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A Randomised Prospective Comparative Study for Comparison of Dexmedetomidine and Ketamine vs Propofol and Ketamine for Procedural Sedation in Pediatric Patients Undergoing Minor Cardiac Procedures in Cardiac Catheterization Laboratory

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Abstract: ***The study compared dexmedetomidine-ketamine vs propofol-ketamine combination for pediatric cardiac catheterization in terms of hemodynamic stability, respiratory variables and recovery time. It concluded that dexmedetomidine-ketamine combination is a safe practical alternative, without any hemodynamic or respiratory effects during cardiac catheterization laboratory procedure but with some delayed recovery. The strength of this study was the adequate sample size, objective measure of outcome of interest, wide range of patient population and randomization of the intervention.***

Keywords: comparative, randomized, sedation, cardiac, catheterization, dexmedetomidine, ketamine, propofol, airway, saturation, blood pressure, heart rate, recovery, stable, pediatric, stewards

1. Introduction

Management of children with acute and chronic diseases require invasive or non-invasive approaches. Adequate depth of sedation has been recommended for optimum procedural outcomes. Traditionally Propofol has been preferred agent because of the ease of titration and rapid emergence post procedure.

In patients with comorbidities propofol may cause high incidences of hypotension, hypoventilation and apnea[(1)]. However these adverse effects are generally dose dependent and vary amongst patients. There has been search for alternative agents due to these above mentioned adverse effects.

Propofol[(3)], Ketamine[(4, 5)]and Dexmedetomidine[(6, 7)] are being used for periprocedural sedation. Goals of anaesthesia being analgesia, amnesia, anxiolysis and lesser separation anxiety, along with maintenance of airway, ventilation, acid base balance and thermoregulation. Anesthetic agents use should provide hemodynamically stable and smooth recovery[(8)].

Most commonly performed cardiac catheterization procedures are diagnostic catheterization, interventional procedures like aortic coarctation angioplasty/ballooning, pulmonary artery-angioplasty, patent ductusarteriosus stenting/device occlusion, device closure of ventricular septal defect, atrial septal defect, Dilatation of aortic/mitral/pulmonic valves[(9)].

Various periprocedural sedative agents which are hemodynamically stable along with least respiratory depression effects have been published [(10, 11)].

In this study we have compared the hemodynamic responses and the recovery time associated with the administration of Dexmedetomidine and Ketamine vs Propofol and Ketamine.

2. Materials and Methods

A randomized prospective comparative study was conducted after taking approval from institutional ethics committee. We included all paediatric patients of either sexes who were posted for various diagnostic or therapeutic cath lab procedures from September2018-April 2020. Children with chromosomal abnormalities or other multiple congenital anomalies, history of drug allergy, requiring mechanical ventilation or inotropic support, with hepatic or renal dysfunction were excluded.

Randomization was done by computer generated random numbers. Continuous data were summarized as Mean ± SD (standard deviation) while discrete (categorical) data in number and percentage. Quantitative data were analyzed by, mean, SD, Unpaired and paired “T” test .Qualitative data were analysed by percentage, Chi square test, fisher exact test.

Heart rate (HR), Mean arterial pressure (MAP), Saturation (Spo2) as determined by pulse oximetry were recorded during the procedure and postoperatively, heart rate and SpO2 were recorded every 5 mins. Recovery time was noted. Scores were assigned on admission to Post anesthetic room where the routine vital signs were measured. Repeated scoring were performed every 10 minutes till the patient recovered up to score of 6 according to the Stewards Simplified Post-anesthetic Recovery Score.[(12)]

Source of data:
The study population was randomly divided into two groups with 40 patients in each group.
Group I consisted of 40 patients received Dexmedetomidine IV infusion 1 µg/kg over 10 min + ketamine 1 mg/kg IV bolus for induction and then maintenance by IV infusion of 0.5 µg/kg/h of Dexmedetomidine and 1 mg/kg/h of Ketamine.

Group II consisted of 40 patients received Inj.Propofol1mg/kg and Inj. Ketamine 1 mg/kg IV for induction and then maintenance by IV infusion of 100 µg/kg/min of Propofol and 1 mg/kg/h of Ketamine.

Pre anaesthetic evaluation:

All patients underwent pre anaesthetic check-up one day prior to the day of procedure. The purpose and nature of study were fully explained to all patients' guardians and a written & informed consent was obtained.

