Research Article

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Hemodynamic Effects of Dexmedetomidine in Pediatric Cardiac Transplantation Recipients during Cardiac Catheterization

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Abstract

Background: Pediatric heart transplant recipients routinely undergo surveillance cardiac catheterizations requiring various levels of sedation often using Dexmedetomidine. The transplanted heart is removed from direct sympathetic nervous innervations and, as a result, has a blunted chronotropic response to maintain cardiac output in response to hypotension. The hemodynamic effects of Dexmedetomidine in pediatric heart transplant recipients undergoing procedural sedation in the cardiac catheterization laboratory has yet to be studied extensively. We therefore conducted a retrospective evaluation at our center evaluating hemodynamic aspects of Dexmedetomidine in pediatric heart transplant patients. We believe this is a unique dataset with very valuable lessons for multiple centers using this technique for sedation in pediatric heart transplant recipients.

Objective: To determine if Dexmedetomidine is a hemodynamically stable sedative agent in pediatric Orthotropic Heart Transplant Recipients (OHTR).

Design: All OHTR <21 years of age undergoing sedated cardiac catheterizations between 1/2010 and 5/2012 were retrospectively reviewed. Dexmedetomidine was administered as a bolus (0.5-1 mcg/kg over 10 minutes) and/or an infusion (0.5-2 mcg/kg/h). Demographic and hemodynamic data were compared between patients sedated with Dexmedetomidine and those receiving other agents.

Setting: Single center study at a University hospital.

Participants: All OHTR <21 years of age undergoing sedated cardiac catheterizations between 1/2010 and 5/2012.

Intervention: Dexmedetomidine was administered as a bolus (0.5-1 mcg/kg over 10 minutes) and/or an infusion (0.5-2 mcg/kg/h).

Measurements: 158 procedures met inclusion criteria. Dexmedetomidine was used in 64% of OHTR: 59% of whom received other sedatives in addition to Dexmedetomidine. Patients receiving Dexmedetomidine and those who did not were similar in pre procedure blood pressure and shortening fraction. The Dexmedetomidine group had a lower mean age (12.5 yrs vs. 15.2 yrs, p=0.001) and higher mean pre-procedure heart rate (108 vs. 99 bpm, p=0.001). The incidences of bradycardia, hypotension and receiving an intervention for either were similar between groups. A decrease in heart rate greater than 20% from baseline was more likely in patients receiving Dexmedetomidine.

Conclusion: Dexmedetomidine administration in pediatric OHTR was not associated with clinically significant bradycardia or hypotension and is a hemodynamically stable sedative in this population.

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Introduction

Dexmedetomidine is a selective alpha$_2$ adrenergic agonist that has sedative, analgesic and anxiolytic properties. Dexmedetomidine does not result in respiratory depression, appears to mimic natural sleep and has centrally mediated anxiolytic effects [1,2]. This quality along with short half life of 6 minutes and terminal half life of 2 hours has led to its increasing use in the cardiac catheterization laboratory as part of a procedural sedation regimen [3-6]. Since the actions of Dexmedetomidine are mediated by α2 adrenoreceptors, Dexmedetomidine has been associated with hypotension and bradycardia [7]. It decreases blood pressure, heart rate and circulating catecholamine's in a dose dependent manner [7]. Although approved for mechanically ventilated adults for periods less than 24 hours, experience is increasing in using this medication in children.

Pediatric heart transplant recipients routinely undergo surveillance cardiac catheterizations requiring various levels of sedation [8]. The transplanted heart is removed from direct sympathetic nervous innervations and, as a result, has a blunted chronotropic response to maintain cardiac output in response to hypotension [9,10]. The hemodynamic effects of Dexmedetomidine in pediatric heart transplant recipients undergoing procedural sedation in the cardiac catheterization laboratory has yet to be studied extensively.

There is data regarding the use of Dexmedetomidine in one small study of pediatric heart transplant recipients undergoing cardiac

catheterization. Dexmedetomidine was administered to twelve patients as a rapid bolus of either 0.25 or 0.5 mcg/kg over 5 minutes [11]. There was a transient increase in systolic blood pressure, diastolic blood pressure, pulmonary artery pressure, pulmonary capillary wedge pressure and systemic vascular resistance at 1 minute, which returned to near baseline after 5 minutes. This study examined bolus dosing but did not comment on whether the hemodynamic changes seen were clinically significant. The hemodynamic effects of rapid bolus dosing of Dexmedetomidine are different compared to the effects seen when it's administered as an infusion. In adults, Dexmedetomidine administered over 2 minutes, resulting in a biphasic hemodynamic response with an initial increase in blood pressure and reflex bradycardia followed by a stabilization of blood pressure and HR below baseline value [7].

