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Midazolam–ketamine versus dexmedetomidine–ketamine combinations for anesthesia of pediatric patients undergoing cardiac catheterization

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Abstract

Background: The aim of the current study was to compare the effects of midazolam–ketamine versus dexmedetomidine–ketamine combinations on hemodynamics, sedation level, and recovery period in pediatric patients undergoing cardiac catheterization for hemodynamic study.

Patients and methods: Fifty pediatric patients undergoing cardiac catheterization for hemodynamic study were enrolled in the current study. Patients were randomly distributed to one of two equal groups: midazolam–ketamine group (group M) and dexmedetomidine–ketamine group (group D). The patients in group M received intravenous midazolam 0.1 mg/kg and ketamine 1 mg/kg as a bolus for induction, then received an intravenous midazolam infusion of 0.1 mg/kg/h and ketamine infusion of 1 mg/kg/h for maintenance whereas patients in group D received intravenous dexmedetomidine1μg/kg and ketamine 1 mg/kg as a bolus for induction, then received an intravenous dexmedetomidine infusion of 0.5 μg/kg/h and ketamine infusion of 1 mg/kg/h for maintenance. Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SPO_2), and sedation scores were recorded. Recovery time, perioperative adverse events, and total ketamine consumption required for anesthesia maintenance were also recorded.

Results: The HR was significantly lower in group D when compared with group M at 10, 20, and 30 min of the procedure with no significant difference as regards the MAP between the two study groups. There were no statistically significant differences between the two study groups in terms of Ramsay sedation scores. Ketamine consumption in group D was significantly lower than in group M. The recovery time was significantly shorter in group D when compared with group M.

Conclusion: The dexmedetomidine–ketamine combination was superior to midazolam–ketamine combination because of less intraoperative ketamine consumption required for adequate intraoperative sedation and the shorter recovery time.

Keywords: Pediatric cardiac catheterization, Dexmedetomidine, Midazolam, Ketamine

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Background

Management of children with congenital heart disease has been a great challenge for anesthesiologists especially during cardiac catheterization (Abbas et al. 2012). In contrast to cardiac catheterizations in adults, which are often performed in the awake patient with local anesthesia at the puncture site, the technique is usually not feasible in children and adolescents (Vittinghoff 2009). Two basic anesthetic techniques have been used for pediatric cardiac catheterization: one based on heavy sedation that is often used in simple cases and short procedures and the other involves full GA with tracheal intubation in either spontaneously breathing or mechanically ventilated patients (Mohammed et al. 2014).

Ketamine is an *N*-methyl-D-aspartate receptor (NMDA) antagonist with sedative, analgesic, and sympathomimetic effects (Miller et al. 2011). Among its benefits is the ability to protect airway reflexes with minimal effect on ventilatory drive (Bernard et al. 2011), but there are potential problems concerning its use in pediatrics such as emergence delirium (Chun et al. 2016). Midazolam is another commonly used intravenous sedative agent with a rapid onset and relatively rapid recovery compared to other benzodiazepines (Chun et al. 2016). It possesses a sedative, anxiolytic, and amnesic properties (Koruk et al. 2010) and minimal hemodynamic effects in clinically recommended doses for sedation (Frölich et al. 2011). However, the lack of analgesic action is a major concern (Abbas et al. 2012; Chun et al. 2016). Both midazolam and ketamine have been used for sedation in pediatric patients for a variety of procedures. Jobeir et al. (2003) used ketamine and/or midazolam in pediatric patients for sedation during cardiac catheterization. They found that their combination in small doses was safe in children.

Dexmedetomidine is a highly selective alpha-2 adrenoreceptor agonist with sedative, anxiolytic, and analgesic effects (Tosun et al. 2006); besides, it blunts the sympathetic nervous system response to surgical stimulation (Mukhtar et al. 2006). It has a shorter elimination half-life and lower risk of respiratory depression when compared with midazolam (Alhashemi 2006) and used safely in pediatric patients for sedation. However, it can cause dose-dependent hypotension and bradycardia (Tobias and Berkenbosch 2002).

The aim of the present study was to compare the effects of dexmedetomidine–ketamine versus midazolam–ketamine combinations on hemodynamic variables, sedation level, the recovery period, and the perioperative adverse events in pediatric patients undergoing cardiac catheterization.

