



# Comparative Assessment of Propofol and Ketamine on Hemodynamic Indices and Cerebral Oximetry of Pediatric Patients Undergoing Cardiac Catheterization

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Received 2022 June 05; Revised 2022 October 26; Accepted 2022 November 11.

## Abstract

**Background:** Propofol and ketamine are widely used in the induction and maintenance of anesthesia and sedation with different cardiovascular and respiratory effects. In cardiac anesthesia (including pediatric cardiac catheterization), due to the high risk of neurologic complications, cerebral oximetry can effectively monitor cerebral blood oxygen saturation to prevent neurological and respiratory complications.

**Objectives:** This study aimed to compare the effect of propofol and ketamine on hemodynamic indices and cerebral oxygenation results in children undergoing cardiac catheterization.

**Methods:** This clinical trial study was performed on 48 patients who were candidates for cardiac catheterization by easy and continuous sampling. Patients were randomly divided into 2 groups: ketamine and propofol. In the ketamine group, ketamine was injected at a dose of 1-2 mg/kg, and in the propofol group, propofol was injected at a dose of 0.5-1.5 mg/kg. In both groups, incremental doses were repeated as needed. The hemodynamic indices, including blood pressure, heart rate, and peripheral SpO<sub>2</sub>, were recorded. Cerebral regional oxygen saturation (RSO<sub>2</sub>) was recorded using infrared spectroscopic sensors. Data were analyzed using chi-square, independent t-test, paired t-test, and 1-way analysis of variance (ANOVA).

**Results:** The results showed that all demographic characteristics of patients and also the mean duration of catheterization were homogeneous between the 2 groups. Hemodynamic indices (such as systolic, diastolic, and mean arterial blood pressure) did not show a significant difference between the 2 groups; however, in the ketamine group compared to the propofol group, the heart rate was significantly higher, and mean RSO<sub>2</sub> was lower ( $P = 0.023$ ).

**Conclusions:** Propofol has fewer complications than ketamine and is a good drug for sedating children undergoing cardiac catheterization.

**Keywords:** Propofol, Ketamine, Cerebral Oximetry, Cardiac Catheterization

## 1. Background

Cardiac catheterization is one of the most important diagnostic and therapeutic tools and has a long history (1). During cardiac catheterization, what matters the most to pediatricians and cardiologists is the least movement of the patient during the operation (2). There are various approaches to sedating children during cardiac catheterization. The ideal method should be safe and easy to use and provide enough sedative effect, cardiovascular stability, immobility during the procedure, and no residual complications (3).

Propofol is a sedative commonly used in general anesthesia. It has no analgesic effect but has side effects such as dose-related cardiovascular and respiratory suppression,

bradycardia, and severe reduction in blood pressure, arising from the reduction of tissue blood flow and oxygenation (4). The main benefits of this drug include rapid onset of action, reduction of nausea/vomiting, lack of active metabolites, and rapid liver clearance after intravenous injection (5, 6).

Sedatives and analgesics, such as ketamine, are used in painful conditions in children. Ketamine causes severe analgesia, stimulation of the sympathetic nervous system, increased blood pressure, and increased heart rate. Unlike propofol, ketamine has the least cardiovascular and respiratory suppression; protective airway reflexes and spontaneous respiration remain intact (7, 8).

One of the most advanced and newest monitors for

patients under anesthesia is cerebral oximetry by near-infrared spectroscopy (NIRS) through sensors located in the forehead skin. Cerebral oxygenation is affected by variables such as cerebral blood flow (CBF), cerebral metabolic rate of oxygen (CMRO<sub>2</sub>), and mean arterial pressure (MAP) (9). Cerebral oximetry is non-invasive monitoring of cerebral blood oxygen saturation that has a more venous basis (10). It depends on the permeability of the skull and brain tissue to infrared light, through which oxygen saturation of the brain can be easily detected (11, 12).

Different results have been reported in studies comparing the effects of ketamine and propofol in pediatric sedation. Lebovic and colleagues reported that propofol has a much shorter recovery time than ketamine (13). Other studies have confirmed the effect of propofol in reducing recovery time (14, 15). Kariman Majd and colleagues stated that systolic and diastolic blood pressure increased the most after ketamine and decreased the most after propofol injection (14). Akin and colleagues also reported that the propofol-ketamine combination, regardless of longer recovery time, causes fewer changes in patients' hemodynamics than propofol injection alone (16).

