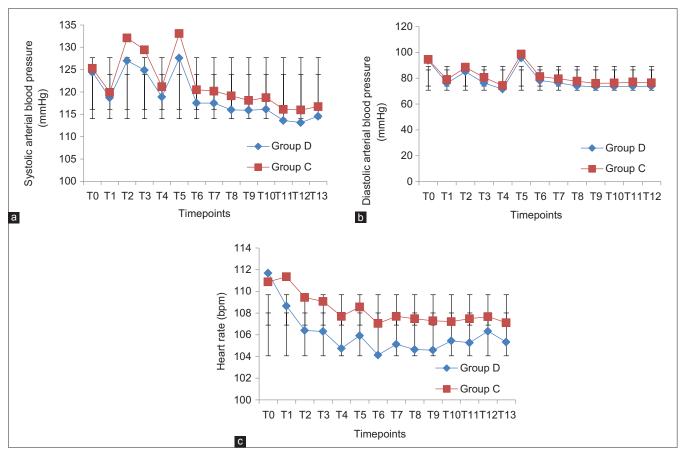


Figure 2: a: Systolic arterial blood pressure of patients; b: Diastolic arterial blood pressure of patients; c: Heart rate of patients. Group D: Dexmedetomidine group; Group C: Control group; T0: Reading at base line before anesthesia; T1: Reading before aortic cross-clamping; T2: Reading 15 min after aortic cross-clamping; T3: Reading 30 min after aortic cross-clamping; T4: Reading before aortic declamping; T5: Reading 15 min after aortic declamping; T6: Reading 30 min after aortic declamping; T7: Reading one hour after aortic declamping; T8: Reading one hour after ICU admission; T9: Reading 6 hours after ICU admission; T10: Reading 12 hours after ICU admission; T11: Reading 24 hours after ICU admission; T12: Reading 48 hours after ICU admission; T13: Reading 72 hours after ICU admission

than Group C (P = 0.046) and treated by bolus of atropine (0.02 mg/kg) [Table 4].

Table 6 shows no difference in the central venous pressure between the two groups through the study (P > 0.05).

Table 4 shows the intra- and post-operative data of the patients. The end-tidal sevoflurane was lower in Group D than Group C (P = 0.026). The total dose of fentanyl was lower in Group D than Group C during surgery (P = 0.034) and during postoperative pediatric cardiac ICU (P = 0.032). There was no significant difference between the two groups in the arterial oxygen saturation (P = 0.665), end-tidal carbon dioxide (P = 0.490), temperature (P = 0.270), duration of anesthesia (P = 0.754), duration of surgery (P = 0.570), mannitol dosage (P = 0.667), and aortic cross-clamping duration (P = 0.162). The amount of blood loss decreased with dexmedetomidine compared to the control group (P = 0.020). The amount of urine output during surgery increased significantly in patients of Group D than Group C (P = 0.024). The extubation was earlier in patients of Group D than Group C (P = 0.043). There was no significant difference between the two groups

regarding the ICU length of stay (P = 0.830) and hospital length of stay (P = 0.928). There were no neurological complications in patients of both groups.

### Discussion

Despite the growing interest in the perioperative uses of dexmedetomidine for pediatric patients with congenital heart disease, its effect on paradoxical hypertension in pediatric patients undergoing aortic coarctation repair is limited. The present study showed that the dexmedetomidine decreased the incidence and severity of the paradoxical hypertension in pediatric patients undergoing aortic coarctation repair. Furthermore, it delayed the onset of occurrence of paradoxical hypertension and decreased the required medications for the treatment of paradoxical hypertension. Dexmedetomidine decreased the required doses of fentanyl and sevoflurane compared to the control group.