Patients and methods

After obtaining approval of research ethical committee of Ain Shams University and patients' guardian written informed consents, the current prospective randomized study was conducted on 50 pediatric patients scheduled to undergo elective cardiac catheterization for hemodynamic study of their congenital heart disease (CHD) in cardiovascular and thoracic surgery academy at Ain Shams University hospitals through the period *from July 2015 to July 2016*.

Inclusion criteria

Pediatric patients with acyanotic heart disease aged from 2 to 15 years of American Society of Anesthesiologists (ASA) classification status II and III were eligible for participation in the study.

Exclusion criteria

Patients requiring mechanical ventilation and intravenous inotropic support and those with cyanotic CHD, second- and third-degree heart block, chromosomal abnormalities or other multiple congenital anomalies, hepatic or renal dysfunction, and allergy to any of the used drugs were excluded.

Patients were randomly divided into two groups using the closed-envelope method: The midazolam–ketamine group (group M) and dexmedetomidine–ketamine group (group D).

Anesthesia technique

The syringes of the given drugs (bolus and infusion) were prepared by an anesthesiologist who was not in charge of the case while the observing anesthesiologist was blinded to the infused drug. The bolus doses of the study drugs midazolam (Dormicum 5 mg/5 ml, La Roche, Switzerland) (0.1 mg/kg), dexmedetomidine hydrochloride (Precedex 200 μg/ 2 ml, Hospira, Inc., Rocky Mount, IL, USA) (1 μg/kg), and ketamine (Ketamine 50 mg/ml, Sigma-Tec Pharmaceuticals Industries, Egypt-SAE) (1 mg/kg) were calculated according to the patient's body weight and diluted in a normal saline solution (NSS) 0.9% to 10 ml in a non-labeled 10-ml identical syringes, and the infusion doses of the study drugs were prepared in non-labeled 50-ml identical syringes and diluted in a normal saline solution (NSS) 0.9% so that midazolam concentration (0.2 mg/ml), dexmedetomidine concentration (1 μg/ml), and ketamine (2 mg/ml) was achieved.

The patients in *group M* received midazolam intravenous bolus (0.1 mg/kg) over 10 min then ketamine intravenous bolus (1 mg/kg) followed by midazolam intravenous infusion using infusion pump (B-Braun, Bethlehem, USA) at 0.5 ml/kg/h and ketamine infusion at 0.5 ml/kg/h while the patients in *group D* received dexmedetomidine bolus (1 μg/kg) over 10 min then ketamine bolus (1 mg/kg) followed by starting of dexmedetomidine infusion at 0.5 ml/kg/h and ketamine infusion at 0.5 ml/kg/h. The

infusion of the study drugs was stopped when the procedure ended and a bandage was applied to the groin.

General preoperative fasting guidelines were followed, and EMLA cream was applied at the proposed site for cannula insertion in all patients 1 h before the procedure, and after patients were admitted to the pediatric cardiac catheter unit, an intravenous catheter was placed and an infusion of ringer solution was started at a rate of 4 ml/kg/h which is administered for the first 10 kg of weight, 2 ml/kg/h for the next 10 kg of weight, and 1 ml/kg/h for any weight over 20 kg. Atropine 0.01 mg/kg was given intravenous 30 min prior to standardized anesthetic induction. On arrival in the catheterization laboratory room, all patients were connected to standard monitors that included five leads electrocardiogram (ECG leads II and V5 were continuously monitored), a noninvasive arterial blood pressure, and a digital pulse oximetry, and the HR, MAP, SpO_2, and Ramsay sedation scores (Ramsay et al. 1974) (Table 1) of all patients were recorded. None of the patients was preoxygenated.

All patients were spontaneously breathing room air. A Ramsay sedation score RSS of 4 is accepted as an adequate sedation level at which the procedure can be started and maintained. Additional intravenous ketamine at a dose of 1 mg/kg was if a patient experienced any discomfort in both groups. The HR, MAP, SpO_2, and Ramsay sedation scores of all patients were recorded after induction and every 10 min thereafter for the duration of the study.

Bradycardia (above 20% decrease in the HR when compared with baseline) was treated with intravenous atropine 0.01 mg/kg, hypotension (MAP< 50 mmHg) was managed by ringer infusion at 3 ml/kg/h (stopped when a MAP value of 50 mmHg was obtained), and if oxygen desaturation (SpO_2 dropped to be < 92%) occurred, oxygen was supplemented at a rate of 4 l/min using a nasal cannula and continued till the end of the procedure. In case of upper airway obstruction (noted by both SpO_2 and patient observation), jaw thrust and insertion of an oropharyngeal Guedel airway was done. If apnea for more than 15 s was noticed, breathing was assisted manually with a Jackson-Rees T-piece system, and for increased salivation, suction was done.

