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COMPARISON OF THE HAEMODYNAMIC EFFECTS OF THE INDUCTION AGENTS KETAMINE VERSUS SEVOFLURANE IN PAEDIATRIC CARDIAC SURGICAL PATIENTS: A RANDOMIZED INTERVENTIONAL STUDY

Anaesthesiology

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ABSTRACT

Background: Sevoflurane is widely used in paediatric anesthesia for induction. Ketamine has been preferred in paediatric cardiovascular anaesthesia. Aim of this study was to compare the haemodynamic effects of ketamine and sevoflurane for anesthesia induction in paediatric patients undergoing cardiac surgery under GA. **Material and Methods:** Sixty children 1-12year age undergoing cardiac surgery under general anaesthesia were included in the study. After randomized into two equal groups, anesthesia induction was started with (2mg/kg) iv ketamine (group A). In the second group, induction was achieved with upto 8% sevoflurane (group B). Haemodynamic parameters (HR, SBP, DBP, MAP) and oxygen saturation were recorded at just after induction, 1, 5, 10, and 20minutes after intubation and any event during induction period was also noted. **Results:** The demographic characteristics of the patients were similar in both the groups. Heart rates and oxygen saturation values were similar between both the groups during the study. However, blood pressure levels were significantly lower in group B after recording baseline values till the intubation time (at 1, 5, and 10 min). Respiratory events, salivation and nausea&vomiting observed during the study were mild and insignificant and no other major side effects are reported in our study. **Conclusion:** Ketamine is a safe and effective induction agent with better haemodynamic stability as compared to sevoflurane in paediatric patients undergoing cardiac surgery under general anesthesia. It is also devoid of major side effects.

KEYWORDS

Anaesthesia induction agents; Ketamine; Sevoflurane; Paediatric cardiac surgery; Haemodynamic parameters

INTRODUCTION

Inhalation anaesthetics and intravenous agents are widely used in paediatric cardiac surgery, Paediatric patients undergoing cardiac surgery are in compromised haemodynamic state and require intensive cardiac monitoring hence choice of the anaesthetic induction agents are important in such patients. A number of factors influence the choice of the anesthetic technique in paediatric patient undergoing cardiac surgery are- heart rate, shunting, myocardial contractility, ventricular dilation and hypertrophy and pulmonary hypertension. The anaesthetic goals remains to maintain these factors.[1]

An ideal induction agent for general anesthesia should have haemodynamic stability, minimal respiratory side effects and rapid clearance.

Ketamine is one of the most popular anesthetic agents in paediatric cardiovascular patients, as it maintains cardiac output and perfusion pressures via sympathetic system stimulation[2]. Ketamine is a unique anaesthetic drug that provides profound analgesia, hypnosis and amnesia. It causes less respiratoy depression than other intravenous anaesthetics at clinically doses and has sympathomimetic properties that make it a useful drug for patients with impaired cardiac function, it also has anti-inflammatory properties that are potentially useful in attenuating the inflammatory response to cardiopulmonary bypass.[3] This agent is also commonly used in catheterization procedures in pediatric cardiac patients and ICU [4,5].

Sevoflurane is currently the most commonly used volatile anaesthetic for inhalational induction because of its lack of pungency and low blood:gas solubility, allowing for a smooth induction of anaesthesia that can provide suitable conditions for airway management with or without adjuvant drugs such as NMBDs or opioids.[6] Sevoflurane is less soluble in blood, produces fewer arrhythmias and decreases contractility less than halothane without changing pulmonary to systemic blood flow ratio in children with congenital heart disease[7]. These features combined with its favourable cardiovascular profile should make it agent of choice for inhalation induction in adult and paediatric anaesthesia. It is the volatile anaesthetic for rapid induction and rapid awakening.

MATERIAL AND METHODS

Study location:

The study will be conducted in department of anaesthesia, Cardiothoracic and vascular surgery operation theatre, S.M.S. Medical College, Jaipur during 2019-20. Due permission from institution ethics committee and research review board and after taking written informed consent from the parents of patient.

Study design:

Hospital Based, Prospective randomized Interventional study.

Sample size:

The sample size calculated is 30 cases in each group would be required at 95% confidence and 80% power to verify the expected minimum 13(±16) bpm difference in change of heart rate from base line to 10 minutes after induction in both study groups as per seed article.[1] So, for study purpose, 30 cases will be taken in each group.

Randomization:

It is a statistical procedure by which the participants will be allocated into two different groups. 60 eligible cases will be randomly allocated in two study groups using computerised random number table.

Study universe:

Paediatric patients of age 1-12 year undergoing cardiac surgeries under general anaesthesia.

Study groups:

The study will be conducted in the following 2 groups of patients. Each group will consist of 30 patients. (n=30/group)

- **Group A (n=30):** Patients will receive inj. ketamine 2mg/kg IV.
- **Group B (n=37):** Patients will receive inhalational sevoflurane (upto8%) ensuring loss of eyelash reflex.