Ketamine and propofol are widely used to induce anesthesia and have markedly opposite cardiovascular and respiratory effects. However, the effects of these drugs on CBF and CMRO<sub>2</sub>, especially in children with congenital heart disease, are not fully understood. Cerebral oximetry is necessary to monitor cerebral blood oxygen saturation during cardiovascular surgical and nonsurgical procedures to prevent neurological complications.

## 2. Objectives

This study aimed to compare the effect of propofol and ketamine on hemodynamic indices and cerebral oxygenation of pediatric patients undergoing cardiac catheterization, considering we could not find any article specifically addressing this issue.

## 3. Methods

This double-blind, randomized clinical trial was performed in a catheterization laboratory. The study group consisted of children referred to diagnostic and therapeutic cardiac catheterization from October 2020 to February 2021.

### 3.1. Inclusion and Exclusion Criteria

Inclusion criteria were children aged 2 months to 14 years who were candidates for cardiac catheterization. Exclusion criteria were parental refusal to participate in the

study, known allergy to ketamine or propofol or any contraindication of their use, a history of seizures or other neurological diseases, significant growth retardation, and renal and hepatic insufficiency. Informed consent was obtained from all children's parents.

### 3.2. Sampling

Sample size calculation was obtained by Altman nomogram with the standardized difference of 1.1% and 95% power. A total of 48 patients were selected by convenience and continuous sampling. They were divided into 2 groups of 24 subjects by simple random sampling using the coin toss method.

### 3.3. Clinical Management

In the first group, ketamine was used for sedation, and in the second group, propofol was used. Thus, after obtaining written consent from the patients' parents, the patients underwent complete cardiopulmonary monitoring and pulse oximetry. A sphygmomanometer cuff was attached to the patient's arm to measure blood pressure, and a pulse oximetry probe was installed on the patient's finger to measure arterial oxygen saturation. Infrared spectroscopic sensors are installed on the right and left sides of the patient's forehead, 2 cm above the eyebrows in the midline of the forehead, according to the manufacturer's instructions to measure RSO<sub>2</sub>. The skin of the forehead area under the sensors was cleaned with alcohol, and the sensors were fixed with a bandage to prevent detachment (8). An antecubital IV line was fixed for drug administration. Patients' hemodynamic indices were measured and recorded. All patients fasted for at least 6 hours before starting sedation. When patients entered the catheterization room, hemodynamic indices and RSO<sub>2</sub> were recorded. Then, under the supervision of an anesthesiologist, patients in both groups were first initially sedated with 0.1 mg of midazolam per kg of body weight, and oxygen therapy with an oxygen mask of 3 L per minute was established for them. In the first group, ketamine at a dose of 1-2 mg per kg of body weight was injected to sedate patients, and if necessary, repeated doses of 1 mg per kg were injected during the procedure. In the second group, propofol at a dose of 0.5-1.5 mg per kg of body weight was gently used for sedation, and as needed, an additional IV bolus dose of 0.5 mg per kg was provided; it was no earlier than 5 minutes from the previous dose. The total anesthetic dose was calculated individually for the final analysis of the 2 groups. A constant interventional cardiologist performed the cardiac catheterization procedure.

### 3.4. Data Collection

For data collection, we used the data recorded from the NIRS monitoring device, which was started at the first moments of patient care, was continued through the operation, and in the post anesthesia care unit (PACU) until patient delivery to the cardiac surgery ward (this device measures the  $\text{RSO}_2$  values, using infrared spectroscopic sensors which are usually placed on the forehead during anesthesia). The protocol for data collection included the following mandatory steps:

- At the time before catheterization as the baseline value;
- During induction of anesthesia;
- Every 5 minutes afterwards (during the procedure until its termination);
- During patient care in PACU.

Also, we measured and recorded the hemodynamic parameters using the following protocol by the cardiopulmonary monitoring device:

- Before starting the procedure;
- Every 5 minutes during the procedure;
- During patient care in PACU.

