

Dexmedetomidine use in a pediatric cardiac intensive care unit: Can we use it in infants after cardiac surgery?

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Objective: To assess clinical response of dexmedetomidine alone or in combination with conventional sedatives/analgesics after cardiac surgery.

Design: Retrospective study.

Setting: Pediatric cardiac intensive care unit.

Patients: Infants and neonates after cardiac surgery.

Measurements and Main Results: We identified 80 patients including 14 neonates, at mean age and weight of 4.1 ± 3.1 months and 5.5 ± 2 kg, respectively, who received dexmedetomidine for 25 ± 13 hours at an average dose of $0.66 \pm 0.26 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. Overall normal sleep to moderate sedation was documented 94% of the time and no pain to mild pain for 90%. Systolic blood pressure (SBP) decreased from 89 ± 15 mm Hg to 85 ± 11 mm Hg ($p = .05$), heart rate (HR) from 149 ± 22 bpm to 129 ± 16 bpm ($p < .001$), and respiratory rate (RR) remained unchanged. When baseline arterial blood gases were compared with the most abnormal values, pH decreased from 7.4 ± 0.07 to 7.37 ± 0.05 ($p = .006$), Po_2 from 91 ± 67 mm Hg to 66 ± 29 mm Hg ($p = .005$), and CO_2 increased from 45 ± 8 mm Hg to 50 ± 12 mm Hg ($p = .001$). At the beginning of the study, 37 patients (46%) were mechanically ventilated; and at 48 hours, 13 patients

(16%) were still intubated and five patients failed extubation. Three groups of patients were identified: A, dexmedetomidine only ($n = 20$); B, dexmedetomidine with sedatives/analgesics ($n = 38$); and C, dexmedetomidine with both sedatives/analgesics and fentanyl infusion ($n = 22$). The doses of dexmedetomidine and rescue sedatives/analgesics were not significantly different among the three groups but duration of dexmedetomidine was longer in group C vs. A ($p = .03$) and C vs. B ($p = .002$). Pain, sedation, SBP, RR, and arterial blood gases were similar. HR was higher in group C vs. B ($p = .01$). Comparison between neonates and infants showed that infants required higher dexmedetomidine doses, $0.69 \pm 25 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$, and vs. $0.47 \pm 21 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ ($p = .003$) and had lower HR ($p = .01$), and RR ($p = .009$), and higher SBP ($p < .001$).

Conclusions: Dexmedetomidine use in infants and neonates after cardiac surgery was well tolerated in both intubated and nonintubated patients. It provides an adequate level of sedation/analgesia either alone or in combination with low-dose conventional agents. (Pediatr Crit Care Med 2009; 10:654–660)

KEY WORDS: sedation; analgesia; infants; dexmedetomidine; cardiac surgery; intensive care unit; neonates

Providing sedation and analgesia in children after cardiac surgery can be challenging. Although our knowledge about sedative agents and their cardiorespiratory interactions has improved during the last two decades, delivering optimal sedation in the postoperative period re-

mains complex. Some of the factors that add to this complexity are the presence of an unpredictable and potentially labile physiology after cardiopulmonary bypass and the inability to accurately assess an infant's level of sedation.

In our institution, a successful effort for fast track and early extubation has been in place for the last 5 yrs. Nonetheless, a significant proportion of patients remain, who could further benefit from newer sedative agents with a better safety profile and less respiratory depression. This is important for infants with both univentricular and biventricular physiology and particularly the ones which are extubated or near extubation. Dexmedetomidine is a highly specific alpha-2 adrenergic receptor agonist with sedative, analgesic, and anxiolytic properties (1). It does not appear to significantly depress respiratory drive, thus interference with weaning from mechanical ventilation is less likely. In fact, it has been used both as a bridge to extubation as

well as in nonintubated patients (2, 3). In our previous study, which was mainly focused on older children after cardiothoracic surgery, dexmedetomidine was found to be well tolerated and provided targeted sedation and analgesia for 93% and 83% of the time, respectively (2). We describe our experience with the use of dexmedetomidine in a much younger and rather more difficult population: Infants, and neonates after congenital cardiac surgery.