Sahu *et al.*<sup>[15]</sup> documented that dexmedetomidine is a safe drug and used as an adjunct for nitroglycerin and nitroprusside in the management of severe paradoxical hypertension. The paradoxical hypertension was severe and not controlled

Table 2: Systolic arterial blood pressure of patients			
Time points	Group D ( <i>n</i> =54)	Group C ( <i>n</i> =54)	Р
Т0	124.44±6.87	125.29±6.95	0.523
T1	118.72±3.52 <sup>†</sup>	119.92±5.40 <sup>†</sup>	0.173
T2	$127.00{\pm}10.80$	132.09±10.28	0.013*
Т3	124.90±8.78	129.45±10.08	0.014*
T4	$118.90 \pm 5.62^{\dagger}$	121.18±5.71	0.039*
T5	127.611±10.32	133.09±11.68	0.011*
Т6	117.53±6.20 <sup>†</sup>	120.51±6.59 <sup>†</sup>	0.017*
Τ7	117.51±5.83 <sup>†</sup>	120.20±6.33 <sup>†</sup>	0.024*
Т8	116.01±7.02 <sup>†</sup>	119.14±7.25 <sup>†</sup>	0.024*
Т9	115.92±5.00 <sup>†</sup>	118.11±6.18 <sup>†</sup>	0.046*
T10	116.13±5.74 <sup>†</sup>	118.75±5.09 <sup>†</sup>	0.013*
T11	113.61±5.20 <sup>†</sup>	116.11±6.16 <sup>†</sup>	0.025*
T12	113.15±4.96 <sup>†</sup>	115.98±6.25 <sup>†</sup>	0.011*
T13	114.57±5.52 <sup>†</sup>	116.74±5.35 <sup>†</sup>	0.040*

Data are presented as mean±SD. \*P<0.05 significant comparison between the two groups,  $^{\dagger}P<0.05$  significant compared to the preoperative reading within the same group. T0: Reading at base line before anesthesia, T1: Reading before aortic cross-clamping, T2: Reading 15 min after aortic cross-clamping, T3: Reading 30 min after aortic cross-clamping, T4: Reading before aortic declamping, T5: Reading 15 min after aortic declamping, T6: Reading 30 min after aortic declamping, T7: Reading 1 h after aortic declamping, T8: Reading 1 h after ICU admission, T9: Reading 6 h after ICU admission, T10: Reading 12 h after ICU admission, T11: Reading 24 h after ICU admission, T12: Reading 48 h after ICU admission, T13: Reading 72 h after ICU admission. Group D: Dexmedetomidine group, Group C: Control group, SD: Standard deviation, ICU: Intensive Care Unit

well by nitroglycerin and nitroprusside in the immediate postoperative period in two cases of aortic coarctation repair. After adding dexmedetomidine (0.5  $\mu$ g/kg/h), the blood pressure was controlled. Furthermore, it helps a smooth transition from intravenous medications to oral drugs to control the blood pressure at a constant level without wide fluctuations in the hemodynamics. Bhana *et al.*<sup>[16]</sup> reported that dexmedetomidine is effective and safe to control the hypertension.

Klamt *et al.*<sup>[17]</sup> evaluated the effects of dexmedetomidine  $(1 \ \mu g/kg/h)$  with fentanyl infusion on blood pressure and heart rate during cardiac surgery in children (aged 1 month–10 years) undergoing surgery to repair congenital heart disease with cardiopulmonary bypass and they found that the systolic blood pressure decreased significantly after 1 h of dexmedetomidine infusion.

Another study evaluated the effect of dexmedetomidine (a loading dose of 1  $\mu$ g/kg) over 15 min before induction followed by infusion of 0.3  $\mu$ g/kg/h during the procedure in high-risk adult patients who underwent aortic vascular surgery with aortic cross-clamping and showed that the dexmedetomidine minimized the fluctuations in arterial blood pressure before, during, and after aortic cross-clamping, and it provides myocardial protection in high-risk patients.<sup>[18]</sup>

Table 3: Diastolic arterial blood pressure of patients			
Time points	Group D ( <i>n</i> =54)	Group C ( <i>n</i> =54)	Р
Т0	93.81±8.23	94.55±7.64	0.628
T1	76.24±5.47 <sup>†</sup>	79.01±7.87	0.035*
T2	85.09±7.41 <sup>†</sup>	88.51±6.66 <sup>†</sup>	0.013*
Т3	76.27±7.59 <sup>†</sup>	$80.63 \pm 9.83^{\dagger}$	0.011*
T4	71.61±5.07 <sup>†</sup>	74.35±6.18 <sup>†</sup>	0.013*
T5	95.72±5.30	98.704±7.28	0.017*
Т6	78.20±7.67 <sup>†</sup>	81.31±6.10 <sup>†</sup>	0.021*
Τ7	76.37±7.01 <sup>†</sup>	79.57±6.52 <sup>†</sup>	0.015*
Т8	74.01±6.48 <sup>†</sup>	77.74±8.63 <sup>†</sup>	0.013*
Т9	73.50±5.76	76.09±7.37 <sup>†</sup>	0.044*
T10	73.53±6.16 <sup>†</sup>	76.33±6.97 <sup>†</sup>	0.029*
T11	73.79±6.60 <sup>†</sup>	77.07±6.79 <sup>†</sup>	0.012*
T12	73.80±5.65 <sup>†</sup>	76.45±7.11 <sup>†</sup>	0.034*
T13	73.38±5.49 <sup>†</sup>	76.03±5.96 <sup>†</sup>	0.018*
	1 00 10	0.05 1 10	

