Which Anesthetic Agent Alters the Hemodynamic Status During Pediatric Catheterization? Comparison of Propofol Versus Ketamine

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Objective: **To compare the effects of propofol and ketamine on systemic and pulmonary circulations in pediatric patients scheduled for elective cardiac catheterization.**

Design: **Prospective, randomized, and blinded.**

Setting: **University hospital.**

Participants: **Children (n = 41) undergoing cardiac catheterization.**

Interventions: **All children were premedicated with oral midazolam 60 minutes before the procedure. Patients were separated into 3 groups according to shunts diagnosed by transthoracic echocardiography before the catheterization procedure: patients without cardiac shunt (Group I, n = 11), left-to-right shunt (Group II, n = 12), and right-to-left shunt (Group III, n = 18). A continuous infusion of propofol (100-200 μg/kg/min) or ketamine (50-75 μg/kg/min) was randomly started in all groups to obtain immobility during the procedure. Hemodynamic data, including systemic venous, pulmonary artery and vein, aortic saturations and pressures, were recorded; Qp/Qs were calculated. The same set of data was recorded before discontinuation of infusions at the end of the procedure.**

Measurements and Main Results: **After the propofol administration, in all 3 patient groups propofol infusion was associated with significant decreases in systemic mean arterial pressure. In groups with cardiac shunts (Group II and III), propofol infusion significantly decreased systemic vascular resistance and increased systemic blood flow, whereas pulmonary vascular resistance and pulmonary blood flow did not change significantly. These changes resulted in decreased left-to-right shunting and increased right-to-left shunting; the pulmonary-to-systemic flow ratio decreased significantly. On the other hand, after ketamine infusion, systemic mean arterial pressure increased significantly in all patient groups, but pulmonary mean arterial pressure, systemic vascular resistance, and pulmonary vascular resistance were unchanged.**

Conclusion: **In children with cardiac shunting, the principal hemodynamic effect of propofol is a decrease in systemic vascular resistance. In children with intracardiac shunting, this results in an increase in right-to-left shunting and a decrease in the ratio of pulmonary to systemic blood flow, which may lead to arterial desaturation. Ketamine did not produce these changes. The authors suggested that during cardiac catheterization in children, both the anesthesiologists and cardiologists need to know that anesthetic agents can significantly alter the hemodynamic status in children with complex congenital heart defects and affect the results of hemodynamic calculations that are important for decision-making and treatment of these patients.**

KEY WORDS: pediatric, cardiac catheterization, propofol, ketamine

THE RAPID TECHNOLOGIC advancement in diagnostic and interventional cardiology has introduced widespread use of cardiac catheterization into the management of congenital heart disease (CHD). These procedures produce challenges for the anesthesiologist because of the increased need to provide support in sedating and/or anesthetizing these patients. The goals for the anesthetic management of children require adequate sedation and immobility. The anesthesiologist must also have a clear understanding of the pathology of the cardiac lesion and recognize the possible circulatory impact of the acutely altered physiologic status. Although a wide variety of pharmacologic agents and techniques have been successfully used for these procedures, studies that have examined the hemodynamic consequences of anesthetic agents mostly focused on changes in heart rate and blood pressure.[1-4] This study was designed to investigate the additional hemodynamic consequences of propofol and ketamine infusions during cardiac catheterization in children with congenital cardiac diseases.

METHODS

After approval of the ethics committee and informed consent from the parent, 41 patients, aged 1 month to 13 years, American Society of Anesthesiologists physical status II and III, scheduled for elective cardiac catheterization for evaluation of congenital heart disease were included in the study. Patients based on the shunt type (diagnosed by transthoracic echocardiography before the catheterization procedure) were separated into 3 groups: patients without a cardiac shunt (Group I, n = 11), patients with a left-to-right shunt (Group II, n = 12), and patients with right-to-left shunt (Group III, n = 18). Exclusion criteria included patients requiring mechanical ventilation or inotropic support. After a minimum fasting period of 4 hours in infants and 6 hours in children, all patients were premedicated with oral midazolam, 0.5 mg/kg, 60 minutes before transfer to the cardiac catheterization labora-

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Table 1. Congenital Cardiac Pathology of All Patients