We sought to examine the hemodynamic effects of Dexmedetomidine in pediatric heart transplant recipients when administered as a slow bolus followed by an infusion in the cardiac catheterization laboratory as part of procedural sedation.

The aim of this study was to determine whether Dexmedetomidine is hemodynamically stable drug to administer to pediatric heart transplant recipients. The study was designed to evaluate the risk of hypotension and bradycardia associated with Dexmedetomidine in comparison to other agents in OHTR patients.

Methods

The institutional review board at our institution approved this study (IRB approval number: 201208032). Parental consent was waived due to the retrospective nature of the study with minimal concerns for loss of privacy. All diagnostic catheterizations performed on pediatric heart transplantation recipients from January 2010 until May 2012 was retrospectively reviewed. All patients less than 21 years of age receiving procedural sedation were included. Procedural sedation was defined as all patients not receiving anesthetic gases or artificial airway devices. Procedures where Dexmedetomidine was administered were compared to those where it was not. Either certified nursing staff or an anesthesiologist provided sedation. The choice of sedative agent used was based on practitioner preference. Dexmedetomidine was administered as a bonus of 0.5-1 mcg/kg over 10 minutes and/or an infusion with rates between 0.5-2 mcg/kg/hour. Other agents used in conjunction with Dexmedetomidine included fentanyl, ketamine, midazolam and propofol. The same agents were also used in the patients who did not receive Dexmedetomidine.

Demographic data including sex, age, weight, pre and post procedural heart rate and blood pressure measurements were collected from electronic medical records. Left ventricular shortening fraction results were obtained from the patients' most recent echocardiogram report prior to the procedure. Maximum and minimum heart rate and blood pressure values recorded at every five to ten minute intervals during the procedure and for the first 30 minutes post procedure were collected from the medical record. Other sedatives administered and doses received were documented. Hypotension and bradycardia were defined by two separate criteria. A 20% decrease from pre-procedural values defined the first criteria. The second criterion was defined according to age appropriate normative values as stated in table 1. Procedures warranting an intervention for either hypotension or bradycardia were recorded. An intervention was defined as either a decrease in Dexmedetomidine dosing or receiving a rescue medication. The reason for intervention and the intervention performed were both documented.

	Systolic Hypotension	Bradycardia
0-2 years	<60mmHg	<75 bpm
3-9 years	<80mmHg	<60 bpm
>9 years	<90mmHg	<60 bpm

Table 1: Definitions Used for Vitals.

Due to intrapatient variability in response to Dexmedetomidine, each exposure to sedation in the cardiac catheterization laboratory was counted as an individual procedure despite several patients undergoing serial catheterizations during the study period.

Demographic data including gender, age, pre procedural vitals, and pre procedural echocardiogram systolic function were compared between the two groups using a student's t-test. Chi square testing was used to compare the incidences of bradycardia and hypotension between the two groups. All statistical analysis was performed using SSPS 21.0 (IMB, Armonk, New York). Statistical significance was defined as a P value ≤ 0.05.

Results

The patient records of 271 procedures were reviewed with 158 procedures meeting inclusion criteria. Several patients underwent serial procedures during the study period, resulting in 87 individual patients included. Demographic data is shown in table 2.

	All Patients (median)	Dex	No Dex
Total	158	101	57
0 - 2 yrs	8	6	2
3 - 9 yrs	28	26	2
>10 yrs	122	69	53
Mean age	13.5	12.5 +/- 5.8	15.2 +/-4.3
% Male	63%	64%	60%
Weight	5-80 kg (42 kg)	5-72 kg (47 kg)	7-80 (52 Kg)
Shortening Fraction	35%	35%+/- 5.8	33% +/- 7.3
Pre-procedure HR	106	108 +/- 16.8	99 +/- 18.0
Pre Systolic BP (mmHg)	118	117+/- 17.9	119 +/- 12.3

Table 2: Demographic Data.