Data are presented as mean±SD. \*P<0.05 significant comparison between the two groups,  $^{+}P<0.05$  significant compared to the preoperative reading within the same group. T0: Reading at base line before anesthesia, T1: Reading before aortic cross-clamping, T2: Reading 15 min after aortic cross-clamping, T3: Reading 30 min after aortic cross-clamping, T4: Reading before aortic declamping, T5: Reading 15 min after aortic declamping, T6: Reading 30 min after aortic declamping, T7: Reading 1 h after aortic declamping, T8: Reading 1 h after ICU admission, T9: Reading 6 h after ICU admission, T10: Reading 12 h after ICU admission, T11: Reading 24 h after ICU admission, T12: Reading 48 h after ICU admission, T13: Reading 72 h after ICU admission. Group D: Dexmedetomidine group, Group C: Control group, SD: Standard deviation, ICU: Intensive Care Unit

The systolic and diastolic arterial blood pressure decreased with dexmedetomidine compared to the control group and this may be related to many factors: (1) the decrease in heart rate with dexmedetomidine;<sup>[19-23]</sup> (2) the decrease of catecholamines release;<sup>[9-12]</sup> (3) the inhibitory effect on the renin-angiotensin system;<sup>[13,14]</sup> (4) the diuretic effect and increased amount of urine output;<sup>[12,14]</sup> (5) it provides sedation and analgesia, and preserving the psychomotor function while the patients are calm and resting comfortably.<sup>[24]</sup>

Tokuhira *et al.*<sup>[25]</sup> studied the effect of dexmedetomidine (0.3–0.4  $\mu$ g/kg/h without a loading dose), for postoperative sedation in 9 pediatric patients who had undergone Fontan procedure for congenital heart disease and reported a stable mean arterial blood pressure and central venous pressure.

Nishibe *et al.*<sup>[26]</sup> showed that the perioperative dexmedetomidine infusion (0.4–0.8  $\mu$ g/kg/h) decreased the pulmonary artery pressure and transpulmonary pressure gradient after a bidirectional superior cavopulmonary shunt in 29 pediatric patients < 12 months of age and the same finding was reported by Lazol *et al.*<sup>[27]</sup>

Contrary to the present study, Friesen *et al.*<sup>[28]</sup> studied the effects of dexmedetomidine loading (1  $\mu$ g/kg, 0.75  $\mu$ g/kg, or 0.5  $\mu$ g/kg) on the hemodynamics of children undergoing

Variables	traoperative da Group D ( <i>n</i> =54)		Р
Paradoxical	Group $D(n=34)$	Group C $(n-34)$	1
hypertension			
Incidence	9	20	0.011*
Onset	16.87±6.35	14.15±6.24	0.026*
Severity	4	14.13±0.24	0.020
Nitroglycerine	4	20	0.001
Nitroprusside	2	8	0.046*
Esmolol	-	6	0.040
Hypotension	10	3	0.038*
Bradycardia	8	2	0.038
Blood loss (ml)	368.18±55.37	396.50±68.82	0.040*
End-tidal	1.60±0.49	$1.83\pm0.57$	0.020*
sevoflurane (%)	1.00±0.49	1.85±0.57	0.020
Fentanyl dose	9.64±4.20	$11.64 \pm 5.43$	0.034*
(µg/kg) during	7.04-4.20	11.04-0.40	0.054
surgery			
Total fentanyl dose	15.45±5.20	$18.16 \pm 7.54$	0.032*
(µg/kg) in PSICU			
(48 h)			
End-tidal carbon	36.32±1.48	36.18±1.85	0.665
dioxide (mmHg)			
Arterial oxygen	99.07±0.73	98.96±0.91	0.490
saturation (%)			
Temperature (°C)	37.02±0.31	37.08±0.25	0.270
Duration of	140.556±24.27	142.13±27.73	0.754
anesthesia (min)			
Duration of surgery	$116.48 \pm 21.92$	$119.25 \pm 28.30$	0.570
(min)			
Mannitol (g)	3.92±1.20	3.82±1.18	0.667
Aortic	37.59±7.69	35.611±6.93	0.162
cross-clamping(min)			
Urine output during	$150.92 \pm 28.03$	139.25±24.86	0.024*
surgery (ml)			
Extubation time (h)	$18.38 \pm 6.82$	20.98±6.32	0.043*
ICU length of	4.12±0.96	4.16±1.01	0.830
stay (days)			
Hospital length of	$12.98 \pm 3.27$	$13.03 \pm 3.15$	0.928
stay (days)			
Neurologic	-	-	
complications			

