

Comparing the Effects of Propofol-Ketamine and Sevoflurane-Ketamine on Emergence Delirium and Pain after General Anesthesia in Pediatric Patients Undergoing Interventional Cardiac Angiography

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Background: Emergence delirium (ED) is a frequent postoperative complication in children. Its prevalence is about 25-80% and is observed more commonly with rapid-acting volatile anesthetics than the older inhalation agents.

Methods: 30 patients aging between 2 to 8 years were included in this randomized double blind study. We compared the effect of combination of two anesthetic drugs, Propofol-Ketamine and Sevoflurane-Ketamine, on ED and pain after general anesthesia in pediatric patients undergoing interventional cardiac angiography. Agitation was measured by PAED (Pediatric Anesthesia Emergence Delirium) scoring system and pain by the CHEOPS (Children's Hospital of Eastern Ontario Scale).

Results: Emergence delirium in 10th minute of recovery was higher in propofol group (7.6 ± 4.47 vs 5.07 ± 3.31 , $p=0.047$) but it was the same between the groups during the rest of recovery times. Pain scores were higher only at the moment of entrance to recovery room in sevoflurane group (6.27 ± 1.99 vs 5.1 ± 1.06 , $p<0.001$). Mean recovery time was shorter in the sevoflurane group than in the propofol group (33.83 ± 15.239 vs 51.67 ± 20.585 , $p=0.02$). Nausea and vomiting was more frequent in the sevoflurane group (6.6% vs 0%, $p, 0.001$), which needed no treatment.

Conclusion: There are some minor differences between sevoflurane-ketamine and propofol-ketamine anesthesia. If the length of recovery is not an issue and the patients are not at high risk of nausea and vomiting, either sevoflurane-ketamine combined anesthesia or propofol-ketamine infusion can be suitably used to anesthetise patients for the pediatric cardiac catheterization procedures.

Keywords: Ketamine; Propofol; Sevoflurane; Ketofol; Pediatric cardiac catheterization; emergence delirium

Emergence Delirium (ED) is a frequent postoperative complication especially in young children undergoing specific surgical procedures [1-6]. It is defined as a dissociated state of consciousness in which the child is inconsolable, irritable, uncompromising or uncooperative, typically thrashing, crying, moaning, or incoherent [4]. ED's prevalence is about 25-80% in children according to ED's definition and its scaling system [7-8] ED that occurs within 30 minutes of anesthesia is known as a self-limited phenomenon with variable duration. Children may hurt parents, nurses or themselves during emergence delirium [9-

10]. Older drugs such as halothane are being replaced by sevoflurane in pediatric surgeries and its usage is expanding every day [11] so reports of ED occurrence due to sevoflurane usage has increased. Our study compared the effect of combination of two anesthetic drugs, propofol-ketamine and sevoflurane-ketamine, on ED and pain score after general anesthesia in pediatric patients who were undergoing interventional cardiac angiography.

Methods

This randomized double blind study was performed in Children's Medical Center cardiac catheterization room from 2013 to 2014. The study was performed according to Helsinki statement. The study was approved by the ethic committee of Tehran University of medical sciences and written informed consents were taken from the parents or legal guardians of the patients. Patients were children between 2-8 years old with American society of Anesthesiologist (ASA) class I or II who were planned to have interventional cardiac angiography. The exclusion criteria were congenital genetic disorders, sensitivity to the study drugs, behavioral disorders, antipsychotics' usage and

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non Persian speaking parents. Based on 80% power, 60 patients were included in this study and were randomly allocated into two equal groups based on block randomization method.

All of the children received 0.5mg/kg midazolam syrup 20 minutes before induction of anesthesia. They also received Eutectic Mixture of Local Anesthetics (EMLA) topical cream bilaterally on the inguinal area, at which interventionist's needle was expected to insert. In the sevoflurane group, induction of anesthesia was done using 1mg/kg ketamine and 1 MAC (Minimum Alveolar Concentration) Sevoflurane. After enough anesthetic depth, a proper-size laryngeal mask airway (LMA) was inserted and 0.66 MAC sevoflurane was used for the maintenance of anesthesia. In the propofol group, induction was performed, based on 1mg/kg propofol and 1mg/kg ketamine. After reaching enough anesthetic depth, an LMA was inserted and anesthesia was maintained using Ketofol, based on 100µg/kg/min of either ketamine or propofol.