Table 1 Ramsay sedation score (Ramsay et al. 1974)

1. Patient is anxious, agitated, or restless.
2. Patient is co-operative, oriented, and calm.
3. Patient is responsive to verbal command only.
4. Patient exhibiting brisk response to light glabellar tap or to an auditory stimulus.
5. Patient exhibiting a sluggish response to light glabellar tap or to an auditory stimulus.
6. No response to any of these stimulations.

Infusion of drugs was stopped when a bandage was applied to the groin. The patients were observed until their recovery scores, modified from the method of Steward (1975) (Table 2), became 6, and the time from stopping the drugs till reaching recovery score of 6 was recorded and then they were transferred to the pediatric ICU.

Outcome measures

The primary outcome of this study was to assess the parameters indicating quality of sedation (Ramsay sedation scores) which was recorded at 10-min intervals till the end of the procedure. The recovery time after discontinuation of the infusion of the study drugs (time to steward score of 6). The secondary measures include hemodynamics (MAP& HR) and respiratory variables (SpO_2) which were recorded which was recorded at 10-min intervals after the initial measurement till the end of the procedure and the total ketamine consumption for the procedural sedation. Other secondary measures included incidence of perioperative adverse events like hypotension hypertension, bradycardia, tachycardia, oxygen desaturation, laryngospasm nausea and vomiting, and shivering were recorded during the procedure.

Statistical analysis

Sample size calculation was performed by GPower® version 3.1.5 computer software [Franz Faul, Universita¨ t Kiel, Germany, 2012], and the sample size of 25 patients in each group was calculated for 80% power, 95% confidence interval, and 5% alpha error. Patients' data were collected, tabulated, and then analyzed using SPSS version 16.0 computer software (Chicago, IL, USA). Data are presented as means ± standard deviation. Comparison of numerical variables including (age, weight, duration of cardiac catheterization, HR, MAP, SpO_2, recovery time, and total ketamine consumption) between the two study groups was performed with an unpaired Student's t test and within the same group was performed using paired Student's t test while the comparison of categorical variables including (sex, side effects, and number of patients requiring additional ketamine doses) between the two study groups was performed by chi-square test. The sedation score was analyzed with a Mann–Whitney U test. P values less than 0.05 were considered statistically significant.

Results

Demographic data and procedure duration

There were no statistically significant differences between the two study groups regarding age, weight, sex, and the duration of cardiac catheterization (Table 3).

Table 2 Modified steward recovery scoring system (Steward 1975)

Consciousness	Airway	Motor
Awake 3 Responds to verbal stimuli 2 Responds to tactile stimuli 1 Not responding 0	Cough on command or cry 2 Maintains good airway 1 Requires airway assistance 0	Moves limbs purposefully 2 Non purposeful movement 1 Not moving 0

Hemodynamic measurements

Regarding MAP changes in the study groups

Baseline MAP was comparable between the two study groups with no statistically significant difference ($P > 0.05$). In group D, the MAP dropped significantly after induction and in all the subsequent recordings when to be significantly lower than baseline values ($P < 0.05$) with no intergroup significant difference ($P > 0.05$). In group M, there was no significant difference between MAP recordings and the baseline values **(**Table 4**).**

Regarding HR changes in the study groups

Baseline HR was comparable between the two study groups with no statistically significant difference ($P > 0.05$). After induction, there was no significant difference between group D and group M ($P > 0.05$). In group D, the HR dropped significantly after 10 min of induction and in all the subsequent recordings to be significantly lower than baseline values ($P < 0.05$) and significantly lower when compared with group M ($P < 0.05$). In group M, there was no significant difference between HR recordings and the baseline values **(**Table 5**).**

Peripheral oxygen saturation (SpO_2)

Baseline SPO_2 was comparable between the two study groups with no statistically significant difference ($P > 0.05$). In all the subsequent recordings, there was no significant difference between group D and group M as regards the SPO_2 ($P > 0.05$) (Table 6). Two patients developed oxygen desaturation (SpO_2 dropped to be < 92%) in each group which responded promptly to oxygen supplementation at a rate of 4 l/min using a nasal cannula (Table 9). No patient had apnea or required the use of assisted ventilation in both study groups.