Besides thorough clinical examination like history, general examination and systemic examination, the following investigation were done to exclude any systemic illness and also for ASA grading

Investigations-Complete blood count, Chest X-ray, Electro cardiogram, Serum Creatinine & Blood Urea Nitrogen, Liver Function tests, Echocardiography, Ultrasound of abdomen, Coagulation profile.

Anaesthesia Technique

According to hospital policy, all children were kept fasting as per the fasting guidelines of ASA:

After midnight: Stop non-clear liquids and solids (this includes any food and also hard candy or gum)

6 hrs before arrival: Stop infant formula.

4 hrs before arrival: Stop breast milk.

2 hrs before arrival: Stop clear liquids (water, clear apple juice).

An intravenous line was accessed with appropriate size cannula and i.v. fluid was started. Baseline parameters like pulse rate & SpO2, blood pressure and ECG were recorded by using pulse oximeter, NIBP monitor and ECG monitor.

Heart rate (HR), oxygen saturation (SpO2), and respiratory rate (RR) were recorded continously during the procedure, while Mean arterial pressure (MAP) was recorded every 5 minutes during the procedure.

The patients were premedicated with glycopyrrolate(10 µg/kg) and midazolam (50 µg/kg) intravenously (IV) 10 min before taking the child inside the catheterization laboratory where appropriate measures to prevent hypothermia to child were undertaken.

In group I, patients received Inj. Dexmedetomidine IV infusion 1 µg/kg over 10 min + Inj. ketamine 1 mg/kg IV bolus for induction and then maintenance by IV infusion of 0.5 µg/kg/h of dexmedetomidine and 1 mg/kg/h of ketamine.

In group II, patients received Inj.propofol 1mg/kg and Inj. ketamine 1 mg/kg IV for induction and then maintenance by IV infusion of 100 µg/kg/min of propofol and 1 mg/kg/h of ketamine.

Additional doses of ketamine 0.5 mg/kg IV bolus were administered when a child showed discomfort in both the groups.

Postoperatively, heart rate and SpO2 were recorded every 10 min. Recovery time was noted down. Scores were assigned on admission to Post-anesthetic room where the routine vital signs were measured. Repeated scoring was performed every 10 minutes till the patient recovered up to score of 6 according to the Stewards Simplified Post-anesthetic Recovery Score.

3. Results

A total of 80 children were recruited in this study. There was no significant difference between the two groups with respect to patient characteristics, type and mean duration of surgery.

The patient's age and weight were comparable in two groups [Tables.1]. The mean age in DK group was 5.4 (±2.84) years and in PK group was 5.375 (±2.55) years with p = 0.967. The mean weight in DK group was 18.05 (±7.67) kg and in PK group was 19.72 (±9.62) kg with p = 0.392. By using unpaired t-test, p > 0.05, therefore there was no significant difference between mean age and weight between the two groups. Mean duration of surgery/procedure in group DK was 58.65±11.88 and group PK was 57.42 ± 7.84 min.[Table 7] The two groups were comparable with respect to type of surgery/procedure [Table 5]. Heart rate was significantly lower in DK group at 5, 10, 15, 20, 25 min post induction in comparison to PK group. Later on, the heart rate continued to be lower in both the groups but it was not statistically significant.[Table 2] There was no statistically significant difference between the two groups in mean BP. [table 6

There was no significant difference between mean SpO2 in group DK and group PK from baseline to 60th min [Table 4]. There was no significant difference between the respiratory rate in group DK and group PK from baseline to 60th min [Table 3]. Recovery was significantly delayed in DK group 38.8 ± 6.29 min versus 30.05 ± 3 min in PK group (P ≤ 0.05) [Table 1]. Additional ketamine consumption was significantly higher in DK group (15 patients in DK) than in PK group (02 patients in PK) (P ≤ 0.05) [Table 8].

Table 1: Comparison of Mean Age, Mean Weight and Mean Recovery Time in two groups: Group D+K and Group P+K

Mean ± SD	Group D+K (N=40)	Group P+K (N=40)	P value
Age (in years)	5.4±2.84	5.375±2.55	0.967
Weight (in kg)	18.05±7.67	19.725±9.62	0.392
Recovery time (in mins)	38.8±6.29	30.05±3	<0.001