After the operation was finished and the patients gained consciousness, the LMA was removed and the patients were transferred to the recovery room. At the recovery room, patients' agitation and pain scores were registered at the first minute and then every ten minutes for an hour. Both the registrar and the recovery nurse were blinded to the study. Agitation was measured by PAED (Pediatric Anesthesia Emergence Delirium) scoring system (Table 1) from zero to twenty and pain by the CHEOPS (Children's Hospital of Eastern Ontario Scale) (Table 2). Vital signs, bronchospasm, laryngospasm, nausea and vomiting and other probable variables were registered and treated in the recovery room. After reaching the discharge criteria of recovery room based on Aldrete score 9 to 10 (Table 3), the length of stay in the recovery room was recorded and the patient was discharged and transferred to the post-cath unit.

Results

There were no significant differences in demographic data between the two groups. Mean age was 4.2±2.28 years in sevoflurane group years 4.5±2.08 years in propofol group (p=0.52). 46.7% of sevoflurane group and 50% of propofol group were females while 53.3% of sevoflurane group and 50% of propofol group were males (p=0.72). Mean weight in sevoflurane group was 14.83±6.265 and in propofol group was 17.83±8.263 (p=0.085) (Figure 1-2).

Pain scores were higher at the moment of entrance to recovery room in sevoflurane group (6.27 ± 1.99 versus 5.1 ± 1.06; p < 0.001). Although emergence delirium was higher in the propofol group, the difference was significant only in the 10th minute, (7.6 ± 4.47 versus 5.07 ± 3.31; p=0.047). Four patients of sevoflurane group (6.6%) had nausea and vomiting, while none of the patients in the propofol group had nausea and vomiting (p<0.001). Four patients of sevoflurane group (6.6%) needed opioids at the time of entrance to the recovery room. No patient in the propofol group needed opioids (p<0.001). No further opioid was needed during the rest of recovery time in the groups. Mean time of recovery room stay was 33.83±15.23 minutes in sevoflurane group and 51.67±20.85 minutes in propofol group (p= 0.02).

Table 1- Pediatric anesthesia emergence delirium (PAED) scale

	Score
The child makes eye contact with the caregiver	4 = not at all
The child's actions are purposeful	3 = just a little
The child is aware of his/her surroundings	2 = quite a bit
	1 = very much
	0 = extremely
The child is restless	0 = not at all
	1 = just a little
The child is inconsolable	2 = quite a bit
	3 = very much
	4 = extremely

Figure 1- Comparison of PAED scores between the groups

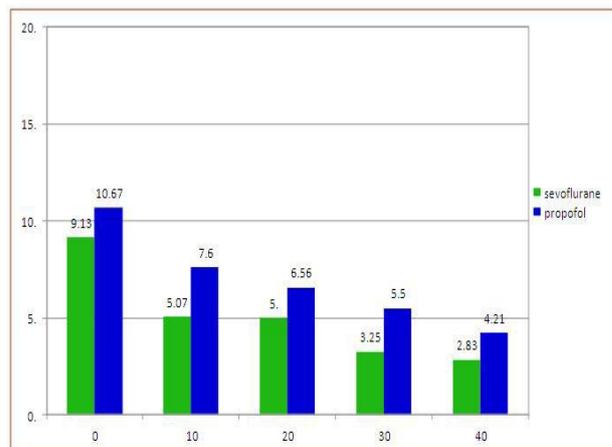
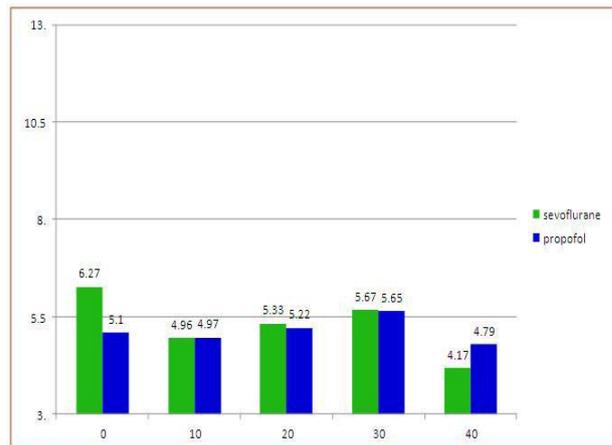


Figure 2- Comparison of CHEOPS scales between the groups



**Table 2- Children's Hospital Eastern Ontario Pain Scale (CHEOPS)
(Recommended for children 1-7 years old) - A score greater than 4 indicates pain**