Table 3 Demographic patients' characteristics and procedure duration (data are presented as mean ± SD or ratio)

	Group D ($n = 25$)	Group M ($n = 25$)	*P* value
Age (years)	6.3 ± 2.6	5.8 ± 3.1	0.539
Weight (kg)	20.53 ± 7.24	18.94 ± 8.56	0.481
Gender (M/F)	15/10	14/11	0.774
Duration of cardiac catheterization (min)	38.65 ± 7.34	37.55 ± 6.21	0.570

Ramsay sedation score

There was no statistically significant difference between the two study groups in terms of Ramsay sedation scores **(**Table 7**).**

Total procedural ketamine consumption

Ketamine consumption required for anesthesia maintenance was significantly higher in group M (a total of 2. 15 ± 1.43 mg/kg/h) when compared with group D (a total of 1.35 ± 0.75 mg/kg/h) ($P < 0.05$). Eleven patients in group M versus five patients in group D required supplemental doses of ketamine ($P > 0.05$).

Recovery time

Recovery time being assessed by using the Steward scoring system (Steward score of 6 or higher) was significantly shorter in group D when compared with group M ($P < 0.05$) (Table 8).

Regarding the incidence of adverse events in the studied groups

The perioperative adverse events were evaluated and recorded in the two study groups **(**Table 9**)**.

Discussion

The goals of anesthetic management during cardiac catheterization are to provide adequate sedation, analgesia, immobility, and hemodynamic stability (Mukhtar et al. 2006). The aim of the current study was to compare the effects of dexmedetomidine–ketamine and midazolam–ketamine combinations on hemodynamics, sedation level, recovery period, and the perioperative adverse events in 50 pediatric patients undergoing cardiac catheterization for hemodynamic study.

The results of the current study showed that in group D, the MAP dropped significantly after induction and in all the subsequent recordings when compared with baseline values ($P < 0.05$) with no intergroup significant difference ($P > 0.05$). Although the drop in the MAP was statistically significant, it was clinically insignificant as the MAP remained within the normotensive range in most patients except for two patients who developed hypotension and responded promptly to the fluid bolus. Also, the HR was significantly lower in group D at 10, 20, and 30 min post-induction when compared with baseline values ($P < 0.05$) and with the HR in group M ($P < 0.05$). Although the drop in the HR was statistically significant, it was clinically insignificant as the HR remained within the normal range in most patients except for three patients who developed bradycardiaand responded promptly to intravenous atropine 0.01 mg/kg. Ketamine was used at the same dose regimen for induction and maintenance in both groups and the significant difference in the HR between both groups could be

Table 4 Comparison of MAP (mmHg) in the studied groups (data are presented as mean ± SD)

MAP	Group D ($n = 25$)	Group M ($n = 25$)	P value
Baseline	85.45 ± 6.22	83.52 ± 5.57	0.253
After induction	78.32 ± 5.43*	80.61 ± 4.35	0.106
10 min	74.73 ± 6.16*	77.21 ± 5.12	0.122
20 min	76.42 ± 5.89*	79.34 ± 6.60	0.105
30 min	78.82 ± 6.22*	80.65 ± 5.87	0.290

*Statistically significant (P value < 0.05) (when compared with baseline value)

contributed to the well-known central sympatholytic properties of dexmedetomidine when compared with midazolam.

Mester et al. (2008) used ketamine and dexmedetomidine combination for sedation in pediatric cardiac catheterization, and they reported that this combination provides effective sedation for cardiac catheterization in infants and children without significant effects on cardiovascular or ventilatory function. Also, Joshi et al. (2017) compared dexmedetomidine and ketamine versus propofol and ketamine for procedural sedation in a pediatric cardiac catheterization laboratory. HR was significantly lower in the dexmedetomidine and ketamine group at 5, 10, 15, 20, and 25 min post-induction in comparison to the propofol ketamine group with no intergroup significant difference as regards the MAP, and they reported that the use of dexmedetomidine ketamine combination is a safe alternative and without any significant hemodynamic or respiratory effects during the cardiac catheterization procedure. There have been an increasing number of reports on the combination of ketamine with dexmedetomidine, particularly in pediatric patients (Frölich et al. 2011; Mester et al. 2008; Joshi et al. 2017; Tobias 2012). The combination of ketamine with dexmedetomidine can serve not only to eliminate the slow onset of sedation, but also to prevent the bradycardia and hypotension that occur when dexmedetomidine is used as a sole agent (Tobias 2012).

