Effect of Sevoflurane and Propofol on pulmonary arterial pressure during cardiac catheterization in children with congenital heart diseases

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Abstract

Background: The aim of this study was to investigate the effect of sevoflurane and propofol on pulmonary arterial pressure during cardiac catheterization in children with congenital heart diseases.

Methods: In order to reach the research goals, 80 patients with congenital heart disease who had referred to Modarres Hospital, Iran for cardiac catheterization were selected as sample. They were divided into two groups for treatment with propofol or sevoflurane. In children in the sevoflurane group, anesthesia began initially with higher concentrations of sevoflurane (4-6%) and spontaneous respiration by face mask with suitable size and gradually the concentration of gas was reduced by increasing the anesthetic depth and anesthesia was continued with 1 MAC inhaled Sevoflurane based on age and individual characteristics of each patient and spontaneous respiration. In the other group, propofol drug (50-70 μg/ kg/min) was injected by perfusion pump. Cardiac catheterization was performed by injection of lidocaine into the catheter entrance i.e. the femoral vessel when the anesthetic depth reached to Ramsay Sedation Score = 3 and BIS = 65-85. Meanwhile, in the groups of sevoflurane and Propofol, systolic and diastolic blood pressure in pulmonary patients was recorded before andduring catheterization. T-test was used to analyze the data.

Results: The findings showed that there was no significant reduction in systolic and diastolic pulmonary arterial pressure in the sevoflurane group in the pretest or posttest, while in the propofol group, systolic and diastolic blood pressure were significantly reduced in the pulmonary artery.

Conclusion: According to the results, it can be concluded that Propofol is considered more appropriate than Sevoflurane for cardiac catheterization in children with congenital heart disease and anesthesiologists can use Propofol as a suitable alternative for sevoflurane.

Key words: Congenital heart disease, Anesthesia, Pulmonary artery pressure, Clinical symptoms

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Introduction

One of the most common congenital diseases of children is abortion of the heart. Among the congenital anomalies in infants, the cardiovascular system causes most deaths. The incidence of congenital heart disease is approximately 8% in 1,000 live births, and if one of the first-degree relatives is afflicted with CHD, the incidence reaches 2-6% (Bernstein, 2,000). Pulmonary artery pressure (PHT) occurs in many congenital heart diseases, and the status of the pulmonary vascular system is often the key to clinical manifestations, period of illness, and curative treatment with surgical methods (Barst, 2001; Qureshi, 2002). By definition, the increase of 25 mm Hg in average pulmonary arterial pressure at rest time and more than 30 mm Hg during activity is said to be pulmonary arterial pressure, whether it is due to increased blood flow or increased vascular resistance (Barst, 2001). The increase in pulmonary vascular resistance leads to double-sided or right-to-left shunting through a congenital communication defect that occurs between the systemic and pulmonary blood stream, which is defined as the Isenmenger syndrome, which is proven by cardiac catheterization (Bernstein, 2000). Patients with PHT may be resistant to medical treatment and ultimately progress to cardiac dysfunction and death, so assessing the severity of illness and the ability to predict the likelihood of death is an important factor in decision-making in these patients.

The goal of sedation during cardiac catheterization in sick children is immobilization, numbness and stability in the respiratory and cardiac system (Lebovic et al., 1992). Induction of anesthesia, intubation and respiration through the device during cardiac catheterization may result in severe changes in respiratory and cardiac indices. For this reason, the use of relaxation method for cardiac catheterization while conscious is preferable to the general anesthetic method. The anesthesiologist plays an important role in this regard (Reich et al., 1989). Regarding the inhalation anesthetics, although halothane was thought to be a mild inhaler inducing good intubation for many years, however, since the introduction of sevoflurane in the early 90's, sevoflurane has been widely used instead of halothane (Jellish Et al., 2005). Now, this question is discussed as to whether sevoflurane can create conditions for an effective and rapid intubation such as thiopental and succinylcholine alone. There are many studies suggesting the successful use of sevoflurane in the intubation condition (Woods, 2005).

Thwaites et al. (1999) showed that sevoflurane can be a satisfactory alternative to the standard method of Succinylcholine chloride and Propofol when children are under non-emergency conditions. Still, studies in this area seem to be inadequate (Woods, 2005).