MATERIALS AND METHODS

This retrospective case series study was approved by the Institutional Review Board of the University of Pittsburgh Medical Center/Children's Hospital of Pittsburgh. To follow our institution's policy, parental informed consent for investigational use of a drug was obtained for all patients younger than 1 year. Infants and neonates who were admitted to the cardiac intensive care unit (CICU) from January 2004 to May 2007 and had received dexmedetomidine were included.

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Dexmedetomidine was started as a continuous infusion, at a dose of $0.1\text{--}1.25 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. If it was considered necessary, a $1 \mu\text{g}/\text{kg}$ bolus at a rate of $0.1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ was given. According to the clinical practice in our CICU, the decision to give a bolus and the exact initial infusion dose was based on the physician's judgment and the level of sedation that the patient had before the initiation of the infusion, i.e., the degree of residual intraoperative anesthesia. Twenty minutes after the onset of the infusion, if sedation/analgesia were considered inadequate by the bedside nurse and by the physician on duty, dexmedetomidine infusion was increased by $0.1\text{--}0.3 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. If sedation/analgesia was still inadequate 20 minutes after the change of the infusion dose, a rescue agent was administered if necessary, and dexmedetomidine infusion was further increased to a maximum of $1.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. The maximum infusion dose of $1.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ was a consensus decision among the intensivists and pharmacists involved with the care of CICU patients. Given the lack of an established sedation protocol and the diversity of our patient population, the rescue agents were multiple and included fentanyl, morphine, midazolam, lorazepam, ketamine, and chloral hydrate.

Heart rate (HR), systolic blood pressure (SBP), respiratory rate (RR), and sedation and analgesia scores were recorded by the nursing staff at baseline, i.e., measurement within 1 hour before starting dexmedetomidine, and every hour thereafter. Arterial blood gas (ABG) results also were recorded every 1–4 hrs as clinically indicated. A hypertensive or hypotensive episode was defined as a 30% change from baseline and/or if the SBP was below or

above the 5th to 95th percentile for age. A bradycardic episode was defined as a 30% change from baseline and/or if the HR was below the fifth percentile for age. Low RR rate was defined as a RR below the fifth percentile for age. Sedation was assessed using a pediatric intensive care unit sedation scale ranging from 0 to 3 (0, none, alert, or normal sleep, easy to arouse; 1, mild sedation, occasionally drowsy, easy to arouse; 2, moderate sedation, frequently drowsy but easy to arouse; 3, severe sedation, somnolent, difficult to arouse). Analgesia was assessed with two 0–10 pain score scales: The FLACC (face, legs, activity, cry, and consolability) for patients older than 2 months old, and the CRIES (cries, requires oxygen for saturation less than 95%, increased vital signs, expression, sleepless) for patients 0–6 months old (4, 5). A pain score of 0 was considered pain free, 1–3 mild pain, 4–7 moderate pain, and 8–10 severe pain. The targeted level of sedation and analgesia was 0–2 and 0–3, respectively. Data were collected for as long as the dexmedetomidine infusion was being administered to a maximum of 48 hours.

Absolute exclusion criteria for the use of dexmedetomidine included decompensated heart failure, acute hemodynamic instability, septic shock, and ventricular arrhythmias. Relative exclusion criteria included a high RACHS-1 (risk adjustment for congenital heart surgery) score, 5 and 6 (6).