The current study showed that there was no significant difference regarding the Ramsay sedation scores between the two study groups. These findings were consistent with

Table 5 Comparison of heart rate (beat/min) in the studied groups (data are presented as mean ± SD)

HR	Group D ($n = 25$)	Group M ($n = 25$)	P value
Baseline	114.82 ± 15.73	112.3 ± 17.3	0.527
After induction	109.24 ± 13.34	114.12 ± 15.14	0.232
10 min	93.16 ± 11.25*,**	110.64 ± 12.91	< 0.05
20 min	92.45 ± 10.81*,**	112. 15 ± 11.36	< 0.05
30 min	94.37 ± 11.62*,**	115.34 ± 12.72	< 0.05

*Statistically significant (P value < 0.05) (when compared with baseline value)
**Statistically significant (P value < 0.05) (group D versus group M)

Table 6 Comparison of SPO_2 in the studied groups (data are presented as mean ± SD)

SPO_2	Group D ($n = 25$)	Group M ($n = 25$)	P value
Baseline	97.48 ± 1.98	97.91 ± 1.72	0.416
After induction	96.35 ± 1.63	96.18 ± 1.45	0.698
10 min	97.15 ± 1.83	96.45 ± 2.17	0.223
20 min	97.63 ± 2.35	96.73 ± 1.98	0.149
30 min	97.79 ± 2.16	97.12 ± 2.61	0.327

those reported by (Koruk et al. (Frölich et al. 2011) who compared the dexmedetomidine–ketamine and midazolam–ketamine combinations for sedation in pediatric patients undergoing extracorporeal shock wave lithotripsy (ESWL). Our observation is that the sedation was satisfactory in both study groups, but this was at the expense of the significantly higher ketamine consumption in group M when compared with group D ($P < 0.05$). The anesthetic sparing effect of intravenous dexmedetomidine was better when compared with intravenous midazolam which was proved in multiple previous studies (Feng et al. 2017; Kumari et al. 2018), and this was attributed to that dexmedetomidine not only has sedative anixolytic properties but also has also analgesic one (Tosun et al. 2006) while midazolam has sedative anixolytic amnesic properties (Koruk et al. 2010) and lacks the analgesic one(Chun et al. 2016).

We determined the depth of sedation according to the Ramsay sedation score, but bispectral index (BIS) was not used as a monitor for depth of sedation. The BIS monitor has been suggested for use in monitoring sedation of pediatric patients in the outpatient setting (Overly et al. 2005), but it should be noted that BIS readings depend on the specific sedative used and ketamine paradoxically increases BIS in spite of deep levels of sedation (Hans et al. 2005).

The results of the current study showed that there was no intergroup significant difference regarding SPO2 recordings ($P > 0.05$). Two patients developed oxygen desaturation (SpO2 dropped to be < 92%) in each group which responded promptly to oxygen supplementation at a rate of 4 l/min using a nasal cannula, and no patient had apnea and those results were similar to those obtained by(Koruk et al. (Frölich et al. 2011). Another study by Tammam (2013) compared the efficacy of

Table 7 Sedation scores of two groups. Values are median (min–max)

Sedation scores	Group D ($n = 25$)	Group M ($n = 25$)
Baseline	2 (1–3)	2 (1–3)
After induction	4 (2–6)	4 (2–5)
10 min	4 (4–6)	4 (4–6)
20 min	4 (4–6)	4 (4–6)
30 min	4 (4–6)	4 (4–6)

Table 8 Recovery time in the studied groups (data are presented as mean ± SD)

Parameter	Group D ($n = 25$)	Group M ($n = 25$)	P value
Recovery time (minutes)	9.32 ± 4.51	16.21 ± 5.52	< 0.05

dexmedetomidine, ketamine, and a mixture of both for pediatric sedation and reported the efficacy of sedation of dexmedetomidine–ketamine combination with minimal affection on hemodynamic and respiratory variables when compared with the other groups. El Sayed et al. (2015) compared dexmedetomidine ketamine and fentanyl-ketamine combinations for sedation in patients undergoing extracorporeal shock wave lithotripsy. In their study, there was no significant difference between the two groups as regards the respiratory variables. And they attributed that to the usage of ketamine in both groups which keep the hemodynamics and respiration stable. This also could explain the stability of oxygen saturation in most of the patients in our study especially those in midazolam ketamine group; it is known that benzodiazepines can produce dose-dependent respiratory depression; this could be minimized by the coadministration of ketamine while the great advantage of dexmedetomidine for procedural sedation or sedation in the intensive care unit is the lack of respiratory depression (Na et al. 2011; Buck 2010).