Propofol is a relatively new intravenous anesthetic. This drug is very useful for calming, relaxation, and at higher doses, it is a great general anaesthetic. Propofol is a sleeping drug with an unknown mechanism and is responsible for impaired cardiovascular and is respiratory system dependent on dose. It also has direct antinociceptive effect, and does not have analgesic effects like benzodiazepines (Greff, 1999).
Propofol is used to make calm and conscientious sleepiness to induce and to maintain conscious calmness. The pharmacokinetics of this drug have made it an effective agent for Conscious calmness (Liberman et al., 1985). Its mechanism of action is to increase gamma aminobutyric acid, activating chlorine canals as a result of the activity of inhibitory neurons in the hippocampus. In addition, it prevents the release of acetylcholine in the hippocampus and prefrontal cortex.

The main benefits of this drug include the onset of fast effects, the lack of active metabolites, and rapid liver cleansing after intravenous injection (Patterson et al., 1991). This medication in elderly patients may be associated with a reduction in high blood pressure and, consequently, a decrease in tissue hemorrhage and oxygenation (Kirkpatrick et al., 1988). Other studies have reported hemodynamic impairment of Propofol injection in children (Short, 1991). The reduction in hypoproteinemia caused by Propofol injection in children at the onset of anesthesia may be between 28- 31% (Goh et al., 2005), and the reduction in blood pressure induced by Propofol injection in cardiovascular patients may be very severe (Patrick et al., 1985).

In a study, the effects of anesthesia with ketamine and Propofol in children with congenital heart disease were investigated for cardiac catheterization (Zeynep Tosun et al., 2006). In this study, the amount of intraoperative movement in the second group receiving less ketamine was slightly higher than the first group, but this difference was not statistically significant, while the duration of waking patients in the same group was shorter with a lower dose of ketamine. In other items, the hemodynamic changes, respiratory conditions, and arterial blood gas were the same in both groups. The researchers concluded that a combination of both doses of ketamine and Propofol for cardiac catheterization was effective in these children, although children who received more ketamine were statistically significantly later awake and conscious, but this was acceptable to the researchers.

In another study, the effects of Propofol and ketamine were investigated on systemic blood and pulmonary flow in children undergoing cardiac catheterization. In this study, patients were divided into three groups without intra-cardiac shunt, with left to right shunt and right to left shunt. The findings showed that in all patients, all of the three groups who were under continuous infusion of Propofol had a significant decrease in the mean systemic arterial pressure. In two groups of patients who had cardiac shunt, Propofol infusion resulted in a clear reduction of systemic vascular resistance and a significant increase in systemic blood flow, while the resistance of pulmonary vessels and blood flow did not change significantly.

These changes significantly and statistically reduced the ratio of pulmonary blood flow to the systemic, resulting in a decrease of left-to-right shunt and an increase of right-to-left shunt. After infusion of ketamine, the mean systemic arterial pressure was increased significantly in all groups of patients, while the median pulmonary arterial pressure, resistance to pulmonary and systemic arteries remained unchanged (Zeynep Tosun et al., 2006).

The effects of sevoflurane on pulmonary arterial pressure or pulmonary vascular resistance, as well as the possible effects on the pulmonary blood flow have been highlighted in studies that have mainly been focused on reducing pulmonary arterial pressure and reducing pulmonary arterial pressure, but these effects on the pulmonary artery that has been damaged previously, or pulmonary arterial pressure has been increased, it is not so noticeable. In the initial studies to evaluate the effects of sevoflurane, 21 individuals who were healthy and without need for surgery were voluntarily subjected to anesthesia with sevoflurane, isoflurane or combination of sevoflurane and 60% nitrous oxide. Studies and performed tests in these subjects showed that sevoflurane did not change much on heart rate, reduced the resistance of arterial vessels and systemic vessels, and decreased the resistance of the pulmonary artery and increased blood flow (Hala et al., 2016). Alawi Tabatabaei (2016) compared the effects of two anesthetic methods with combination of ketamine/sevoflurane and ketamine/Propofol combination on cardiovascular variables in children with diagnostic cardiac angiography. They concluded that the use of ketamine and Propofol or ketamine and sevoflurane did not significantly differ in hemodynamic indexes of patients. However, it should be emphasized that patients receiving sevoflurane had higher systolic blood pressure and shorter recovery time. Regarding the relatively high use of sevoflurane and Propofol and the lack of studies in this field, this study aimed to investigate the effect of sevoflurane and Propofol on pulmonary arterial pressure during cardiac catheterization in children with congenital heart disease.

