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Research Article

Ketamine–propofol versus ketamine fentanyl for anesthesia in pediatric patients undergoing cardiac catheterization: A prospective randomized study

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KEYWORDS

Pediatric anesthesia;
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Abstract *Objective:* The aim of the study was to assess, compare the safety and efficacy of continuous IV administration of a combination of ketamine–propofol versus ketamine fentanyl for anesthesia in children undergoing cardiac catheterization procedures with RT to Lt Shunt.
Methods: Thirty-six children aged from 1 to 8 years, with RT to Lt Shunt scheduled for Cardiac catheterization in Mansoura Children Hospital were included in this study. Patients in group KP (n = 18) received ketamine (1 mg/kg) and propofol (2 mg/kg) as induction agents followed by combination of ketamine (25 μg/kg/min) and propofol (25 μg/kg/min) for maintenance of anesthesia. On other hand, patients in group KF (n = 18) received ketamine (1 mg/kg) and fentanyl (1 μg/kg) as induction agents followed by combination of ketamine (25 μg/kg/min) and fentanyl (0.75 μg/kg/min) for maintenance of anesthesia. Hemodynamic, oxygenation, recovery variables and side effects were recorded.

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Results: There were no statistical significant differences with age, sex, duration of anesthesia. There were statistical significant decreases in mean arterial blood pressure (MAP), systemic vascular resistance (SVR), pulmonary to systemic vascular resistance ratio in KP group. Additionally, Sao_2 and Pao_2 after anesthesia in KF group were statistically significant higher than the other group. Also there was significant prolongation of time to full recovery in KF group compared with KP group. *Conclusion:* We concluded that a combination of ketamine–fentanyl is safer and more efficacious than ketamine–propofol for pediatric cardiac catheterization although it was associated with prolonged recovery time.

1. Introduction

Cardiac catheterization procedures often require an anesthetic technique that ensures a still patient with stable hemodynamics [1]. To achieve this goal, different anesthetic drugs have been used either alone or in combination such as ketamine, propofol [2,3], remifentanil [4], sevoflurane [5], meperidine, and chlorpromazine [6]. To our knowledge, no ideal single or the combination anesthetic drugs have gained acceptance universally.

A combination of propofol and ketamine have been used in pediatric patients undergoing cardiac catheterization and found to be safe [1,7]. However, the use of combination was associated with hypotension during induction, psychic disturbances and cardiovascular stimulation [8].

Fentanyl is considered to be cardiac stable drugs, so it is one of the principle opioids used in cardiac anesthesia. However it may cause a dose dependent degree of bradycardia and hypoventilation [9]. Ketamine/fentanyl combination has not used before in pediatric patients undergoing cardiac catheterization. We hypothesized that it could be beneficial in pediatric patients with Rt to Lt shunt undergoing cardiac catheterization.

In this study we aimed to evaluate and compare between the efficacy and safety of two different anesthetic technique in cardiac catheterization patients with RT to Lt Shunt (propofol/ketamine versus ketamine/fentanyl) regarding hemodynamic and oxygenation parameters as well as side effects.

2. Patients and methods

After institutional ethical committee approval and written informed parental consent, 36 children with American Society of Anesthesiologists grade (ASA) II, III scheduled for elective cardiac catheterization in Mansoura Children Hospital. Inclusion criteria include children 1–8 years with RT to Lt Shunt scheduled for diagnostic or interventional cardiac catheterization. Exclusion criteria include the need for mechanical ventilation, or inotropic support. The procedure was performed after a minimal fasting period of 2–4 h for fluids and 6 h for solid food.

On arrival at the catheterization room, a canula was inserted in a peripheral vein after application of Lidocaine/Prilocaine cream. Patients were premedicated with iv midazolam 0.05 mg/kg and atropine, 0.02 mg/kg. They were monitored with electrocardiography, noninvasive blood pressure measurements, respiratory rate, and pulse oximetry. Baseline blood pressure and heart rate were obtained before induction. The end-tidal CO_2 waveform was monitored by graphic display. Heart rate, mean arterial blood pressure (MAP) and arterial oxygen consumption were reported. Systemic vascular resistance (SVR), pulmonary vascular resistance (PVR) and pulmonary to systemic vascular resistance ratio were calculated. Blood for analysis of arterial oxygen saturation (Sao_2), arterial oxygen tension (Pao_2) was obtained from the superior vena cava. The cardiologist who performed catheterization gave us the baseline values of these variables.