Table 1: Comparison of Mean Heart Rate in two groups: Group D+K and Group P+K

Heart rate recording time (Beats/min)	Mean Heart rate of Group D+K (N=40)	Mean Heart rate of Group P+K (N=40)	P value
baseline	112.125±16.53	113.5±13.82	0.688
5 mins	101.725±13.31	108.425±13.6	0.029
10 mins	101±14.76	107.425±13.6	0.022
15 mins	97.7±15.53	104.375±12.67	0.038
20 mins	95.875±15.54	102.375±13.03	0.046
25 mins	94.775±15.15	104.2±13.31	0.004
30 mins	98.85±16.36	104.975±11.25	0.055
35 mins	99.875±15.05	103.925±11.71	0.183
40 mins	102.425±14.73	103.025±13.7	0.851
45 mins	102.85±16.07	108.025±11.47	0.101
50 mins	105.75±15.09	107.6±11.24	0.536
55 mins	105.825±15.07	108.4±11.61	0.395
60 mins	107.725±15.7	110.575±12.23	0.368

Table 2: Comparison of Mean Respiratory Rate in two groups: Group D+K and Group P+K

Respiratory rate (Breaths/min) Recording time	Mean Respiratory rate of Group D+ K (N= 40)	Mean Respiratory rate of Group P+K (N=40)	P value
Baseline	23.55±5.87	24±5.13	0.716
5 min	19.725±4.67	20.025±4.81	0.778
10 min	18.65±4.92	19.875±4.21	0.235
15 min	20.2±4.44	20.45±5.35	0.821
20 min	21.15±5.2	20.8±5.34	0.767
25 min	19.925±4.2	19.675±3.46	0.772
30 min	20.625±4.68	21.125±5	0.646
35 min	21.5±5.22	20.8±3.98	0.502
40 min	20.125±5.1	19.925±4.19	0.849
45 min	21.25±4.82	20±4.81	0.249
50 min	21.025±4.37	21.1±3.6	0.933
55 min	20.35±5.99	20.825±5.25	0.707
60 min	21.775±5.53	21.75±5.02	0.983

Table 3: Comparison of Mean SPO_2 (Pulse Oximetry) in two groups: Group D+K and Group P+K

Spo2 Recording time	Mean Spo2 of Group D+K (N=40)	Mean Spo2 of Group P+K (N=40)	P value
Baseline	99.75±0.44	99.85±0.36	0.269
5 min	99.625±0.49	99.75±0.44	0.1
10 min	99.575±0.5	99.675±0.47	0.362
15 min	99.425±0.87	99.65±0.53	0.168
20 min	99.6±0.63	99.8±0.41	0.096
25 min	99.55±0.64	99.75±0.49	0.121
30 min	99.6±0.63	99.8±0.46	0.111
35 min	99.575±0.64	99.725±0.51	0.247
40 min	99.6±0.63	99.75±0.59	0.275
45 min	99.85±0.36	99.95±0.22	0.14
50 min	99.625±0.74	99.85±0.36	0.90
55 min	99.775±0.42	99.9±0.3	0.133
60 min	100±0	100±0	1.00

Table 4: Comparison of Types of Procedures in two groups: Group D+K and Group P+K

Procedure	Group D+K (N=40)	GROUP P+K (N+40)
ASD Device closure	6(15%)	7(17.5%)
Balloon dilatation of mitral valve	6(15%)	6(15%)
Balloon dilatation of aortic valve	2(5%)	1(2.5%)
Diagnostic cath.	11(27.5%)	10(25%)
VSD Device closure	04(10%)	05(12.5%)
PDA Device closure	11(27.5%)	11(27.5%)

Table 5: Comparison of Mean MAP in two groups: Group D+K and Group P+K

MAP recording time	Mean of MAP of GROUP D+K (N=40)	Mean of MAP of GROUP P+K (N=40)	P Value
Baseline	63.325±5.05	62.6±6.25	0.47
5 mins	60.375±4.54	60.4±5.93	0.28
10 mins	59.35±2.23	59.125±4.72	0.41
15 mins	60.075±2.98	59.275±4.88	0.11
20 mins	60.55±2.12	59.175±4.79	0.06
25 mins	59.9±2.39	59.8±2.52	0.23
30 mins	61.025±2.22	60.175±2.51	0.30
35 mins	61.125±2.75	60.275±2.44	0.37
40 mins	61.525±3.57	60.6±2.39	0.08
45 mins	61.875±2.59	61±2.08	0.68
50 mins	60.925±2.8	60.75±2.03	0.39
55 mins	61.4±2.97	60.35±2.71	0.1
60 mins	62.6±2.35	62±1.71	0.36

Table 6: Comparison of Mean Duration of Procedure in two groups: Group D+K and Group P+K

Duration of procedure (in mins)	Group D + K (n =40)	Group P + K (n=40)	P value
Mean ± SD	58.65±11.88	57.425±7.84	0.59 NS