Propofol Infusion Groups	Ketamine Infusion Groups
Group I (n = 4)	Group I (n = 7)
PS + TGA (repaired)	Subaortic stenosis
PS	Subvalvular PS + TGA (repaired)
PS + TOF (repaired)	PS
PS	Aortic coarctation
Group II (n = 8)	PS
AS + VSD	Aortic coarctation
VSD	Aortic coarctation
VSD	Group II (n = 4)
VSD + PS + BT shunt	Aortic coarctation + ASD
VSD + PH	VSD + PS
VSD + PH	VSD + PS
VSD	VSD
VSD + PS	—
Group III (n = 9)	Group III (n = 9)
TOF + BT shunt	TOF + BT shunt
TOF	TOF + BT shunt
UVH. + PDA	TOF
AVSD + PS	TOF
AVSD + BT Shunt	VSD + AVSD + PAB.
TOF	AVSD + PAB.
TOF	TOF
TOF	TGA + ASD + BT shunt
TGA + ASD + PAB + BT shunt	TOF

Abbreviations: PS, pulmonic stenosis; TGA, transposition of great arteries; TOF, tetralogy of Fallot, AS, aortic stenosis; VSD, ventricular septal defect; BT, Blalock-Taussig shunt; PDA, patent ductus arteriosus; ASD, atrial septal defect; PAB, pulmonary artery banding; PH, pulmonary hypertension; UVH, univentricular heart; AVSD, atrioventricular septal defect.

tory. A reliable intravenous catheter was secured and maintenance fluid (1/4 normal saline in 5% to 10% dextrose) was started at a rate of 100 mL/kg/24 hours.

On arrival in the catheterization laboratory, patients were monitored with an electrocardiogram (lead II), a noninvasive blood pressure device, and a pulse oximeter (Nellcor Inc., Hayward, CA). Under local anesthesia, a 5F or 6F catheter was inserted percutaneously into the femoral artery by the cardiologist (who was blinded to the study drug). Left heart catheterization was done with a pigtail catheter entering the aorta and left ventricle. A right heart catheterization was also performed with a Berman angiographic balloon catheter passed from the femoral vein into the right atrium, right ventricle, and pulmonary artery under fluoroscopic control by the cardiologist. The arterial and right heart catheters were attached to pressure transducers (Model 1280; Hewlett Packard, Waltham, MA) for continuous pressure readouts. During initial placement of the sheaths, intravenous thiopental, 2 to 3 mg/kg, was administered to keep the patient appropriately sedated. In an attempt to reduce the effect of thiopental on hemodynamic measurements, data were not recorded within 10 minutes of the thiopental.

After insertion of the catheters, systemic venous, pulmonary artery and vein, and aortic pressures were recorded. Analyses of blood gases from the same sites were performed, and oxygen saturations were recorded. Pulmonary and systemic blood flow (Qp, Qs) were calculated by the Fick principle. Pulmonary and systemic vascular resistances were calculated. All groups of patients were allocated via a randomization-generated computer program to receive either a propofol infusion (100-200 μg/kg/min) or ketamine infusion (50-75 μg/kg/min) for the duration of the procedure. Two sets of data were obtained: the first before the administration of the propofol or ketamine infusion and the second before discontinution of the infusions when a steady state was achieved during the procedure. All patients breathed spontaneously, and supplemental oxygen was not provided until completion of the study.

Results were expressed as mean ± SD. Statistical analysis was performed by using the statistic package named Graphadprism (GraphPad Software, Inc. England). Within each group, values before and after the infusions were compared and differences between the groups were analysed by using a Mann Whitney *U* and Wilcoxon analysis; $p < 0.05$ was considered statistically significant.

RESULTS

Forty-one children were enrolled. All patients completed the study protocol and no patient required supplemental oxygen. Patients' demographic data are presented in Tables 1 and 2. Group I (n = 11) patients had no cardiac shunt; 7 patients received ketamine, and 4 patients received propofol. In Group II (n = 12), patients had a left-to-right cardiac shunt, 4 patients received ketamine, and 8 patients received propofol. Children in Group III (n = 18) had right-to-left shunt; 9 patients received ketamine, and 9 patients received propofol. Arterial blood gas analysis and hemodynamic data of Group I (no intracardiac shunting) are shown in Table 3.