Data are presented as mean $\pm$ SD, *n* (%).\**P*<0.05 significant comparison between the two groups. Group D: Dexmedetomidine group, Group C: Control group, SD: Standard deviation, ICU: Intensive Care Unit, PSICU: Pediatric cardiac surgical ICU

cardiac catheterization and they documented that the mean arterial blood pressure and indexed systemic vascular resistance increased significantly.

The heart rate decreased with dexmedetomidine compared to the control group, and this may be mediated by enhancement of vagal neural activity,<sup>[19,20]</sup> depression of the sinus node, and atrioventricular node,<sup>[21,22]</sup> in addition to the decrease in catecholamines release in the blood.<sup>[29]</sup> The decrease in heart rate resulted in a decrease in cardiac output, therefore decrease in blood pressure.<sup>[30-33]</sup>

The amount of blood loss decreased in the dexmedetomidine group compared to the control group, and this may be a result of decreased blood pressure with dexmedetomidine more than the control group.<sup>[34-36]</sup>

Dexmedetomidine increased the urine output, and this may be related to the inhibitory effect of dexmedetomidine on the renin angiotensin system, antidiuretic hormones,<sup>[14]</sup> and the increase of atrial natriuretic peptide release resulting in natriuresis.<sup>[37]</sup>

The extubation time was shorter with dexmedetomidine compared to the control group, and this may be related to the decreased dose of fentanyl.<sup>[38,39]</sup>

The present study showed that the dexmedetomidine was associated with hypotension and bradycardia more the control group and these findings were documented by previous studies.<sup>[16,40-42]</sup>

Our study recognizes some limitations such as a small number of patients and limited articles which studied the effect of dexmedetomidine on the paradoxical hypertension to compare the results of the present study.

### Conclusion

Dexmedetomidine is safe in pediatric patients undergoing aortic coarctation repair. It minimized the incidence and severity of paradoxical hypertension and delayed its onset. It decreased the requirement for the antihypertensive, inhalational agents, and opioids. Hypotension and bradycardia are the most common side effect of dexmedetomidine.

#### Acknowledgment

The authors appreciate the help and support of the staff-nurses in the operative rooms and pediatric cardiac ICU to achieve this work.

### Financial support and sponsorship

Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

#### References

- Canniffe C, Ou P, Walsh K, Bonnet D, Celermajer D. Hypertension after repair of aortic coarctation – A systematic review. Int J Cardiol 2013;167:2456-61.
- Dittrich S, Germanakis J, Dittrich H, Daehnert I, Ewert P, Alexi-Meskishvili V, *et al.* Comparison of sodium nitroprusside versus esmolol for the treatment of hypertension following repair of coarctation of the aorta. Interact Cardiovasc Thorac Surg 2003;2:111-5.
- Sealy WC. Paradoxical hypertension after repair of coarctation of the aorta: A review of its causes. Ann Thorac Surg 1990;50:323-9.
- Goodall MC, Sealy WC. Increased sympathetic nerve activity following resection of coarctation of the thoracic aorta. Circulation 1969;39:345-51.
- 5. Werning C, Schönbeck M, Weidmann P, Baumann K, Gysling E, Wirz P, et al. Plasma renin activity in patients with coarctation of