Item	Behavioral		Definition	Score
Cry	No cry	1	Child is not crying.	
	Moaning	2	Child is moaning or quietly vocalizing silent cry.	
	Crying	2	Child is crying, but the cry is gentle or whimpering.	
	Scream	3	Child is in a full-lunged cry; sobbing; may be scored with complaint or without complaint.	
Facial	Composed	1	Neutral facial expression.	
	Grimace	2	Score only if definite negative facial expression.	
	Smiling	0	Score only if definite positive facial expression.	
Child Verbal	None	1	Child not talking.	
	Other complaints	1	Child complains, but not about pain, e.g., "I want to see mommy" or "I am thirsty".	
	Pain complaints	2	Child complains about pain.	
	Both complaints	2	Child complains about pain and about other things, e.g., "It hurts; I want my mommy".	
	Positive	0	Child makes any positive statement or talks about others things without complaint.	
Torso	Neutral	1	Body (not limbs) is at rest; torso is inactive.	
	Shifting	2	Body is in motion in a shifting or serpentine fashion.	
	Tense	2	Body is arched or rigid.	
	Shivering	2	Body is shuddering or shaking involuntarily.	
	Upright	2	Child is in a vertical or upright position.	
	Restrained	2	Body is restrained.	
Touch	Not touching	1	Child is not touching or grabbing at wound.	
	Reach	2	Child is reaching for but not touching wound.	
	Touch	2	Child is gently touching wound or wound area.	
	Grab	2	Child is grabbing vigorously at wound.	
	Restrained	2	Child's arms are restrained.	

**Table 2- Children's Hospital Eastern Ontario Pain Scale (CHEOPS)
(Recommended for children 1-7 years old) - A score greater than 4 indicates pain (Continued)**

Legs			
Neutral	1	Legs may be in any position but are relaxed; includes gentle swimming or separate-like movements.	
Squirm/kicking	2	Definitive uneasy or restless movements in the legs and/or striking out with foot or feet.	
Drawn up/tensed	2	Legs tensed and/or pulled up tightly to body and kept there.	
Standing	2	Standing, crouching or kneeling.	
Restrained	2	Child's legs are being held down.	

Table 3- Post Anesthetic Recovery Scoring System (Aldrete Score)

Activity	Respiration	Circulation	Consciousness	Oxygen Saturation
2: Moves all extremities voluntarily/ on command	2: Breaths deeply and coughs freely	2: BP + 20 mm of preanesthetic level	2: fully awake	2: Spo2 > 92% on room air
1: Moves 2 extremities	1: Dyspneic, shallow or limited breathing	1: BP + 20-50 mm of preanesthetic level	1: Arousable on calling	1: Supplemental O2 required to maintain Spo2 >90%
0: Unable to move extremities	0: Apneic	0: BP + 50 mm of preanesthetic level	0: Not responding	0: Spo2<92% with O2 supplementation

Discussion

The higher PAED scale in the propofol group in the 10th minute is in contrast with other studies. However, the results might be different with larger sample size. Aouad expressed that single dose administration of propofol at the end of strabismus surgery in children significantly increased the incidence and intensity of ED [12]. In Abu-shahwan study, it was reported that adding 1mg/kg propofol leads to a significant decrease in ED after general anesthesia with sevoflurane in children undergoing non-painful procedures such as MRI [13].

According to our results, overall pain incidence and CHEOPS scale were not statistically different among the two groups, so it seems that Propofol and Sevoflurane have the same analgesic effect for this procedure.

Pieters demonstrated that pediatrics who was anesthetized with Propofol for Adenotonsillectomy had significantly less pain after surgery than those who had received sevoflurane. There was no significant difference in ED severity and occurrence between two groups [11]. In this study, none of the patients in the propofol group had CHEOPS scale more than 10 so there was no need to use opioids in that group; but four patients in the sevoflurane group had CHEOPS scale more than 10 so that opioids were administered. There was no significant difference between two groups which may be justified with wider data distribution and higher CHEOPS standard deviation in the sevoflurane group. It seems that pain incidence in sevoflurane group was higher; that may be due to fast recovery after sevoflurane induction.

Stay time in recovery room was significantly shorter in sevoflurane group which may be related to the inhalation administration, chemical properties and pharmacokinetic of sevoflurane. In Shukry's study, the perioperative infusion of 0.2 microg.kg (-1).h (-1) dexmedetomidine decreased the incidence and frequency of ED in children after sevoflurane-based general anesthesia without prolonging the time to extubate or discharge [14]. Four cases had nausea and

vomiting in sevoflurane group, while there were no reports of that in propofol group which was expected and is related to the propofol's anti- nausea effect. This was statistically different and those patients who had nausea and vomiting in sevoflurane group didn't need any treatments in our study, so there was not any difference between two groups regarding nausea and vomiting.

Conclusion

According to the results of this study, despite some minor differences between two groups, sevoflurane-ketamine and propofol-ketamine can be used interchangeably to anesthetise patients for the pediatric cardiac catheterization procedures. Post anesthesia agitation and delirium is different only in 10th minute. Pain scores and need for opioids were different only at the first minute. Using sevoflurane for induction of anesthesia in children for angiographic cardiac intervention is accompanied with higher rate of nausea and vomiting, which needs no treatment. Using propofol-ketamine for anesthesia in these patients is accompanied with longer recovery times.

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