Propofol infusion was associated with significant decreases in mean systemic arterial pressure (SMAP). Arterial blood gas analysis and hemodynamic data of Group II and III (left-to-right and right-to-left intracardiac shunting) are shown in Tables 4 and 5. Group III patients suffered from cyanotic heart disease and had significantly lower baseline SaO_2 values than patients in Group I and Group II. In both groups with a shunt (Groups II and III) significant decreases in systematic vascular resistance (SVR) and significant increases in Qs followed; whereas pulmonary vascular resistance (PVR) and Qp did not change significantly. These changes resulted in a significant increase in the ratio of pulmonary to systemic resistance and significant decrease in the ratio of Qp/Qs.

In all 3 patient groups, ketamine infusion was associated with significant increase in mean systemic arterial pressure ($p < 0.05$), but no statistical difference was found in SVR, PVR, PVR/SVR, and Qp/Qs.

DISCUSSION

Several different anesthetic agents have been safely used for cardiac catheterization in patients with CHD who now remain relatively immobile and sedated during the procedure. The maintenance of spontaneous ventilation without supplemental oxygen and the effects of anesthetic agents on the magnitude and direction of intracardiac shunt are very important so that the hemodynamic data obtained by the cardiologist will be meaningful. In this study, the hemodynamic effects of propofol

Table 2. Demographic Data of All Patients

	Age (yr)		Weight (kg)	
	Propofol	Ketamine	Propofol	Ketamine
Group I	3.07 ± 2.41	6.10 ± 3.30	11.25 ± 4.1	19.81 ± 7.19
Group II	4.51 ± 3.58	6.22 ± 6.72	15.03 ± 7.58	16.75 ± 14.24
Group III	3.25 ± 2.63	4.03 ± 3.3	11.44 ± 4.74	14.06 ± 5.78

Table 3. Arterial Blood Gas Analysis Data and Hemodynamic Data of Group I (No Intracardiac Shunting)

Variable	Before Propofol	After Propofol	Before Ketamine	After Ketamine
Arterial pH	7.35 ± 0.42	7.33 ± 0.20	7.33 ± 0.4	7.32 ± 0.12
$PaCO_2$ (mmHg)	37 ± 6	39 ± 2	36 ± 6	35 ± 4
PaO_2 (mmHg)	98 ± 10	93 ± 14	97 ± 9	93 ± 14
SaO_2 (%)	96 ± 1.5	95 ± 1.1	95 ± 1.0	94 ± 1.8
HR (beats/min)	96.75 ± 60.91	119.8 ± 20.52	101.9 ± 19.61	104.7 ± 19.64
SMAP (mmHg)	73.75 ± 3.59	65.50 ± 1.91*	70.77 ± 14.01	78.0 ± 13.43*†
PMAP (mmHg)	14.50 ± 3.69	19.25 ± 4.78	19.86 ± 10.12	20.14 ± 10.88
Qp (L/min/m²)	4.53 ± 0.76	6.85 ± 5.30	6.29 ± 5.69	6.71 ± 5.86
Qs (L/min/m²)	4.89 ± 0.25	5.15 ± 0.59	5.25 ± 2.85	7.87 ± 7.02
Qp/Qs	0.92 ± 0.13	1.28 ± 0.89	1.08 ± 0.26	0.93 ± 0.13
PVR (wood units/m²)	1.11 ± 1.31	1.72 ± 2.29	3.03 ± 1.57	2.97 ± 1.69
SVR (wood units/m²)	13.88 ± 2.07	12.67 ± 5.07	15.88 ± 6.78	12.91 ± 6.73
PVR/SVR	0.75 ± 0.7	0.11 ± 0.11	0.17 ± 0.07	0.24 ± 0.15

NOTE. Data are mean ± SD.

Abbreviations: HR, heart rate; SMAP, systemic mean arterial pressure; PMAP, pulmonary mean arterial pressure; Qp, pulmonary blood flow; Qs, systemic blood flow; Qp/Qs, pulmonary to systemic blood flow ratio; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; PVR/SVR, pulmonary to systemic resistance ratio.

*Data before and after were compared (significance set at $p < 0.05$).