Materials and Methods

The study was a single-blind clinical trial. The research population was all patients with congenital heart disease in the age range of three months to 12 years and 80 patients with congenital heart disease were selected by available sampling method who were referred to Modarres Hospital, Iran for diagnostic and therapeutic measures under cardiac catheterization. The samples were divided into two groups: Propofol and sevoflurane.

The sample size was 80 individuals based on similar research ($p \leq 0.05$) and a test power of 80%. The criteria for entering the study included: the age of patients between 3 months and 12 years old, congenital heart disease, stable hemodynamic symptoms, absence of pulmonary, renal, hepatic, and co-abnormalities, etc., no history of drug allergy or allergies to food, ASA class 2-3, lack of infectious diseases and withdrawal criteria included: respiratory distress, apnea or a clear drop in arterial oxygen saturation, severe hemodynamic impairment and need for treatment during catheterization, stable cardiac arrhythmia requiring interventional therapy, ventilation disorder requiring interventional and respiratory support and seizure during prognosis. Ethical Criteria in this study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences.

After diagnosis of the patient as an appropriate case, the necessary explanations were given to the parents of the patient about the method of implementation and the benefits and possible complications of participating in the project, and written consent was obtained from them. Intervention was performed without cost to the patient. Before the intervention, parents were asked to fill out a demographic questionnaire including gender, age, and history of previous treatments, background history of the disease and the duration of the symptoms.

Regarding moral considerations, the patient's parents were assured that their lack of cooperation with the doctor and the hospital would not affect their treatment and all patient information would be kept confidential. After entering the heart catheterization department, details of the followed cases were recorded comprising hemodynamic baseline values, such as heart rate, and respiratory rate per minute, cystic and diastolic blood pressures, arterial pulse oxygen saturation in the room, the presence or absence of cyanotype of the child, as well as tests, blood, biochemistry and electrolyte and liver enzymes, thyroid and renal function tests, as well as those observed in scans and grafts.

The use of any medication or nutritional supplement, a history of drug allergy or allergy to food, and other cases was also noted and recorded in the patient records. All patients were to be NPO according to the age and specific characteristics of the period before lung catheterization, in which case their parents were provided with explanations and warnings. One hour before catheterization, 0.5 mg/kg oral midazolam was prescribed as a premedication. Peripheral venous catheter was embedded before the start of the procedure. In children in the sevoflurane group, anesthesia initially began with higher concentrations of sevoflurane (4-6%) and spontaneous respiration by face mask and gradually reduced the concentration of gas by increasing the anesthetic depth, and continuous anesthesia with 1 MAC of inhalant sevoflurane based on age and individual characteristics of each patient and spontaneous breathing.

In the other group, Propofol 50-70 μg/kg/min was injected through a perfusion pump, and when the depth of anesthesia reached the appropriate level (Ramsay Sedation Score = 3 and BIS = 65-85), the cardiac catheterization was performed with lidocaine injection at the catheter entrance i.e. femoral vessels. Systemic hemodynamic symptoms, systolic and diastolic blood pressure of the pulmonary artery were recorded after catheter entrance into the pulmonary artery. In analyzing data, mean, standard deviations, frequency, tables and charts were used to categorize and summarize the collected data. In the study of statistical pre-requisites, considering the number of observations in each distribution, the Kolmogorov-Smirnov test was used to verify the distribution of data. According to statistical hypotheses, paired t- test was used ($p<0.05$) using statistical package version 22. In all analyses, the significance level was considered as $p <0.05$.

Results

The participants in this study consisted of 35 females (43%) and 45 males (57%). The mean age for sevoflurane was 0.24 ± 2.1 years and in the Propofol group was 7.4 ± 0.54 years. Table 1 shows the changes in systolic and diastolic blood pressure from pre-test to post-test.

Table 1: Descriptive statistics of the research

Variables	Sevoflurane group		Propofol group	
	Pre-test	Post-test	Pre-test	Post-test
Systolic pressure of pulmonary artery	22.37± 7.7	224.37± 7.2	261.51± 6.9	232.37± 6.4
Diastolic pressure of pulmonary artery	92.37± 2.31	91.87± 2.46	99.77± 2.05	88.87± 1.94

Pulmonary artery systolic blood pressure

The results of Kolmogorov-Smirnov test showed that the distribution of data was normal (P>0.05). In this study, systolic blood pressure in patients with pulmonary artery was measured. Then, two anesthetic drugs, sevoflurane and Propofol, was imposed on patients under cardiac catheterization depending on the type of group.