Table 7: Comparison of Mean Additional Consumption Ketamine Boluses (in %) of in two groups: Group D+K and Group P+K

Additional ketamine doses	Group D+K (N=40)	Group P+K (N=40)	P Value
Yes	15(37.5%)	6(15%)	0.022
No	25(62.5%)	34(85%)	
Total	40(100%)	40(100%)	

4. Discussion

Cardiac catheterization differs amongst paediatric and adults in terms of requirement of procedure, patterns of diseases, need of general anesthesia or sedation to evaluate the heart and its anomalies. Most commonly performed procedures include device closures, angiolpasty, valvuloplasty, diagnostic and electrophysiologic studies.

In our study, we have compared the combinations of Group I D+K (Dexmedetomidine-Ketamine) versus Group II P+K (Propofol-Ketamine) in 80 patients undergoing cardiac catheterization for the purpose of evaluation of hemodynamic stability and recovery time .In this study, we observed decrease in the heart rate more significantly in Group I(Dexmedetomidine-Ketamine group) for the first 25 minutes post induction .Decrease in the heart rate persisted in both the groups till the end of procedure afterwards, statistically insignificant.

We found the heart rate significant lower in the group I (Dexmedetomidine-Ketamine) than Group II (Propofol-ketamine) which is similar to a study conducted by Tosun Z et al. in 2006, [(11)]who studied the effects of combination of Dexmedetomidine-Ketamine andPropofol-Ketamine in terms of hemodynamics, sedation level and recovery period in pediatric patients posted for cardiac catheterization studies.

We found no significant difference amongst the two groups in terms of hemodynamics and respiratory parameters (Spo2 and Respiratory rate) which is similar to a study conducted by Ali NP et al. in 2015[(13)] who also found insignificant difference in terms of recovery pattern and hemodynamics in the two groups of Dexmedetomidine-Ketamine and Propofol-Ketamine in patients undergoing pediatric cardiac catheterization.

Propofol has been used for providing paediatric cardiac catheterization due to the rapid emergence which it provides, as also studied by Gozal D et al. in 2001[(14)]. They found Propofol as an adequate sedative agent for pediatric cardiac catheterization.

We found the hemodynamic changes after ketamine administration were insignificant and it did not altered the clinical status and cath study. Similarly, Morray JP et al. in 1984[(15)] studied the hemodynamic changes of ketamine in patients with congenital heart disease. They too concluded that it can be used as an sedative agent in paediatric cath study as it did not altered the information obtained by cardiac catheterization.

Dexmedetomidine, an alpha 2 agonist has been used as an sedative, analgesic and anxiolytic agent .It periprocedural use reduces anesthetic requirements and the symapthetic response to the surgical stimulation. A study conducted by Munro HMet al. in 2007 [(10)] showed it to be a suitable

alternative agent with Propofol/ Ketamine or without them for sedation in paediatric cardiac catheterization.

We concluded that the recovery time was delayed in the group I (Dexmedetomidine-Ketamine group) as compared to Group II(Propofol-Ketamine group) (38.8 ± 6.29 min versus 30.05 ± 3) $p \leq 0.05$. Similar study conducted by Heard C et al. in 2008[16] observed the significantly longer recovery period with Dexmedetomidine-Midazolam group as compared to Propofol. Thimmarayappa A et al. in 2015[17] too concluded that average recovery time is prolonged after dexmedetomidine sedation after stopping of infusion.

Our study observed high utilization of Ketamine boluses in Group I D+K (Dexmedetomidine-Ketamine group) as compared to Group II P+K (Propofol-Ketamine group). none of the patients developed any adverse effects like increased secretions, convulsion, laryngospasms etc. Tosun Z et al. in 2006 [11] too noticed similar high utilization of Ketamine in Dexmedetomidine group as compared to Propofol group.

This study which compared the dexmedetomidine and ketamine versus propofol and ketamine combinations on hemodynamic stability, respiratory variables, and recovery time in children undergoing minor cardiac procedures in cardiac catheterization laboratory concludes that the use of Dexmedetomidine-Ketamine combination is a safe, practical alternative, without any hemodynamic or respiratory effects during the cardiac catheterization laboratory procedure but with some delayed recovery. The strength of this study was the adequate sample size, objective measure of outcomes of interest, wide range of patient population, and randomization of the intervention. The limitation of this study was the lack of masking of the intervention and that majority of the patients were clinically stable, thus limiting the application of the findings on clinically unstable patients with co-morbidities.

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