Dexmedetomidine was administered in 101 procedures. In 80 of these, Dexmedetomidine was administered as both a bolus and an infusion. In 19 procedures, it was administered as an infusion alone and twice only a bolus. Other sedative agents were used in addition to Dexmedetomidine in 60 cases (Table 3). Pre procedure blood pressure and shortening fraction were similar in procedures where Dexmedetomidine was administered compared to those where it was not. In the Dexmedetomidine group, the mean age was lower (12.5 yrs vs. 15.2 yrs, p=0.001) and the mean pre procedure heart rate was higher (108 vs. 99 bpm, p=0.001) (Table 2).

A decrease in heart rate greater than 20% from baseline was more likely when Dexmedetomidine (p=0.001) was administered. The incidence of receiving an intervention (p=0.310), bradycardia for age (p=0.702), hypotension for age (p=0.059) or decrease in blood

	# Patients (%)
Total Dexmedetomidine	101 (64%)
Dex bolus + infusion	80 (79%)
Dex infusion only	19 (19%)
Dex bolus only	2 (2%)
Adjunct agents given	60 (59%)

Table 3: Sedation Regimen Used.

pressure greater than 20% from baseline (p=0.126) was similar in procedures with Dexmedetomidine compared to those without (Figures 1-5).

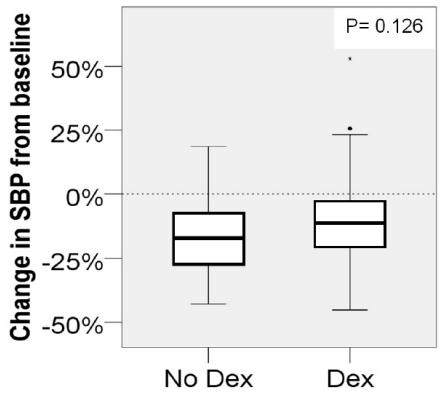

Figure 1: Change in systolic BP from baseline.

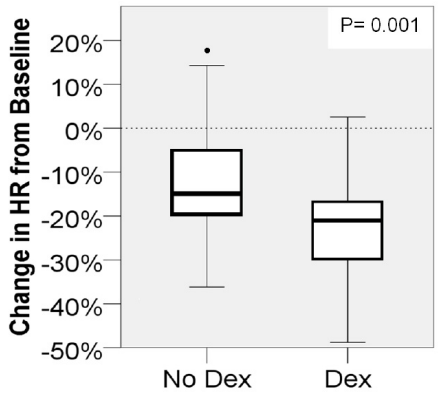

Figure 2: Change in HR from baseline.

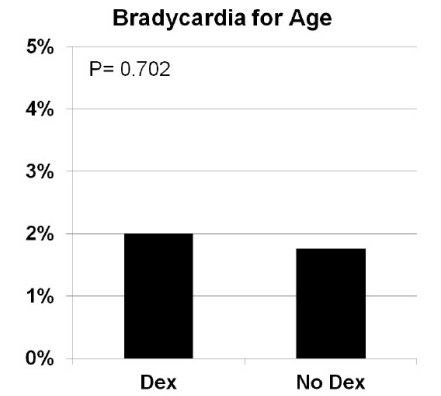

Figure 3: Bradycardia for age.

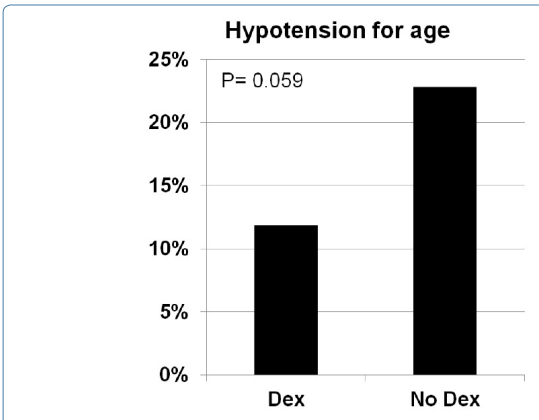

Figure 4: Hypotension for age.

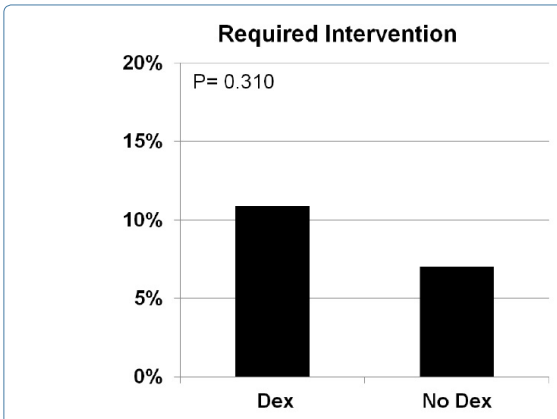

Figure 5: Required intervention.