### 3.5. Data Analysis

Data were analyzed using SPSS version 26 (SPSS Inc., Chicago, Ill, USA), as well as using descriptive statistics, Fisher exact test, chi-square, Mann-Whitney, independent t test, paired t test, and independent *t* test. *P* values less than 0.05 were considered statistically significant.

## 4. Results

The results showed that 41.7% of patients in the ketamine group and 58.3% in the propofol group were males. The mean age of patients in the ketamine group was  $63.37 \pm 53.12$  and in the propofol group was  $62.04 \pm 59.83$  months. Statistical tests showed no statistically significant difference in all demographic characteristics, diagnosis of disease, and catheterization time between the 2 groups, and they were homogeneous (Table 1).

The total anesthetic doses in the 2 study groups were as follows:

- In the first group (ketamine) =  $6 \pm 3.8$  mg/kg;
- In the second group (propofol) =  $5.5 \pm 3$  mg/kg.

Data analyses showed that systolic, diastolic, and mean arterial blood pressure, as well as peripheral blood oxygen saturation and recovery time between the 2 groups, had no statistically significant difference, but the heart rate was significantly higher in the ketamine group than in the propofol group (Table 2).

The results showed that cerebral oximetry was not significantly different in the 2 groups before the intervention; however, cerebral oximetry significantly decreased in the ketamine group than in the propofol group after the intervention (Table 3).

## 5. Discussion

The sedative effects of anesthetic drugs (such as ketamine and propofol) have been studied in various studies. In this study, we investigated the sedative effects of ketamine and propofol on hemodynamic and cerebral oximetry parameters in children undergoing cardiac catheterization.

The results of the present study showed that all demographic characteristics, as well as catheterization time between the 2 groups, had no statistically significant difference and were homogeneous. The homogeneity of demographic characteristics between the 2 groups minimizes the effect of confounding variables that could affect the results; therefore, the changes in hemodynamic parameters, as well as brain oximetry results, can be more decisively attributed to the effects of these 2 drugs.

The present study showed that the heart rate was significantly higher in the ketamine group than in the propofol group. These results are consistent with Kariman Majd et al. (14), Shetabi et al. (17), and Yazdi et al. (18). However, they are in contradiction with the results of Maneglia and Cousin (19) and Shahryari et al. (20). In these studies, it was stated that the heart rate in patients sedated with ketamine and propofol had no statistically significant difference. It seems that the increased heart rate in the ketamine group was due to an increase in sympathetic stimulation.

Consistent with Shahryari et al. (20) and Yazdi et al. (18), our results showed no statistically significant difference between the 2 groups in terms of mean arterial blood oxygen saturation; however, it is contrary to the study of Greeley et al. (21). Arterial blood oxygen saturation is affected by various factors, and due to the lack of differences between blood pressure indices in this study, arterial oxygen saturation did not show a significant difference.

In this study, systolic, diastolic, and mean arterial blood pressure indices were not significantly different between the 2 groups. These results are consistent with Shahryari et al. (20) and Shetabi et al. (17) but in contradiction with Kariman Majd et al. and Yazdi et al., Kariman Majd et al. stated that propofol injection led to increased blood pressure and ketamine injection caused hypotension (14). Yazdi et al. also stated that both systolic and diastolic blood pressure indices significantly increased in the ketamine group than in the propofol group (18). However, Greeley et al. showed that blood pressure decreased

**Table 1.** Demographic Characteristics of Patients in the 2 Groups<sup>a</sup>

Groups	Ketamine (24 Patients)	Propofol (24 Patients)	P Value (Test Type)
<b>Sex</b>	0.248 (chi-square)		
Female	10 (41.7)	14 (58.3)	
Male	14 (58.3)	10 (41.7)	
<b>Age (mo)</b>	63.37 ± 53.12	62.04 ± 59.83	0.935 (independent <i>t</i> test)
<b>Weight (kg)</b>	17.29 ± 12.84	18.12 ± 14.14	0.832 (independent <i>t</i> test)
<b>Diagnosis of disease</b>	0.068 (fisher exact test)		
ASD	2 (8.4)	1 (4.2)	
AVSD	1 (4.2)	3 (12.6)	
TF	4 (16.7)	2 (8.4)	
VSD	5 (20.8)	2 (8.4)	
AS	0 (0)	1 (4.2)	
Other	12 (50)	15 (62.5)	
<b>Catheterization time (min)</b>	46.25 ± 9.58	42.08 ± 8.58	0.120 (independent <i>t</i> test)

Abbreviations: ASD, atrial septal defect; AVSD, atrioventricular septal defect; TF, tetralogy of fallot; VSD, ventricular septal defect; AS, aortic stenosis.