Patients were divided into three groups: A, dexmedetomidine only ($n = 20$); B, dexmedetomidine with sedatives/analgesics ($n = 38$); and C, dexmedetomidine with both sedatives/analgesics and fentanyl infusion ($n = 22$). Three major comparisons of data were performed: between baseline and while on dexmedetomidine infusion; among groups A, B, and C; and between neonates and infants. Baseline vital signs were compared with the lowest values and baseline ABGs with the lowest pH, base excess, Po_2 , and the highest CO_2 levels while receiving dexmedetomidine. Categorical

variables were reported as frequencies and percentages. Continuous variables were reported as mean \pm SD if the distribution was normal and as median with range if the distribution was not normal. Paired Student's *t* test or the Wilcoxon test, depending on the distribution of the data being analyzed, was used to compare continuous variables before and during dexmedetomidine infusion. Groups A, B, and C, were analyzed by the analysis of variance test or Kruskal-Wallis test, depending on the distribution, followed by the Bonferroni equation or the Dwass-Steel-Chritchlow-Fligner test, respectively, for between-group differences. Pain and sedation scores were analyzed by analysis of variance based on Kruskal-Wallis. Data from neonates and infants were either analyzed by an unpaired Student's *t* test or the Mann-Whitney test. Pearson's correlation coefficient (*r*) was used to identify any correlation between dexmedetomidine dose and vital signs. All reported *p* values were two-tailed, and values of $\leq .05$ were considered statistically significant.

RESULTS

A total of 80 patients (39 males and 41 females) were identified (Tables 1 and 2) and divided into three groups: A, $n = 20$; B, $n = 38$; C, and $n = 22$. Four of these patients were included in our previous report (2). Overall there were 1999 individual hourly points of data collected.

Average age and weight were 4.1 ± 3.1 months and 5.5 ± 2 kg, respectively. Group B had a higher weight compared with group C (*p* = .01). Fourteen patients (17.5%) were neonates with a mean age and weight of 15 ± 9 days and 3.2 ± 0.9 kg, respectively. Seventy-eight surgical procedures were adjusted for severity according to RACHS-1 classification and the median severity score was 2 (range,

Table 1. Cardiac diagnosis/procedures performed

	n (%)
Tetralogy of Fallot	19 (24)
Coarctation of the aorta	14 (17.5)
VSD with or without ASD	12 (15)
Atrioventricular septal defect	9 (11)
Glenn	9 (11)
Hypoplastic or interrupted aortic arch and VSD	3 (4)
Norwood stage I (HLHS)	2 (2.5)
Total anomalous pulmonary venous return	2 (2.5)
Pulmonary valvotomy and VSD	2 (2.5)
Blalock-Taussig shunt	2 (2.5)
Transposition of the great arteries	1
Aortopulmonary window	1
Right ventricle to pulmonary artery conduit	1
Left pulmonary artery augmentation	1
Other ^a	2

ASD, atrial septal defect; HLHS, hypoplastic left heart syndrome; VSD, ventricular septal defect.

^aOne patient s/p cardiac catheterization and one with severe pulmonary hypertension.

Table 2. Baseline patient characteristics

	Group A (n = 20)	Group B (n = 38)	Group C (n = 22)	<i>p</i>
Age (mo)	3.9 ± 3	4.8 ± 3	3.2 ± 3	.12
Weight (kg)	5.5 ± 2	6.1 ± 1.9	4.4 ± 2	.01 ^a
Gender (M, F)	9, 11	18, 20	15, 7	
Mechanically ventilated, n (%)				
On admission	8 (40)	11 (29)	18 (82)	
At 48 hrs	3 (15)	3 (8)	7 (32)	
Vital signs				
HR (bpm)	149 ± 19	146 ± 23	152 ± 24	.52
SBP (mm Hg)	85 ± 12	88 ± 15	82 ± 18	.03 ^b
RR (breaths/min)	32 ± 13	32 ± 12	29 ± 12	.7
CICU length of stay (d)	4 (1–126)	3 (1–87)	8 (2–74)	.005 ^c

CICU, cardiac intensive care unit; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure.

^a*p* = .002 group B vs. C; ^b*p* = .046 group A vs. B and *p* = .017 group B vs. C; ^c*p* = .002 group B vs. C.