The Dexmedetomidine dose was decreased during 11 procedures. In two of these (2%) the patients were noted to have respiratory concerns (upper airway obstruction or shallow breathing). Rescue medications were administered in six procedures (6%) in the Dexmedetomidine group compared to four procedures (7%) in the control group. Rescue medications included dopamine, phenylephrine and/or fluid boluses. In four procedures where the Dexmedetomidine dose was decreased, there was no bradycardia or hypotension.

Discussion

Dexmedetomidine is a α2 adrenoreceptors agonist whose sedative and anxiolytic effects are centrally mediated [1]. It is currently approved by the Federal Drug Administration for intensive care and procedural sedation in the adult population and has gained increasing usage in the pediatric anesthesia regimen. The drug has been reported to be used in procedural sedation, including sedation for gastroenterology, otolaryngology, orthopedic and radiologic procedures [12-18]. Our study demonstrates that the drug can be used without significant hemodynamic effects for procedural sedation in OHTR in the cardiac catheterization laboratory.

Dexmedetomidine is currently recognized as an option for sedation of patients with congenital heart disease [19]. Several studies document its usage as a sedative both intraoperative and in the intensive care unit following cardiac surgery, including in single ventricle patients [20-26]. In the cardiac catheterization laboratory, Deutsh et al., evaluated the usage of Dexmedetomidine in children with congenital

heart disease [27]. Their study included 9 heart transplant recipients in whom non inferiority of Dexmedetomidine combined with sevoflurane was demonstrated for decreased heart rate, but not for hypotension.

According to the International Society for Heart and Lung Transplantation guidelines, pediatric transplant recipients undergo several surveillance cardiac catheterizations [8]. There is limited data regarding the usage of Dexmedetomidine in pediatric heart transplant recipients. There are documented cases of Dexmedetomidine use, including the prevention of post operative withdrawal symptoms follow cardiac transplantation as well its usage to facilitate the extubation of a transplant recipient recovering from acute pneumonia [28,29]. Jooste et al., reported the results of rapid bolus dosing in 12 pediatric heart transplant recipients undergoing routine diagnostic catheterizations [11]. Their study demonstrated a significant transient increase in systemic blood pressure, which returned to baseline within 5 minutes. However, that study only looked at rapid bolus dosing in a small number of patients. While the study by Deutsh et al., also included transplant recipients, only nine such patients were included [27]. Our study is the largest study to look at Dexmedetomidine dosing in pediatric heart transplant recipients receiving bolus and infusion dosing.

Our study shows that although there was a marginally significant difference was found in blood pressure (0.059) among the patients receiving Dexmetomidine there was no hemodynamically significant bradycardia or hypotension warranting clinical intervention in pediatric heart transplant recipients receiving Dexmedetomidine for procedural sedation. A decrease in heart rate greater than 20% compared to baseline values was seen.

In our study population, patients receiving Dexmedetomidine were older. This is reflective of the sedation practice at the study institution. Patients who received the agent also had a higher baseline heart rate. This could explain the finding that, although patients demonstrated 20% decreases in heart rate from baseline, their heart rate remained within normal age values. Despite this, the rates of hypotension and interventions remained the same between patients who did and did not receive Dexmedetomidine.

This study has limitations inherent with its retrospective nature. Choice of sedative agent and rescue intervention was provider dependent and patients were not randomized. As a retrospective study, we were unable to control for the usages and dosages of other sedative agents. Based on the sedation practices of the study institution, the control arm of this study was small. However, our study does provide support for future prospective studies to further delineate the hemodynamic effects of Dexmedetomidine in this patient population.

Conclusion

Patients receiving Dexmedetomidine for procedural sedation did not demonstrate hemodynamically significant bradycardia or hypotension warranting clinical intervention. However, heart rate decreases greater than 20% compared to baseline values were seen. Our findings conclude that Dexmedetomidine is hemodynamically safe for procedural sedation for pediatric heart transplant patients without significant hemodynamic effects in the cardiac catheterization laboratory.

Disclosures

We have no disclosures from all the authors.

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