<sup>a</sup> Values are expressed as No. (%) or mean ± SD.**Table 2.** Comparison of Blood Pressure, Heart Rate, Arterial Blood Oxygen Saturation, and Recovery Time Indices Between the 2 Groups

Groups	Ketamine (24 Patients)	Propofol (24 Patients)	P Value (Test Type)
<b>Recovery time (min)</b>	18.12 ± 5.67	17.5 ± 6.25	0.719 (independent <i>t</i> test)
<b>SBP (mmHg)</b>	94.95 ± 12.46	92.26 ± 18.61	0.346 (independent <i>t</i> test)
<b>DBP (mmHg)</b>	57.7 ± 9.05	54.37 ± 13.21	0.313 (independent <i>t</i> test)
<b>MAP (mmHg)</b>	70.12 ± 8.9	66.45 ± 14.65	0.300 (independent <i>t</i> test)
<b>HR (pulse)</b>	141.62 ± 21.93	125.54 ± 25.46	0.023 (independent <i>t</i> test)
<b>SpO<sub>2</sub></b>	95.25 ± 4.56	96.83 ± 4.15	0.215 (independent <i>t</i> test)

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; SpO<sub>2</sub>, saturation of peripheral oxygen.**Table 3.** Comparison of the Cerebral Oxygen Saturation of Patients Within and Between the 2 Groups Before and After the Intervention (Drug Administration)

Group	Ketamine (24 Patients)	Propofol (24 Patients)	P Value (Test Type)
<b>RSO<sub>2</sub> Before the Intervention (%)</b>	75.25 ± 13.02	76.92 ± 9.67	0.644 (independent <i>t</i> test)
<b>RSO<sub>2</sub> after the intervention (%)</b>	70.29 ± 11.21	76.95 ± 8.22	0.023 (independent <i>t</i> test)
<b>P value (test type)</b>	0.002 (paired <i>t</i> test)	0.849 (paired <i>t</i> test)	

sharply following induction with propofol (21). Rau et al. also reported a 30% reduction in blood pressure following propofol injection (22). Also, Aydoğan et al. reported that propofol injection reduced mean arterial blood pressure while its combination with ketamine had fewer hemodynamic changes (23). Ozgül et al. reported a significant change in systolic blood pressure in the propofol group compared to the ketamine group (24). The results of all 5 studies are in contradiction with the results of the present study, and it seems that it is due to the dose differences between the two studies; we used sedation dose while the

other study used higher doses.

The last item studied in this trial was RSO<sub>2</sub> measured by NIRS. NIRS has been studied to estimate mixed venous oxygen saturation (25) and jugular bulb venous saturation (26) in pediatric cardiac catheterization laboratories. The findings of this non-invasive monitor have also been investigated in the presence of other drugs, such as dexmedetomidine. However, a comparative study of the effect of propofol and ketamine on RSO<sub>2</sub> is very limited and mainly performed in adults (27), and the current study is unique in this respect. The results showed that the 2 groups had