1–6). The total CICU length of stay was a median of 4 days (1–126). Group B had a shorter CICU stay when compared with group C ($p = .002$) (Table 2).

Dexmedetomidine Dosing and Duration. Dexmedetomidine was started at a mean of 4 ± 6 hours after arrival from the operating room. A total of 24 patients (30%) received a $0.5\text{--}1 \mu\text{g}/\text{kg}$ loading dose at a rate of $0.1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. The mean dexmedetomidine starting dose was $0.47 \pm 0.29 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ followed by a maintenance infusion of $0.66 \pm 0.26 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. The duration of infusion was 25 ± 13 hrs.

Dexmedetomidine dose requirement between mechanically ventilated and nonmechanically ventilated patients did not differ, $0.62 \pm 0.26 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ vs. $0.68 \pm 0.26 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ ($p = .3$). Similarly, there was no difference in dexmedetomidine dose between patients who received fentanyl infusion (group C) and those who did not (groups A and B): $0.6 \pm 0.21 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ vs. $0.68 \pm 0.28 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ ($p = .2$) (Table 3). Dexmedetomidine duration, however, was longer in group C compared with A ($p = .03$) and compared with B ($p = .002$).

To assess if cumulative experience with the use of dexmedetomidine could have resulted in higher doses, we compared the dexmedetomidine dosage between the first and the last 40 patients. Both starting and maintenance doses were significantly higher in the last 40 patients. Starting dose was 0.34 ± 0.18 vs. $0.6 \pm 0.32 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ ($p < .001$) and maintenance dose was $0.54 \pm 0.2 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ vs. $0.78 \pm 0.26 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ ($p < .001$). Furthermore, we analyzed the amount of times dexmedetomidine was administered above the recommended adult maximum dose of $0.7 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. There were a total of 789 recorded doses (39% of dexmedetomidine infusion time) above the maximum, the majority of which (>75%) were in the last 40 patients, 169 vs. 620.

Rescue Sedative/Analgesic Agents. Groups A and B, which comprised 73% of patients, received dexmedetomidine without any other continuous analgesic or sedative infusion. Group C had an average fentanyl infusion dose of $1.7 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ and it continued for 18 ± 15 hrs. Table 3 shows in detail the requirements of these three groups. There was no significant difference in rescue sedation/analgesia between patients who received fentanyl infusion and patients who did not, 2.8 vs. 2.6 doses per 24 hours of dexmedetomidine infusion, respectively. Overall, fentanyl (40%), mor-

Table 3. Descriptive data on sedatives, analgesics, and hemodynamic infusions among groups A, B, and C during dexmedetomidine infusion

	Group A (n = 20)	Group B (n = 38)	Group C (n = 22)	<i>p</i>
Dexmedetomidine				
Dose ($\mu\text{g}/\text{kg}/\text{hr}$)	0.72 ± 0.31	0.65 ± 0.26	0.6 ± 0.21	.37
Duration/patient (hrs)	24 ± 12	22 ± 11	32 ± 15	.009 ^a
Duration (total patient hrs)	471	820	708	
Fentanyl ($\mu\text{g}/\text{kg}/\text{hr}$)			1.7 ± 1	
Rescue doses ^b (doses/24 DEX infusion hrs)		143 (2.6)	84 (2.8)	
Analgesics (n)		106	46	
Sedatives (n)		37	38	
Milrinone, n (%)	16 (80)	30 (79)	20 (91)	
Dose ($\mu\text{g}/\text{kg}/\text{min}$)	0.91 ± 0.24	0.86 ± 0.24	0.84 ± 0.26	.68
Duration (hrs)	23 ± 11	24 ± 11	32 ± 15	.06
Dopamine, n (%)	2 (10)	8 (21)	6 (27)	
Dose ($\mu\text{g}/\text{kg}/\text{min}$)	2.9 ± 3.1	3.3 ± 0.8	3.7 ± 1.2	.9
Duration (hrs)	5 ± 6	13 ± 9	16 ± 8	.27
Epinephrine, n (%)	0	1 (2)	2 (9)	
Dose ($\mu\text{g}/\text{kg}/\text{min}$)		0.04	0.03 ± 0.02	
Duration (hrs)		14	26 ± 20	
Nitroprusside, n (%)	10 (50)	30 (71)	7 (32)	
Dose ($\mu\text{g}/\text{kg}/\text{min}$)	2.2 ± 1	2.2 ± 1	1.6 ± 0.7	.37
Duration (hrs)	18 ± 10	12 ± 7	16 ± 7	.16
Esmolol, n (%)	0	3 (7)	0	
Dose ($\mu\text{g}/\text{kg}/\text{min}$)		157 ± 42		
Duration (hrs)		14 ± 7		