†Values differed significantly among groups (significance set at $p < 0.05$).

and ketamine infusion were studied in children with congenital heart diseases undergoing cardiac catheterization.

Ketamine is widely used as a constant infusion for maintenance of anesthesia in children for cardiac catheterization. In a retrospective review, ketamine infusion was the technique most frequently preferred by the anesthesiologist.[5] When used as a constant infusion for maintenance of anesthesia during cardiac or noncardiac procedures, the ketamine infusion rate has been 50 μg/kg/min in most of the studies.[6,7] The authors have used the same dose in patients who received supplemental midazolam for premedication and found it satisfactory. Its potential advantages include sympathic stimulation with support of the blood pressure and heart rate, excellent sedation and analgesia, and maintenance of airway reflexes and respiratory drive. However, ketamine is associated with a prolonged recovery period, emergence delirium, and nonpurposeful movements with or without noxius stimuli. In addition, its effects on pulmonary vascular resistance are still controversial. Ketamine was initially considered to increase PVR in adult patients with pulmonary vascular disease.[8,9] However, studies of ketamine in infants with normal or elevated PVR have shown no increase in PVR when ventilation and F_IO_2 are held constant.[10,11] In another report, Santolini et al[12] stated that there were no complications related to a drop in pulmonary blood flow caused by a shunt inversion or by an increase in a right-to-left shunt. In the present study, there were no significant changes after ketamine in SVR, PVR, and Qp/Qs ratio; there was a significant increase in SMAP in all 3 groups.

Table 4. Arterial Blood Gas Analysis Data and Hemodynamic Data of Group II (Left-to-Right Intracardiac Shunting)

Variable	Before Propofol	After Propofol	Before Ketamine	After Ketamine
Arterial pH	7.36 ± 0.03	7.35 ± 0.20	7.34 ± 0.12	7.32 ± 0.49
$PaCO_2$ (mmHg)	35 ± 5.8	37 ± 3	38 ± 4.9	35 ± 5.2
PaO_2 (mmHg)	95 ± 15.45	94 ± 11.02	96 ± 8.15	94 ± 10
SaO_2 (%)	95 ± 2.1	94 ± 1.7	95 ± 2.63	94 ± 3.4
HR (bpm)	111.1 ± 20.69	112.5 ± 26.88	125.8 ± 38.58	122.5 ± 32.6
SMAP (mmHg)	66.46 ± 7.43	57.53 ± 7.67*	63.26 ± 5.88	71.16 ± 5.99*†
PMAP (mmHg)	27.86 ± 18.22	31.00 ± 20.58	37.25 ± 21.45	37.0 ± 23.59
Qp (L/min/m²)	9.12 ± 2.34	12.77 ± 3.5	6.81 ± 0.80	6.71 ± 0.81†
Qs (L/min/m²)	5.31 ± 1.42	7.35 ± 1.71*	3.70 ± 1.95	5.06 ± 1.08†
Qp/Qs	1.74 ± 0.37	1.22 ± 0.32*	2.19 ± 0.97	1.37 ± 0.4
PVR (wood units/m²)	2.16 ± 1.61	1.99 ± 1.79	4.40 ± 3.94	4.30 ± 3.78
SVR (wood units/m²)	13.66 ± 5.12	8.75 ± 2.32*	13.91 ± 4.1	21.33 ± 1.11†
PVR/SVR	0.19 ± 0.17	0.26 ± 0.28*	0.21 ± 0.16	0.27 ± 0.17

NOTE. Data are mean ± SD.

Abbreviations: HR, heart rate; SMAP, systemic mean arterial pressure; PMAP, pulmonary mean arterial pressure; Qp, pulmonary blood flow; Qs, systemic blood flow; Qp/Qs, pulmonary to systemic blood flow ratio; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; PVR/SVR, pulmonary to systemic resistance ratio.

*Data before and after were compared (significance set at $p < 0.05$).

†Values differed significantly among groups (significance set at $p < 0.05$).