Then, the systolic blood pressure of the pulmonary artery was re-recorded. In the next step, the blood pressure of post-test was compared with pre-test using paired t-test to determine whether a change has been established in pulmonary artery systolic blood pressure after anesthetic drugs or not (Table 2).

As can be seen in the table, pulmonary artery systolic blood pressure in the Sevoflurane group in pre-test group was 227, which was decreased to 224 in the post-test, but this decrease was not statistically significant (Fig. 1, p = 0.725). While in the Propofol group, the pulmonary artery systolic blood pressure was 261 in the pretest, which was decreased to 232 in the post-test and this decrease was statistically significant (Figure 1, p = 0.008).

Table 2: Paired t-test for evaluating pre-test and post-test of systolic blood pressure in patients with pulmonary artery disease

Groups	Level	Average	df	t	p-value
Sevoflurane group	Pre-test	227.37± 7.7	39	0.354	0.725
	Post-test	224.37± 7.2			
Propofol group	Pre-test	261.51± 6.9	39	2.81	0.008
	Post-test	232.37± 6.4			

Pulmonary artery diastolic blood pressure

The results of Kolmogorov-Smirnov test showed that the distribution of data was normal (P> 0.05). The paired t-test results are presented in Table 3. As seen in the table, the diastolic blood pressure of the pulmonary artery was 92 in the sevoflurane group in the pre-test, which was decreased to 91 in the posttest, but this decrease was not statistically significant (Fig. 2, p=0.887). While in the Propofol group, the diastolic blood pressure of the pulmonary artery was 99 in pre-test, which was decreased to 88 in the post-test and this decrease was statistically significant (Figure 2, p = 0.001).

Table 3: Paired t-test for evaluating pre-test and post-test of diastolic blood pressure in patients with pulmonary artery disease

Groups	Level	Average	df	t	p-value
Sevoflurane group	Pre-test	92.37± 2.31	39	0.143	0.887
	Post-test	91.87± 2.46			
Propofol group	Pre-test	99.77± 2.05	39	3.442	0.001
	Post-test	88.87± 1.94			

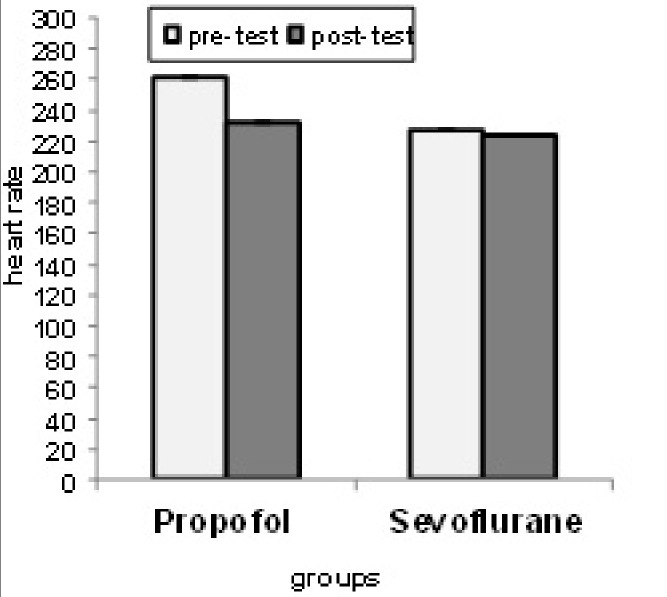

Figure 1: Changes of systolic blood pressure in patients with pulmonary artery disease from pre-test to post-test in two groups

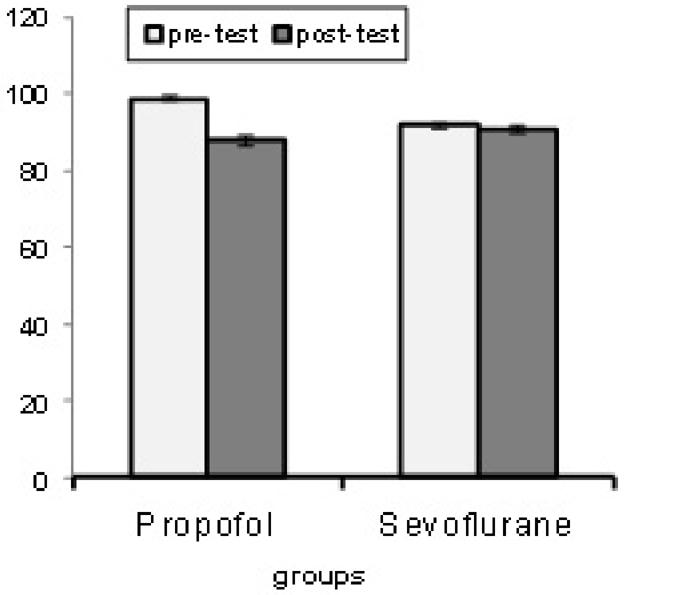

Figure 2: Changes of diastolic blood pressure in patients with pulmonary artery disease from pre-test to post-test in two groups