DEX, dexmedetomidine.

^a $p = .03$ group A vs. C and $p = 0.002$ group B vs. C; ^bgroup A and group B rescue doses are presented as one group; Values are presented as mean \pm SD.

Table 4. Sedation and pain scores

	Group A (n = 20)	Group B (n = 38)	Group C (n = 22)	<i>p</i>
Sedation score (0–3)	1.0 ± 0.4	1.2 ± 0.5	1.4 ± 0.4	.28
Pain score (0–10)	1.7 ± 0.9	2.0 ± 1	1.9 ± 0.7	.62

Values are presented as mean \pm SD.

phine (20%), and chloral hydrate (15%) were the most common rescue drugs used. Midazolam, lorazepam, and ketamine were used less frequently.

Sedation/Analgesia. The overall mean sedation score was 1.2 ± 0.5 . Normal sleep, defined as easily arousable patient without drowsiness, to moderate sedation was documented 94% of the time. In regards to analgesia, the mean pain score was 1.9 ± 0.9 and no pain to mild pain was documented 90% of the time. Among groups A, B, and C, sedation and pain scores were similar (Table 4).

Cardiovascular Effects. Average SBP and HR were statistically lower after dexmedetomidine was initiated. Blood pressure decreased from 89 ± 15 mm Hg at baseline, to an average of 85 ± 11 mm Hg (5% decrease, $p = .006$). HR decreased from 149 ± 22 bpm to 129 ± 16 bpm (13% decrease, $p < .001$) (Fig. 1). Further analysis between baseline and av-

erage lowest values showed a decline in the SBP to 69 ± 11 mm Hg (22% decrease) and HR to 113 ± 15 bpm (24% decrease). Changes in dexmedetomidine dose correlated negatively with HR ($r = -.65$, $p < .001$), and had no correlation with SBP ($r = -.2$, $p = .22$).

Because of lack of data and because the timing of starting dexmedetomidine was not uniform in all patients after surgery, it was difficult to differentiate if hemodynamic changes were secondary to a potential presence of low cardiac output syndrome (LCOS) or dexmedetomidine. Nonetheless, the HR trend and the correlation with dexmedetomidine dosage did not support a worsening LCOS because of dexmedetomidine (Fig. 1). As noted above, the overall HR was lower after initiating dexmedetomidine, in contrast to the expected higher HR seen in LCOS state (7). Additionally, we noticed that during the first 8 hrs, when dexmedeto-