Table 5. Arterial Blood Gas Analysis Data and Hemodynamic Data of Group III (Right-to-Left Intracardiac Shunting)

Variable	Before Propofol	After Propofol	Before Ketamine	After Ketamine
Arterial pH	7.36 ± 0.52	7.34 ± 0.46	7.33 ± 0.5	7.32 ± 0.55
$PaCO_2$ (mmHg)	38 ± 3.78	40 ± 4.6	37 ± 4.15	40 ± 5.33
PaO_2 (mmHg)	52 ± 10	44 ± 14*	56 ± 9.28	52 ± 7.15†
SaO_2 (%)	83 ± 7	76 ± 10*	88 ± 7.9	87 ± 4.6†
HR (bpm)	123.8 ± 21.58	121.4 ± 21.61	111.8 ± 16.51	115.6 ± 19.71
SMAP (mmHg)	71.83 ± 10.82	57.89 ± 10.70*	59.73 ± 10.14	72.14 ± 11.49*†
PMAP (mmHg)	20.78 ± 16.47	21.67 ± 17.12	16.44 ± 12.35	17.44 ± 12.45
Qp (L/min/m²)	8.22 ± 8.35	6.75 ± 4.84	4.30 ± 2.10	4.43 ± 1.47
Qs (L/min/m²)	7.57 ± 3.91	8.68 ± 0.05*	4.33 ± 1.51	5.57 ± 1.49†
Qp/Qs	0.90 ± 0.59	0.60 ± 0.27*	0.99 ± 0.29	1.51 ± 2.08
PVR (wood units/m²)	2.37 ± 2.39	2.75 ± 2.93	1.96 ± 2.04	2.31 ± 1.95
SVR (wood units/m²)	10.67 ± 3.77	7.97 ± 2.30*	13.11 ± 4.74	16.87 ± 5.97†
PVR/SVR	0.37 ± 0.67	0.40 ± 0.57*	0.17 ± 0.22	0.19 ± 0.20

NOTE. Data are mean ± SD.

Abbreviations: HR, heart rate; SMAP, systemic mean arterial pressure; PMAP, pulmonary mean arterial pressure; Qp, pulmonary blood flow; Qs, Systemic blood flow; Qp/Qs, pulmonary to systemic blood flow ratio; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; PVR/SVR, pulmonary to systemic resistance ratio.

*Data before and after were compared (significance set at $p < 0.05$).

†Values differed significantly among groups (significance set at $p < 0.05$).

Propofol is likely to be used increasingly in children with congenital heart disease. It may become a preferred option in hemodynamically stable patients with CHD admitted for cardiac catheterization. Lebovic et al[13] have shown that a propofol infusion with fentanyl analgesia was associated with significantly shorter recovery times than ketamine/midazolam anesthesia in pediatric cardiac catheterization procedures. Despite rapid recovery from anesthesia and less agitation, a potential disadvantage of propofol infusion is the lack of analgesia at subanesthetic plasma concentrations, which may lead to excessive movement. Also respiratory support may be needed because of the high risk of respiratory depression. Every effort is made to maintain spontaneous ventilation and to minimize supplemental oxygen during cardiac catheterization so that the hemodynamic data obtained by the cardiologist will be meaningful. It has been suggested that propofol causes a 20% to 40% decrease in blood pressure, primarily via systemic vasodilation, and the hemodynamic changes induced by propofol may alter the information obtained during cardiac catheterization.[14,15] Its hemodynamic profile may also require caution, especially in patients for whom systemic afterload reduction may be harmful (eg, patients with aortic stenosis) and in cyanotic patients whose pulmonary blood flow depends on the balance between systemic and pulmonary vascular resistance (eg, hypoplastic left heart syndrome after the Norwood palliation). In the present report, propofol's principal effects were reductions in SMAP and SVR in all groups. Because PVR remained constant, the ratio between pulmonary and systemic resistance was increased. In children with a cardiac shunt, the increased PVR/SVR ratio led to a diminished left-to-right shunt, increased right-to-left shunt, and a decrease in Qp/Qs ratio. In cyanotic children, the reduced pulmonary blood flow may increase the risk of arterial desaturation.

During cardiac catheterization, a propofol infusion may increase cyanosis in children with right-to-left cardiac shunts or may change the direction of intracardiac shunt flow, whereas ketamine had a minimal effect on PaO_2 and SaO_2. Interpretation of hemodynamic data obtained during cardiac catheterization of children requires awareness of the cardiac pathophysiology.

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