Anesthesia was induced and maintained with sevoflurane (1–2 minimum alveolar anesthetic concentration)/air through an anesthetist holding a tight and fitted facemask and circle breathing system. The patients' groins were infiltrated with 1% lidocaine for femoral vascular access. As soon as baseline catheterization measurements were obtained, Sevoflurane is stopped and Children were randomly allocated by closed envelope method to receive ketamine 1 mg/kg as a loading dose, and propofol, 2 mg/kg to keep the patient appropriately sedated. Then the infusion mixture of propofol and ketamine was started at an initial rate of 25 μg/kg/min propofol and of 25 μg/kg/min ketamine (KP group). In KF group, ketamine 1 mg/kg, and fentanyl of 1 μg/kg. Thereafter, infusion mixture of fentanyl and ketamine started at an initial rate of 0.75 μg/kg/min fentanyl and of 25 μg/kg/min ketamine. Parameters were reported by anesthetist unaware of the group assignment. Once the drug infusion started, spontaneous movements that interfered with the procedure were treated by the ketamine 0.5 mg/kg intravenously in boluses until its disappearance. All parameters were recorded at baseline and after administration of the drug combination by 10 min. All patients breathed air spontaneously via facemak. Lactated Ringer's solution was infused at the maintenance rate4 ml/Kg/h. Supplemental oxygen 30% was given via facemask in case of a reduction of O_2 saturation more than 5% from baseline. Number of patients requiring additional ketamine doses were reported. The anesthetic drug infusion was discontinued when the groin bandage was applied.

After the procedure was completed, the patients were transferred to the post anesthetic care unit (PACU). Additional ketamine doses were reported. Children were transferred from PACU to cardiac unit if they achieved Modified Aldrete Score of 10 which include five items; Activity, Respiration, Circulation, Consciousness, Saturation [10]. The time to spontaneous eye opening, time to full consciousness, and time to meeting PACU discharge criteria were recorded.

Data are expressed as mean ± SD. Kolmogorov–Smirnov test was done to test the normality of data distribution. Normally distributed data were subjected to parametric tests. A paired *t* test was used to compare within group, while an independent t test was used for comparison between groups. Statistical significance was set at $p < 0.05$. A prior power analysis

Table 1 Patient characteristics, duration of procedures and total dose of ketamine. Data are expressed as mean ± SD.

	KP group	KF group	*p*-Value
Age (years)	5 ± 2.3	4.9 ± 1.4	0.56
Wt (kg)	17.5 ± 4.4	16.5 ± 3.4	0.26
Gender M/F	11/7	10/8	0.45
Procedures duration (min)	14.1 ± 4	16.5 ± 6	0.72

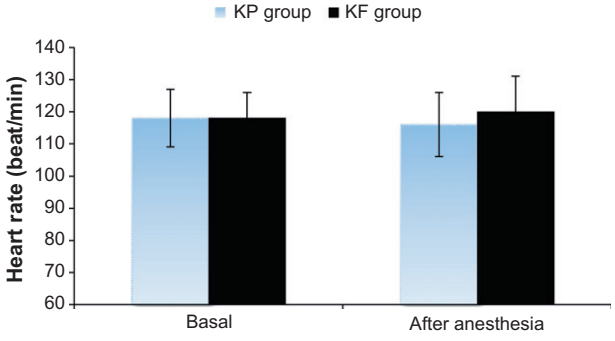

Figure 1 Heart rate (beat/min) changes of the studied groups.

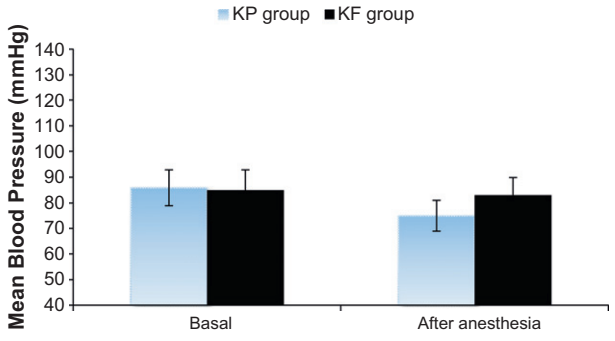

Figure 2 Mean blood pressure (mmHg) changes of the studied groups.

using Epicalc program 2000 indicated that 16 patients in each group would be sufficient to detect a 15% reduction in blood pressure values after anesthesia, with a type-I error of 0.05 and a power of approximately 90%. Extra numbers were taken to avoid defaulters, so each group = 18. The statistical analysis were done by using excel program and SPSS program statistical package for social science version 16.

3. Results

Thirty-six patients were included in the study, 18 patients in each group. There were no statistically significant differences in age, weight and duration of procedures (Table 1). There was no significant difference in heart rate between the two groups (Fig. 1).

With respect to hemodynamic variables, there was significant decrease in mean arterial blood pressure (Fig. 2), and systemic vascular resistance, and significant increase of systemic to pulmonary resistance ratio (Table 2) in KP group comparing with its basal values and comparing with other group. Sao_2 and Pao_2 after drug infusion in KP group were statistically significantly lower than its basal values and corresponding value in KF group (Table 2). Regarding recovery room parameters there was significant increase in time to eye opening, time to full consciousness and time to meeting PACU discharge criteria in the KF group comparing with the KP group (Table 3). The groups did not differ significantly including adverse effects during the 24 h following the procedures (Table 4).