In the current study, the recovery time was assessed using Steward score, and it was significantly shorter in group D when compared with group M ($P < 0.05$). Unlike midazolam, dexmedetomidine had shorter elimination half-life of 2 h (vs 3–4 h for midazolam). This short half-life makes it easier to titrate and faster to recover (Alhashemi 2006). Despite their well-known sedative properties, a previous meta-analysis found no evidence that α2-agonists delay recovery times when used during perioperative period which was attributed to the concomitant anesthetic-sparing of them (Blaudszun et al. 2012), and this was also evident in the current study with the significantly lower total ketamine consumption in group D when compared with group M ($P < 0.05$), only five patients in group D versus 11 patients in group M required supplemental doses of ketamine. Moreover, dexmedetomidine-induced sedation qualitatively resembles normal sleep. This type of sedation is termed as co-operative or arousable, to distinguish it from sedation that is caused by drugs acting on G-aminobutyric acid receptors, such as benzodiazepines or propofol, which reduce consciousness (Yazbek-Karam and Aquad 2006). A finding can be explained by the nature of dexmedetomidine as a sedative not hypnotic agent so patients receiving it will be sedated but easily arousable. Same observation was found by Nasreen et al. (2009) who reported significant reduction in the awakening time in patients receiving dexmedetomidine when compared to the placebo group.

Table 9 The incidence of perioperative adverse events in both study groups

Side effects	Group D ($n = 25$)	Group M ($n = 25$)	P value
Nausea/vomiting	1 (4%)	4 (16%)	0.157
Tachycardia (HR inc > 20% from baseline)	0 (0%)	3 (12%)	0.074
Bradycardia (HR dec > 20% from baseline)	3 (12%)	0 (0%)	0.074
Hypotension	2 (8%)	1 (4%)	0.551
O_2 desaturation (SpO2 dropped to be < 92% from baseline)	2 (8%)	2 (8%)	1
Shivering	0 (0%)	3 (12%)	0.074
Laryngeal spasm	0 (0%)	0 (0%)	–
Increased oral secretions	0 (0%)	1 (4%)	0.312

There was no statistically significant difference between the two study groups as regards the incidence of side effects such as nausea/vomiting, hypotension, hypertension, bradycardia, tachycardia, oxygen desaturation, shivering, increased oral secretions, and laryngospasm.

Study limitations

The current study has several limitations. It was a single-center study. Also, we did not enroll critically ill patients, and the majority of the patients was clinically stable, thus may limit the application of the findings on clinically unstable patients with comorbidities. The small sample size may not have enabled the detection of adverse events that could occur with a low frequency. Also, the cost implications for the drugs used should be considered.

Conclusion

In conclusion, the dexmedetomidine–ketamine combination was superior to midazolam–ketamine combination for sedation in pediatric cardiac catheterization because of less intraoperative ketamine consumption required for adequate intraoperative sedation and the shorter recovery time.

Abbreviations

ASA: American Society of Anesthesiologists; CHD: Congenital heart disease; ECG: Electrocardiography; HR: Heart rate; MAP: Mean arterial pressure; NMDA: *N*-Methyl-D-aspartate; NSS: Normal saline solution; SpO_2: Peripheral oxygen saturation

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Availability of data and materials
The datasets generated during and/or analyzed during the current study are not publicly available due to restrictions based on privacy regulations and informed consent of the guardians of the participants, but are available from the corresponding author on reasonable request.

Authors' contributions
The corresponding author, MAM, contributed to the study conception and design, acquisition of data, and analysis and interpretation of data. The other author, HMF, was responsible for the drafting of the manuscript and its critical revision. Both authors read and approved the final manuscript.

Ethics approval and consent to participate
The current randomized, double blinded, placebo-controlled study was conducted on 50 acyanotic pediatric patients aged from 2 to 15 years who underwent elective cardiac catheterization for haemodynamic study of their congenital heart disease (CHD) in cardiovascular and thoracic surgery academy at Ain Shams university hospitals through the period from July 2015 to July 2016 after obtaining approval of research ethical committee (REC) of Faculty of medicine - Ain Shams University (FMASU) at june 2015 with reference number of FMASU 3274/2015 and patients' guardian written informed consents for acceptance of participation in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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