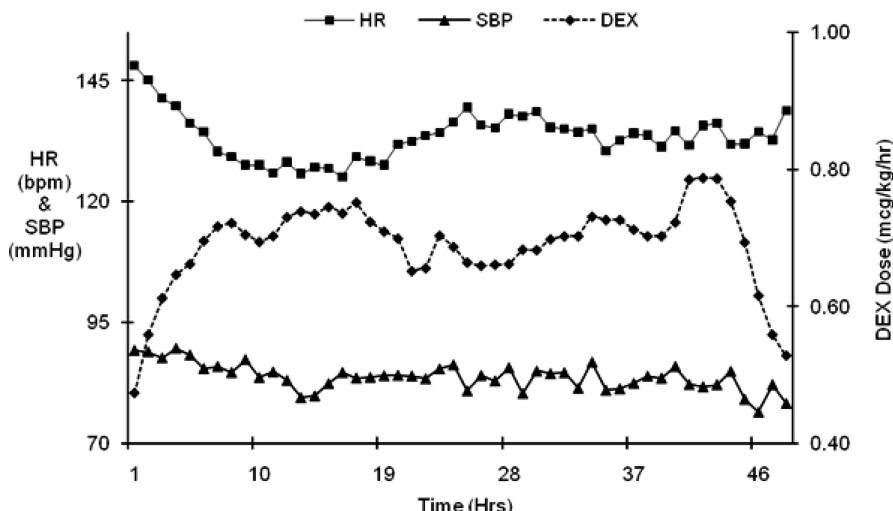


Figure 1. Average heart rate (HR), systolic blood pressure (SBP), and dexmedetomidine (DEX) dose in all patients.

Table 5. Hemodynamic variables in groups A, B, and C during dexmedetomidine infusion

	Group A (n = 20)	Group B (n = 38)	Group C (n = 22)	p
SBP (mm Hg)	85 ± 9	88 ± 11	82 ± 11	.19
HR (bpm)	128 ± 15	126 ± 13	136 ± 17	.03 ^a
RR (br./pm)	32 ± 8	30 ± 8	34 ± 11	.34

SBP, systolic blood pressure; HR, heart rate; RR, respiratory rate.

^ap = 0.01 group B vs. C. Values are presented as mean ± sd.

midine dose increased steadily, there was a large negative correlation with HR ($r = -.9$, $p < .001$). During the 9- to 17-hour period, there was no correlation ($r = .04$, $p = .9$); and during the 18- to 28-hour period, when there was a steady decline in the dexmedetomidine dose, there was also a significant negative correlation ($r = -.7$, $p = .07$). These indirect findings do not support worsening LCOS. Figure 1 shows graphically the HR and SBP trend in relation to dexmedetomidine dose and duration. Because vital signs were documented only every hour, we were not able to detect further changes that may have occurred during the loading dose or with increased dexmedetomidine infusion rate.

Twenty-seven patients (34%) had at least one episode of hypotension and 10 patients (12.5%) at least one episode of bradycardia. Overall, from the 1999 hourly recordings, there were 58 hypotensive events (3%) and 44 bradycardic events (3%). Crystalloid or colloid fluids boluses were administered in 23 patients (29%); however, we could not determine whether these were a part of the postoperative cardiac care or if they were associated with dexmedetomidine administration.

Sixty-six patients were on some inotropic support before dexmedetomidine was started. Table 3 shows the inotropic agent requirements among groups A, B, and C, and Table 5 shows the hemodynamic variables. Overall there was no substantial difference in the hemodynamic infusions, SBP or RR. HR was statistically higher in group C compared with group B ($p = .01$). A total of 50 patients had significant postoperative systemic hypertension requiring sodium nitroprusside (47 patients) and esmolol (three patients). Thirty-three of these belonged to group B.

Nine patients had an arrhythmia before starting dexmedetomidine. The types of arrhythmias included five patients with junctional ectopic tachycardia, two with first and one with third-degree atrioventricular block, and one patient with junctional accelerated rhythm. All arrhythmias recovered to normal sinus rhythm before discharge from the CICU.

Respiratory Effects. Thirty-seven patients (46%) were already intubated at the initiation of the dexmedetomidine infusion. Twenty-four of these were weaned off and extubated while receiving dexmedetomidine. Five patients subsequently

failed extubation while receiving dexmedetomidine. Three had complex CICU courses, with chronic lung disease and previous prolonged intubation, and two were found to have hemidiaphragm paralysis that needed surgical intervention.