4. Discussion

Cardiac catheterization remains the gold standard for detailed diagnosis of complex cardiac anatomic anomalies. Anesthetic management for cardiac catheterization in pediatric patients can be uniquely challenging especially in children with Rt to Lt shunt. In order to obtain meaningful hemodynamic data during cardiac catheterization, it is important to provide stable hemodynamics with no effect on intracardiac shunting and maintain spontaneous ventilation with no supplemental oxygen. Also, it is important that the patients remain immobile during the procedure to avoid cardiac complications, especially perforation [11].

Although, ketamine had been used for sedation in pediatric patients undergoing cardiac catheterization, it resulted in long

Table 2 Hemodynamic and oxygenation variables. Data are expressed as mean ± SD.

Variables	KP group		*p*-Value	KF group		*p*-Value
	Basal	After anesthesia		Basal	After anesthesia	
SVR (dynes/s/cm^5)	1335 ± 492	945 ± 298***	0.003	1403 ± 448	1398 ± 302	0.27
PVR (dynes/s/cm^5)	132 ± 62	130 ± 140	0.22	133 ± 42	135 ± 140	0.15
P/S resistance ratio.	0.11 ± 0.1	0.29 ± 0.1***	0.005	0.13 ± 0.5	0.15 ± 0.2	0.1
O_2 consumption (ml min/m^2)	169 ± 23	180 ± 25	0.41	170 ± 34	179 ± 30	0.37
Pao_2 (mmHg)	54 ± 9	49 ± 10***	0.05	55 ± 10	54 ± 9	0.56
Sao_2 (%)	82 ± 6	75 ± 8***	0.04	80 ± 8	79 ± 10	0.61

SVR = systemic vascular resistance, SBF = systemic blood flow, P/S resistance ratio = pulmonary systemic vascular resistance ratio, Sao_2 = arterial oxygen saturation, Pao_2 = arterial oxygen tension.
$P < 0.05$.
* Significant when compared with basal value in the same group.
** Significant when compared with the other group.

Table 3 Recovery room parameters. Data are expressed as mean ± SD.

Variable	KP group	KF group	*p*-Value
Time to eye opening (min)	11.5 ± 4.4*	16.2 ± 5.1	0.05
Time to full consciousness (min)	42.5 ± 16*	49.2 ± 4.3	0.04
Time to PACU discharge (min)	49. ± 19.4	59.2 ± 17	0.03

PACU, post anesthetic care unit.
* Significant with the other group.

Table 4 Safety and side effects over 24 h. Data are expressed as number (%).

Variable	KP	KF
Respiratory depression	0	0
Excessive salivation	2(11%)	2(11%)
No. of doses of additional ketamine	1(5.5%)	2(11%)
No. of patient showing unpredictable movements	3(16.6%)	2(11%)

recovery period, delirium, and side effects such as tachycardia and hypertension [12]. Also, Propofol has been used for pediatric cardiac catheterization for rapid recovery and smooth induction. However, the decreased systemic vascular resistance and MAP may limit its use [13].

In this study, the use of ketamine/propofol in pediatric patients with Rt to Lt shunt undergoing cardiac catheterization, resulted in significant decreases in mean arterial BP, SVR, which could be explained by predominance of the cardiodepressent effect of propofol [14,15].

This in contrast to Gayatri et al., and Akin et al. [1,7] who proved that there is no significant hemodynamic instability with the use of (KP) combination. This contrast can be explained by firstly, the use of midazolam 0.5 mg/kg before anesthesia. Secondly the use of bolus dose of ketamine 1 mg/kg and propofol 2 mg/kg as the inducting dose. Thirdly, the choice of selected patients who suffering from Rt to Lt shunt that are very sensitive to any cardiodepressent drug and to any hemodynamic changes. On the other hand, our study had confirmed that there were stable hemodynamics in KF and that passes in parallel with Kaynar et al. [16] who advised that small amounts of an opioid such as fentanyl may be administered for procedure sedation, thus allowing the patient to remain stand still and to avoid bleeding complications at the femoral vascular access sites. As an alternative to a volatile anesthesia-based technique, the patient can be managed with total intravenous anesthesia using various combinations of opioids, benzodiazepines, propofol, and ketamine.

Also there was significant decrease in Pao_2 and Sao_2 in ketamine/propofol group comparing with ketamine/fentanyl group. This is in agreement with Williams et al. [17] who proved that the use of ketamine/propofol in Rt to Lt shunt patients causes clinical important changes in cardiac shunt direction and flow with a subsequent decrease in oxygen concentration in blood.

A combination of ketamine/fentanyl group appeared to be free of side effects of ketamine alone [18–20] which result from its sympathetic stimulation. This combination also provides deep sedation of rapid onset with minimal hemodynamic or respiratory compromise.

Finally, we found that the time to full recovery is significantly prolonged in ketamine/fentanyl and that being due to sedating and analgesic effects of both ketamine and fentanyl.

We conclude that the use of ketamine/fentanyl combination, for pediatric patients with Rt to Lt shunt undergoing cardiac catheterization, is safer and more efficacious than ketamine/propofol as it preserved homodynamic variables and oxygenation parameters despite being associated with prolonged recovery time.

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