PROCEDURE:

Institutional ethics committee and research review board approval will be taken prior to the commencement of the study. 60 patients undergoing cardiac surgery under general anesthesia will be selected after applying already mentioned stringent inclusion and exclusion criteria. One day prior to surgery all parents of Patients were explained about the anaesthetic technique and a detailed pre anaesthetic check-up were done. The patients were randomized into two groups of 30 each by using computerised generated random number table. Informed and written consent were taken from patient's parents or relatives. On arrival of patient in the operation theatre fasting status,written informed consent and PAC were checked. Routine noninvasive monitors attached and baseline parameters i.e. Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), oxygen saturation SpO_2 were noted. ECG was attached to the patient. Intravenous line 24 G in upper limb were secured. Patients was induced with study drug. Induction of anaesthesia with Study drug, was given according to group allocation. Study drug in group-A patients were received inj. Ketamine 2mg/kg iv and group-B patients were received inhalational Sevoflurane, its concentration gradually

increases (upto8%) and loss of eyelash reflex were considered to be the end point. Haemodynamic parameters were recorded just after induction Inj. Fentanyl (2mcg/kg) IV. Inj. Rocuronium (0.9 mg/kg) IV were given as a muscle relaxant to facilitate endotracheal intubation. Patient were ventilated with 100% oxygen for 90 seconds. Haemodynamic parameters were also noted just after induction of anaesthesia. Under direct laryngoscopy patient was intubated with appropriate size E.T.T. Bilateral air entry was checked & tube was fixed. Haemodynamic Parameters were noted at 1,5,10 & 20 minutes after intubation. Then surgery was allowed to proceed& anaesthesia was maintained with Oxygen, Sevoflurane &inj.vecuronium and inj. Fentanyl. After completion of surgery patient was shifted to ICU with endotracheal tube in situ.

STATISTICALANALYSIS:

Statistical analysis was performed with the SPSS (Statistical Package for the Social Science), version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by students t-test. Probability was considered to be significant if less than 0.05.

RESULTS

A total of 60 patients were enrolled into the study. No statistically significant differences were found with respect to mean age, weight and gender between ketamine and sevoflurane groups in our study (p>0.05) and thus the results were comparable.

Hemodynamics – The baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable between both the groups. There was no statistically significant difference in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure before induction in both the groups. The significant difference was observed in SBP, DBP and MAP both the groups at just after induction, 1 min., 5min. and 10min. post-intubation, but DBP was also significant at 20min. Hemodynamic parameters SBP, DBP, and MBP were significantly decrease in patients induced with Sevoflurane (group B) as compared to patients induced with Ketamine (group A) and decrease was maximum in group B and minimum in group A at just after induction after that they started increasing. No significant difference was observed in heart rate in both groups in any time interval. No significant side effects or complications were found in any of the study groups.

Thus it shows that Ketamine was comparatively better in maintaining the hemodynamic stability after induction of anaesthesia as compared to Sevoflurane.

MONITORING

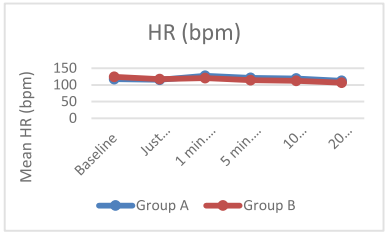
Table-1: Demographic profile:

Demographic data	**Group-A**	**Group-B**	**p-value**
Mean age in years	5.90±3.91	5.27±3.40	0.505 (NS)
Gender (M:F)	19:11	15:15	0.434 (NS)
Mean Weight (kg)	16.36±7.20	15.07±5.59	0.441(NS)

Both the groups were comparable and there was no statistically significant difference regarding age, Sex, weight of patients in two groups.

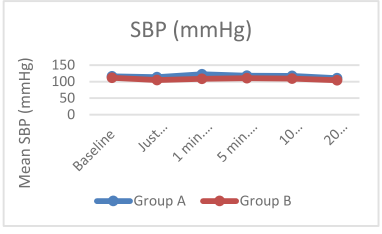
Table-2: Hemodynamic comparison in both the groups

Hemodynamic variables	**Group-A**	**Group-B**	**p-value**
Mean Heart Rate (base line)	117.13	124.13	0.224 (NS)
Mean Heart Rate (just after induction)	115.37	117.10	0.706 (NS)
Mean Heart Rate (1 min post intubation)	127.60	120.20	0.123 (NS)
Mean Heart Rate (5 min post intubation)	121.07	114.23	0.132 (NS)
Mean Heart Rate (10 min post intubation)	119.43	112.17	0.147 (NS)
Mean Systolic BP (base line)	115.90	111.43	0.201 (NS)
Mean Systolic BP (just after induction)	113.47	105.10	0.010 (S)
Mean Systolic BP (1 min post intubation)	122.47	108.63	0.0006 (S)
Mean Systolic BP (5 min post intubation)	118.17	110.33	0.039 (S)
Mean Systolic BP (10 min post intubation)	117.03	109.10	0.038 (S)
Mean Diastolic BP (base line)	73.97	71.63	0.451 (NS)
Mean Diastolic BP (just after induction)	71.90	65.97	0.022 (S)
Mean Diastolic BP (1 min post intubation)	76.47	66.43	0.002 (S)
Mean Diastolic BP (5 min post intubation)	72.23	65.93	0.035 (S)
Mean Diastolic BP (10min post intubation)	70.83	65.70	0.037 (S)