Among the patients who were not intubated at the initiation of dexmedetomidine, none required intubation during the study period. None of the patients had any documented episodes of apnea.

There was no significant change between baseline and overall mean RR, 31 ± 12 breaths/min to 31 ± 9 breaths/min ($p = .83$). However, a comparison between baseline and the lowest mean RR, 20 ± 6 breaths/min [35% drop] showed a significant difference ($p < .001$). There were 31 patients with 108 recorded episodes consistent with low RR for age (5% incidence). When we analyzed dexmedetomidine dose in relation to the RR, we did not find any significant correlation ($r = -.05$, $p = .76$).

ABGs were statistically different when baseline values were compared with the most abnormal ABGs while on dexmedetomidine. These changes included lower pH level, 7.40 ± 0.1 to 7.37 ± 0.1 ($p = .006$), mild CO₂ retention, 45 ± 8 to 50 ± 12 mm Hg ($p = .001$), and lower Po₂ levels, 91 ± 67 mm Hg to 66 ± 29 mm Hg ($p = .005$). The timing of these most abnormal ABGs ranged from 2 to 25 hrs after starting dexmedetomidine, with an average of 4 ± 7 hrs. These ABG changes did not differ among groups A, B, and C (Table 6).

Gastrointestinal Effects. Twenty-one patients (26%) were fed during the dexmedetomidine infusion. One episode of vomiting was documented in one patient.

Neonates vs. Infants. A subgroup analysis was performed comparing neonates (n = 14) with infants (n = 66) (Table 7). Dexmedetomidine dose was statistically lower in neonates ($p = .003$). Sedation and analgesia scores and rescue sedatives were similar in both groups. HR and RR were statistically higher and SBP was lower in neonates.

Safety and Adverse Events. Two patients had changes in the cardiorespiratory variables that may have been attributed to dexmedetomidine and thus it was discontinued. The first was a 2-mo-old patient with aortic coarctation repair who had received dexmedetomidine for 8 hrs before discontinuation ($0.4 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$). At the time, this patient was simultaneously treated with nitroprusside ($2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) for hypertension when a

Table 6. Comparison of arterial blood gas changes in groups A, B, and C

	Group A (n = 20)	Group B (n = 38)	Group C (n = 22)	p
pH				
Baseline	7.4 ± 0.06	7.41 ± 0.06	7.39 ± 0.09	.6
Lowest	7.37 ± 0.05	7.38 ± 0.05	7.36 ± 0.06	.2
CO ₂ , mm Hg				
Baseline	45 ± 6	46 ± 7	45 ± 11	.9
Highest	54 ± 19	48 ± 8	50 ± 8	.4
PO ₂ , mm Hg				
Baseline	86 ± 54	100 ± 72	79 ± 71	.1
Lowest	73 ± 36	69 ± 26	55 ± 25	.07
Base excess, mmol/L				
Baseline	2 ± 4	4 ± 4	3 ± 6	.4
Lowest	1 ± 4	2 ± 4	1 ± 3	.5

Values are presented as mean ± SD.

Table 7. Neonates vs. infants

	Neonates (n = 14)	Infants (n = 66)	p
Group A, B, C (n)	3, 7, 4	17, 15, 34	
Dexmedetomidine			
Dose (μg/kg/hr) ^a	0.47 ± 21	0.69 ± 25	.003
Duration (hrs) ^a	27 ± 17	25 ± 13	.6
Rescue sedative/analgesic doses n (doses/24 DEX infusion hrs)	43 (2.6)	184 (2.7)	
Pain score ^b	2 (0.8–2.4)	2 (0–4)	.5
Sedation score ^b	1.4 (0–2)	1 (0–2.3)	.06
Vital signs			
HR (bpm) ^a	140 ± 10	127 ± 15	.001
SBP (mm Hg) ^a	77 ± 9	87 ± 10	< .001
RR (breaths/min) ^b	37 (17–55)	28 (18–68)	.009
RACHS-1 ^b	3 (1–4)	2 (1–6)	.1
CICU stay (d) ^b	8 (2–30)	4 (1–126)	.67

DEX, dexmedetomidine; HR, heart rate; SBP, systolic blood pressure; RR, respiratory rate; CICU, cardiac intensive care unit; RACHS-1, Risk Adjustment for Congenital Heart Surgery Classification.