Discussion and Conclusion

The aim of this study was to evaluate the effect of sevoflurane and Propofol on pulmonary arterial pressure during cardiac catheterization in children with congenital heart disease. The results showed that the effect of Propofol was statistically significant on the reduction of systolic and diastolic pulmonary arterial pressure during cardiac catheterization while the effect of Sevoflurane was not significant. The comparison of the mean values showed that pulmonary artery systolic blood pressure was decreased from 261 mmHg to 232 mmHg and the pulmonary artery diastolic blood pressure ranged from 99 to 88 mmHg. Propofol leads to a greater reduction in blood pressure than Sevoflurane (Peishun et al., 2016). The findings of this study were in line with the results of previous studies. For example, Kariman Majd et al. (2006) examined the effect of various proportions of Propofol and ketamine on hemodynamic changes in patients. Their findings showed that the Propofol group experienced a greater reduction in pulmonary artery systolic and diastolic blood pressure in comparison to the ketamine group. Kirkpatrick et al. (1988) also found that blood pressure reduction is very intense in the elderly after induction with Propofol, and the drop in pressure is lower in the younger group. In other studies, the effects of Sevoflurane and Propofol have been compared.

For example, Inh et al. (2009) investigated and compared inhaled inductive anesthetics and preservation of anesthesia (VIMA) with sevoflurane with complete intravenous anesthesia (TIVA) with Propofol and remifentanil for adrenalin, norepinephrine, cortisol, and Glucose and IL-6 plasma in four levels of basal level, induction of anesthesia, secretion and separation of the device. The findings showed that the levels of glucose, cortisol, adrenaline and noradrenaline in the TIVA group were significantly lower than the VIMA group. But there was no difference between the two groups at IL-6 level. Weale et al. (2003) found that in a clinical trial on 49 children under the age of 5 years, remifentanil infusion (1 μg/kg/min and further) can prevent glucose increase associated with phase before heart surgery bypass.

There are many hypotheses about the effect of these drugs on hyperglycemia during surgery. Studies in pigs and humans have shown that sevoflurane reduces insulin secretion and, as a result, reduces the use of glucose (Tanaka et al., 2005).

Also, anesthesia with sevoflurane in comparison with Propofol provides better glycolysis in skeletal muscle cells in induction of ischemia with tourniquet (Carles et al., 2008). In contrast, Propofol decreases the activity of sympathetic nerves (Ebert et al., 1992). Apparently, the mechanism of glucose metabolism is different in anesthesia with Propofol with anesthesia surgery with sevoflurane (Kitamura et al., 2009). The probable mechanism of Propofol effect can be expressed in such a way that it can inhibit the activity of the sympathetic nervous system more than parasympathetic. In fact, bradycardia and ascites have been observed after induction of anesthesia, which sometimes leads to recommend prescribing anticholinergic drugs at a time when there is a potential for vagus stimulation with Propofol prescription. Propofol reduces the resistance of peripheral arteries and blood pressure, which is most commonly observed with the same thiopental value. Vessel smooth muscle relaxation by Propofol is essentially related to the activity of vascular spasm nerves in the sympathetic nervous system. The effect of the negative inotropy of Propofol may be the result of inhibition of intracellular calcium intake. The effect of Propofol on blood pressure may be worse in patients with hypovolemic, elderly, and left ventricular dysfunctional patients with coronary artery disease. Despite the decrease in blood pressure, heart rate often remains fast and unchanged (Reves et al., 2000). Some studies concluded that cognitive function in the sevoflurane group was better than the Propofol group in elderly subjects after general surgery (Kheirkhah, 2014). According to the results of this study, it can be concluded that for cardiac catheterization in children with congenital heart disease, Propofol is more appropriate than sevoflurane. Anesthesiologists can use Propofol as a good alternative to sevoflurane.

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