Table 5: Heart rate of patients				
Time points	Group D ( <i>n</i> =54)	Group C ( <i>n</i> =54)	Р	
Т0	111.68±6.91	110.88±6.30	0.533	
T1	108.66±4.53 <sup>†</sup>	111.35±6.25	0.012*	
T2	$106.40 \pm 6.82^{\dagger}$	109.44±7.52	0.030*	
Т3	106.31±6.18 <sup>†</sup>	109.07±7.05 <sup>†</sup>	0.033*	
T4	104.75±6.44 <sup>†</sup>	$107.70 \pm 7.78^{\dagger}$	0.034*	
Т5	105.92±5.03 <sup>†</sup>	108.57±6.88 <sup>†</sup>	0.024*	
Т6	104.14±5.28 <sup>†</sup>	107.05±8.05 <sup>†</sup>	0.029*	
Τ7	105.13±4.31 <sup>†</sup>	107.70±7.67 <sup>†</sup>	0.034*	
Т8	104.64±5.42 <sup>†</sup>	107.48±7.55 <sup>†</sup>	0.027*	
Т9	104.59±6.10 <sup>†</sup>	107.29±7.46 <sup>†</sup>	0.042*	
T10	105.44±7.00 <sup>†</sup>	107.22±8.38 <sup>†</sup>	0.215	
T11	105.27±7.19 <sup>†</sup>	107.48±8.91 <sup>†</sup>	0.160	
T12	106.33±5.72 <sup>†</sup>	107.68±7.13 <sup>†</sup>	0.280	
T13	105.33±7.12 <sup>†</sup>	107.11±9.35 <sup>†</sup>	0.269	

Data are presented as mean±SD. \**P*<0.05 significant comparison between the two groups, <sup>†</sup>*P*<0.05 significant compared to the preoperative reading within the same group. T0: Reading at base line before anesthesia, T1: Reading before aortic cross-clamping, T2: Reading 15 min after aortic cross-clamping, T3: Reading 30 min after aortic cross-clamping, T4: Reading before aortic declamping, T5: Reading 15 min after aortic declamping, T6: Reading 30 min after aortic declamping, T7: Reading 1 h after aortic declamping, T8: Reading 1 h after ICU admission, T9: Reading 6 h after ICU admission, T10: Reading 12 h after ICU admission, T11: Reading 24 h after ICU admission, T12: Reading 48 h after ICU admission, T13: Reading 72 h after ICU admission. Group D: Dexmedetomidine group, Group C: Control group, SD: Standard deviation, ICU: Intensive Care Unit

the aorta. A comment of the pathogenesis prestenotic hypertension. Circulation 1969;40:731-7.

- Markiewicz A, Wojczuk D, Kokot F, Cicha A. Plasms renin acitivity in coarctation of aorta before and after surgery. Br Heart J 1975;37:721-5.
- Benedict CR, Grahame-Smith DG, Fisher A. Changes in plasma catecholamines and dopamine beta-hydroxylase after corrective surgery for coarctation of the aorta. Circulation 1978;57:598-602.
- Bojar RM, Weiner B, Cleveland RJ. Intravenous labetalol for the control of hypertension following repair of coarctation of the aorta. Clin Cardiol 1988;11:639-41.
- Mukhtar AM, Obayah EM, Hassona AM. The use of dexmedetomidine in pediatric cardiac surgery. Anesth Analg 2006;103:52-6.
- Snapir A, Posti J, Kentala E, Koskenvuo J, Sundell J, Tuunanen H, *et al.* Effects of low and high plasma concentrations of dexmedetomidine on myocardial perfusion and cardiac function in healthy male subjects. Anesthesiology 2006;105:902-10.
- Ammar AS, Mahmoud KM, Kasemy ZA, Helwa MA. Cardiac and renal protective effects of dexmedetomidine in cardiac surgeries: A randomized controlled trial. Saudi J Anaesth 2016;10:395-401.
- Xu H, Aibiki M, Seki K, Ogura S, Ogli K. Effects of dexmedetomidine, an alpha2-adrenoceptor agonist, on renal sympathetic nerve activity, blood pressure, heart rate and central venous pressure in urethane-anesthetized rabbits. J Auton Nerv Syst 1998;71:48-54.
- Gellai M, Ruffolo RR Jr. Renal effects of selective alpha-1 and alpha-2 adrenoceptor agonists in conscious, normotensive rats. J Pharmacol Exp Ther 1987;240:723-8.
- Villela NR, do Nascimento Júnior P, de Carvalho LR, Teixeira A. Effects of dexmedetomidine on renal system and on vasopressin plasma levels. Experimental study in dogs. Rev Bras Anestesiol 2005;55:429-40.