^aValues as mean ± SD; ^bvalues as median with range.

dose of hydralazine was administered. The patient's SBP decreased from a baseline of 81 to 65 mm Hg, a 19% change, and the decision was made to discontinue both the nitroprusside and dexmedetomidine infusions. Blood pressure returned to baseline within 15 mins. The second patient was also a 2-mo-old with coarctation of the aorta repair who had received dexmedetomidine for 11 hrs (0.7 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$). The patient's HR had decreased from baseline of 115 bpm to 89 bpm, a 23% change and although normotensive at the time with no signs of LCOS, a precautionary decision was made by the physician on call to discontinue dexmedetomidine. HR recovered to 127 bpm within 1 hr without any further interventions.

DISCUSSION

Dexmedetomidine has been increasingly used in our CICU for sedation, analgesia, and other off-label indications. With growing experience, we have ex-

panded its use from adolescents and young adults to infants and neonates, and to more complex cardiac surgeries. In our previous study, although only seven patients were younger than 1 yr, we noticed that this younger population had a tendency toward a higher dexmedetomidine dose requirement (2).

In this report, which included only infants and neonates, the dexmedetomidine dose was higher compared with our previous results in older children, 0.66 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ vs. 0.4 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ (2). We also found that with increasing experience, the dose had increased to 0.78 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. Although these dose ranges are relatively high, they are still within the range published in both adult and pediatric literature (8–10). Two pediatric pharmacokinetic studies by Petroz et al (11) and Diaz et al (12), although limited by the number of infants included, showed that children had similar and predictable pharmacokinetics com-

pared with adults. In reference to our minority neonatal subgroup of patients, we found that the dexmedetomidine dose was lower compared with the older infant population. Given the small number of patients, we can only speculate why there was such a difference. One possibility is that due to the immature neonatal kidney function, the renally excreted dexmedetomidine accumulates over time and thus the requirement is less. The lower SBP and higher RR and HR are likely explained by the age difference.

Dexmedetomidine decreases opioid and benzodiazepine requirements, possibly due to a synergistic or additive effect, and in some studies it has been used as a single agent for sedation (13, 14). In 25% of the patients in this report, dexmedetomidine was administered as the sole sedative/analgesic agent; approximately half of the patients required occasional rescue boluses and 27% required an additional low-dose fentanyl infusion. A comparison between patients who received additional fentanyl infusion and those who did not showed that there was no difference in either sedation or pain score and both groups received equal amounts of rescue sedative/analgesic boluses. Providing an adequate level of analgesia with the least amount of side effects is of paramount importance, and has been shown to decrease cardiorespiratory morbidity and, therefore, hospitalization time. This is rather important, taking into consideration that most CICU patients have several noxious stimuli, including chest tubes and chest incisions as well as the need for mechanical ventilation. Our results are in agreement with those of Tobias and Berkenbosch (15), who demonstrated that the use of dexmedetomidine in pediatric ICU patients was superior to midazolam infusion based on supplemental rescue dose requirements. The study by Tobias and Berkenbosch was a small randomized trial, in mechanically ventilated infants and children, and it compared dexmedetomidine infusion at two different doses, 0.25 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ and 0.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ with midazolam 0.22 $\text{mg}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. At a dose of 0.25 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$, dexmedetomidine was equivalent to midazolam. At 0.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$, dexmedetomidine provided more effective sedation as demonstrated by the need for fewer bolus doses of morphine, a decrease in the 24-hr requirements for supplemental morphine, as well as a decrease in the total number

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