a statistically significant difference in terms of  $\text{RSO}_2$ ; thus,  $\text{RSO}_2$  was significantly lower in the ketamine group than in the propofol group.  $\text{RSO}_2$  decreased significantly in the ketamine group than in the propofol group before the intervention. These results are in contradiction with the results of Duran *et al.*, showing that the results of brain oximetry were significantly lower in the propofol group than in the ketamine group after induction of sedation (11). However, other studies have shown that ketamine has a negligible effect on  $\text{CMRO}_2$  and no effect on CBF (28). In these studies, the effects of the drug on CBF were due to its metabolic effect but not vasodilatory effect (29). However, there are conflicting results in this area; for instance, Strelbel *et al.* reported that inhibition of arterial hypertension with esmolol did not prevent the ketamine-induced increase in CBF velocity and suggested that ketamine increased CBF velocity via a direct effect rather than a secondary effect caused by a change in arterial pressure and/or  $\text{PaCO}_2$  (30). Another explanation for the ketamine-induced increase in CBF is that ketamine-induced central nervous excitation stimulates cerebral metabolism (31). On the other hand, Sakai *et al.* suggested ketamine had no effect on the cerebral artery blood flow velocity or the cerebrovascular  $\text{CO}_2$  response (32). However, recent studies suggest a ketamine-induced increase in CBF (33), at times leading to significant changes in  $\text{CMRO}_2$  and/or  $\text{rCMRO}_2$  (34). On the other hand, propofol is believed to reduce CBF,  $\text{CMRO}_2$ , and intracranial pressure, but more precisely, normal cerebral circulation and metabolism are maintained in the presence of propofol, especially if the hemodynamic indices do not change dramatically, as happened in our study (35).

Can relatively inconsistent findings of this study with other studies about the effect of ketamine on CBF and  $\text{RSO}_2$  be attributed to increased brain metabolism over increased CBF?

Ketamine increases the body's basal metabolism, leading to an increase in the oxygen consumption of the whole body and brain tissues. As a result,  $\text{RSO}_2$  and brain oximetry decrease. The effect of anesthetic drugs on brain autoregulation is not fully understood, especially in children. CBF increases rapidly from 7 months to 6 years of age and declines thereafter (36). Can immaturity of cerebral autoregulation in children affect the obtained results? In the absence of cerebral autoregulation, CBF depends on systemic arterial pressure. Sub-anesthetic doses of ketamine that do not significantly alter the hemodynamics indices of the child cannot lead to an increase in CBF and subsequent increase in  $\text{RSO}_2$ . However, studies in children with larger sample volumes for sub-anesthetic doses of the drug that do not cause dramatic hemodynamic changes are necessary.

### 5.1. Conclusions

Comparing the effect of ketamine and propofol on hemodynamic and  $\text{RSO}_2$ , hemodynamic symptoms did not change significantly, except for the heart rate in the ketamine group; however,  $\text{RSO}_2$  was lower in the ketamine group. Therefore, we conclude that propofol, due to less complication than ketamine, is a good drug for sedating children undergoing cardiac catheterization.

### 5.2. Limitations

Like other studies, the present study has its limitations. Individual, social, psychological, and family differences are among the uncontrollable variables that can affect the outcome of the research. The number of patients in the study groups did not seem to be sufficient. With the increasing number of patients, the difference between the 2 groups could be statistically significant in some variables.

### 5.3. Suggestions

In the present study, some important variables in evaluating the research results (such as environmental conditions, type of drug used, etc.) have not been studied. Therefore, further research is recommended to investigate the effect of these variables. It is also recommended to conduct more research with a higher number of samples in different research environments to compare with the results of the present study.

### Acknowledgments

We would like to express our sincere gratitude for the cooperation of all the esteemed officials of Shahid Modares Hospital in Tehran and all the esteemed staff of the angiography department.

### Footnotes

**Authors' Contribution:** K. F. and M. S. N. had substantial contributions to the conception of the work and collected data. A. D. contributed to the acquisition, analysis, or interpretation of data for the work. K. F. and M. S. N. drafted the work, and A. D. critically alternated the work. All the authors approved the final version for publication. All the authors take into account the responsibility for all aspects of the work and its related accuracy and integrity of any part of the work.

**Clinical Trial Registration Code:** Iranian clinical trial number: IRCT20180724040575N1 (<https://en.irct.ir/trial/50809>)

**Conflict of Interests:** The authors have no conflicts of interest to declare.

**Data Reproducibility:** The data presented in this study are uploaded during submission as a supplementary file and are openly available for readers upon request.

**Ethical Approval:** The Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study (code: IR.SBMU.REC.1398.137) (ethics.research.ac.ir/IR.SBMU.REC.1398.137).

**Funding/Support:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Informed Consent:** Written consent was obtained from all patients' parents.

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