Table 6: Central venous pressure of patients				
Time points	Group D ( <i>n</i> =54)	Group C ( <i>n</i> =54)	Р	
Т0	10.53±1.46	10.22±1.73	0.316	
T1	9.89±1.93	$10.02 \pm 1.69$	0.710	
Т2	10.45±1.28	10.73±1.53	0.304	
Т3	11.30±1.61	10.76±1.75	0.098	
T4	11.22±1.35	10.83±1.52	0.161	
Т5	10.77±1.60	10.41±1.33	0.206	
Т6	11.25±1.37	11.42±1.64	0.560	
Τ7	11.13±1.44	11.42±1.36	0.284	
Т8	10.75±1.92	11.20±1.57	0.185	
Т9	10.24±1.65	11.39±1.32	0.219	
T10	9.75±1.80	10.12±1.57	0.257	
T11	10.48±1.55	10.64±1.36	0.569	
T12	10.45±1.70	10.72±1.58	0.356	
T13	10.73±1.40	10.47±1.59	0.369	
	1 000 41			

Data are presented as mean±SD. \*P<0.05 significant comparison between the two groups,  $^{+}P$ <0.05 significant compared to the preoperative reading within the same group. T0: Reading at base line before anesthesia, T1: Reading before aortic cross-clamping, T2: Reading 15 min after aortic cross-clamping, T3: Reading 30 min after aortic cross-clamping, T4: Reading before aortic declamping, T5: Reading 15 min after aortic declamping, T6: Reading 30 min after aortic declamping, T7: Reading 1 h after aortic declamping, T8: Reading 1 h after ICU admission, T9: Reading 6 h after ICU admission, T10: Reading 12 h after ICU admission, T11: Reading 24 h after ICU admission, T12: Reading 48 h after ICU admission, T13: Reading 72 h after ICU admission. Group D: Dexmedetomidine group, Group C: Control group, SD: Standard deviation, ICU: Intensive Care Unit

- 15. Sahu MK, Manikala VK, Singh SP, Bisoi AK, Chowdhury UK. Use of dexmedetomidine as an adjunct in the treatment of paradoxical hypertension after surgical repair of coarctation of the aorta in infants. The systolic and diastolic pressure decreased significantly with dexmedetomidine compared to nitroglycerine. Ann Card Anaesth 2015;18:437-40.
- 16. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-8.
- Klamt JG, de Andrade Vicente WV, Garcia LV, Ferreira CA. Effects of dexmedetomidine-fentanyl infusion on blood pressure and heart rate during cardiac surgery in children. Anesthesiol Res Pract 2010;2010:1–7.
- Soliman R, Zohry G. The myocardial protective effect of dexmedetomidine in high-risk patients undergoing aortic vascular surgery. Ann Card Anaesth 2016;19:606-13.
- Kamibayashi T, Hayashi Y, Mammoto T, Yamatodani A, Sumikawa K, Yoshiya I, *et al.* Role of the vagus nerve in the antidysrhythmic effect of dexmedetomidine on halothane/epinephrine dysrhythmias in dogs. Anesthesiology 1995;83:992-9.
- Ross CA, Ruggiero DA, Reis DJ. Projections from the nucleus tractus solitarii to the rostral ventrolateral medulla. J Comp Neurol 1985;242:511-34.
- Robertson HA, Leslie RA. Noradrenergic alpha 2 binding sites in vagal dorsal motor nucleus and nucleus tractus solitarius: Autoradiographic localization. Can J Physiol Pharmacol 1985;63:1190-4.
- Hammer GB, Drover DR, Cao H, Jackson E, Williams GD, Ramamoorthy C, *et al.* The effects of dexmedetomidine on cardiac electrophysiology in children. Anesth Analg 2008;106:79-83.
- 23. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology

1992;77:1134-42.

- Chrysostomou C, Di Filippo S, Manrique AM, Schmitt CG, Orr RA, Casta A, *et al.* Use of dexmedetomidine in children after cardiac and thoracic surgery. Pediatr Crit Care Med 2006;7:126-31.
- Tokuhira N, Atagi K, Shimaoka H, Ujiro A, Otsuka Y, Ramsay M, *et al.* Dexmedetomidine sedation for pediatric post-Fontan procedure patients. Pediatr Crit Care Med 2009;10:207-12.
- Nishibe S, Imanishi H, Mieda T, Tsujita M. The effects of dexmedetomidine administration on the pulmonary artery pressure and the transpulmonary pressure gradient after the bidirectional superior cavopulmonary shunt. Pediatr Cardiol 2015;36:151-7.
- Lazol JP, Lichtenstein SE, Jooste EH, Shiderly D, Kudchadker NA, Tatum GH, *et al.* Effect of dexmedetomidine on pulmonary artery pressure after congenital cardiac surgery: A pilot study. Pediatr Crit Care Med 2010;11:589-92.
- Friesen RH, Nichols CS, Twite MD, Cardwell KA, Pan Z, Pietra B, et al. The hemodynamic response to dexmedetomidine loading dose in children with and without pulmonary hypertension. Anesth Analg 2013;117:953-9.
- Kalman JM, Munawar M, Howes LG, Louis WJ, Buxton BF, Gutteridge G, *et al.* Atrial fibrillation after coronary artery bypass grafting is associated with sympathetic activation. Ann Thorac Surg 1995;60:1709-15.
- Howlin F, Brenner M. Cardiovascular assessment in children: Assessing pulse and blood pressure. Paediatr Nurs 2010;22:25-35.
- Greeley WJ, Kern FH. Anesthesia for pediatric cardiac surgery. In: Miller RD, editor. Anesthesia. 4<sup>th</sup> ed. New York: Churchhill Livingstone Inc.; 1994. p. 1811-4.
- Strafford MA. Cardiovascular physiology. In: Motoyama EK, Davis PJ, editors. Smith's Anesthesia for Infants and Children. 6<sup>th</sup> ed. St. Louis: C.V. Mosby Company; 1996. p. 76-81.
- 33. McAuliffe G, Bissonnette B, Cavallé-Garrido T, Boutin C. Heart rate and

cardiac output after atropine in anaesthetised infants and children. Can J Anaesth 1997;44:154-9.

- Rashwan DA, Rashwan SA, Talaatb NN. Dexmedetomidine infusion in adult patients undergoing open nephrolithotomy: Effects on intraoperative hemodynamics and blood loss; a randomized controlled trial. Egypt J Anaesth 2015;31:321-5.
- Ibraheim OA, Abdulmonem A, Baaj J, Zahrani TA, Arlet V. Esmolol versus dexmedetomidine in scoliosis surgery: Study on intraoperative blood loss and hemodynamic changes. Middle East J Anaesthesiol 2013;22:27-33.
- Mizrak A, Karatas E, Saruhan R, Kara F, Oner U, Saricicek V, *et al.* Does dexmedetomidine affect intraoperative blood loss and clotting tests in pediatric adenotonsillectomy patients? J Surg Res 2013;179:94-8.
- Venn RM, Bryant A, Hall GM, Grounds RM. Effects of dexmedetomidine on adrenocortical function, and the cardiovascular, endocrine and inflammatory responses in post-operative patients needing sedation in the Intensive Care Unit. Br J Anaesth 2001;86:650-6.
- Shehabi Y, Ruettimann U, Adamson H, Innes R, Ickeringill M. Dexmedetomidine infusion for more than 24 hours in critically ill patients: Sedative and cardiovascular effects. Intensive Care Med 2004;30:2188-96.
- Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesth Analg 2004;98:153-8.
- Ebert T, Maze M. Dexmedetomidine: Another arrow for the clinician's quiver. Anesthesiology 2004;101:568-70.
- Hosokawa K, Shime N, Kato Y, Taniguchi A, Maeda Y, Miyazaki T, *et al.* Dexmedetomidine sedation in children after cardiac surgery. Pediatr Crit Care Med 2010;11:39-43.
- 42. Tobias JD, Gupta P, Naguib A, Yates AR. Dexmedetomidine: Applications for the pediatric patient with congenital heart disease. Pediatr Cardiol 2011;32:1075-87.