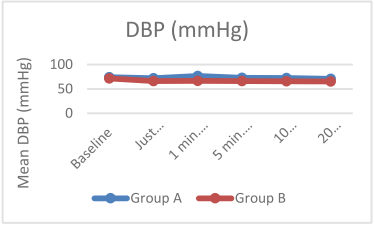


Graph 1: Mean Heart rate comparision in both the groups

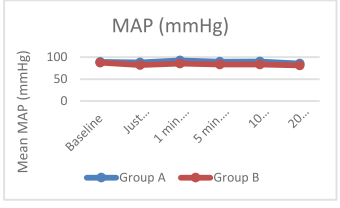
The baseline heart rate was comparable between the two groups with no statistical significant difference (p>0.05)). Both the groups showed decrease in the HR when compared to the baseline just after induction, and decrease in HR less in group B (117.10±16.79) compared to group A (115.37±18.61). In group A there was increase in HR after intubation till 10minutes, But in group B the HR was not increase above the baseline after intubation. There was no statistically significant difference observed between the two groups in the heart rate at any time interval.



Graph 2: Mean systolic blood pressure comparision in both the groups. Significant difference in SBP was observed between the groups at just after induction, 1 min., 5min., and 10 min. post intubation, but was not significant at 20min. post intubation.



Graph 3: Mean diastolic blood pressure comparison in both the groups. Significant difference in DBP was observed between the groups at just after induction, 1 min., 5min., 10 min. and 20 min. post intubation.



Graph 4: Mean diastolic blood pressure comparison in both the groups

The baseline mean arterial pressure was comparable between the groups with no statistical significant difference (p>0.05). Significant difference in MAP was observed between the groups at just after induction, 1 min., 5min., and 10 min. post intubation, but was not significant at 20min. post intubation. Mean MAP was significantly lower in Group B as compared to Group A.

Table-3: Complications or side effects

	Group-A	Group-B	p-value
Nausea and Vomiting	4	1	0.350 (NS)
Salivation	4	1	0.350 (NS)
Respiratory events	0	3	0.236 (NS)
Emergency agitation	0	0	-

Eight cases had complications in group A, 5 cases had complications in group B. 5 cases had nausea and vomiting, 5 cases had salivation, 3 cases had respiratory events, Out of the 5 cases of nausea and vomiting 4 cases were from group A and 1 case from group B. Out of 5 cases of salivation 4 were from group A, while 1 from group B. Out of 3 cases with respiratory events all were from group B.

None of the cases had emergence agitation during intra operative or post-operative period. In terms of development of either intra-operative or post-operative complications, the difference between the two groups was not found to be statistically significant (Table-3).

DISCUSSION

The aim of the study was to compare the hemodynamic effects of the induction agents ketamine versus sevoflurane in paediatric patients undergoing cardiac surgeries under general anaesthesia.

The study involved 60 paediatric patients of ASA II & III physical status. They were randomized in to 2 groups: Group – A (Ketamine) and Group – B (Sevoflurane) and following parameters were analysed.

- Hemodynamic parameters.
- Complications or side effects.

Both the groups were comparable and there was no statistically significant difference regarding age, sex, body weight of patients in two groups.

In this study, the mean baseline heart rate was comparable in both the groups with no statistical significant difference ($p>0.05$). Both the groups showed decrease in the HR when compared to the baseline just after induction, and decrease in HR less in group B (117.10±16.79) compared to group A (115.37±18.61). In group A there was increase in HR after intubation till 10minutes, But in group B the HR was not increase above the baseline after intubation. After induction there was no statistically significant difference observed between the two groups in the heart rate at any time interval. The reduction in HR after induction occurred due to the abolition of the sympathetic drive. Very similar results were found in studies conducted by A R Tavakollian et al.[8] Rivenes et al.[9] Sungur Ulke et al.[2] Hasija S. et al.[1] All these studies including our study show consistent findings with regard to heart rate. This shows that both the drugs are comparable with regard to effect on heart heart.

The significant difference in SBP, DBP and MAP was observed between the groups at just after induction, 1 min., 5min. and 10min. post-intubation, but DBP was also significant at 20min. post-intubation. We observed that there was significant decrease in SBP, DBP, MAP after induction till 10 minutes of post-intubation in patients induced with Sevoflurane (group B) as compared to patients induced with Ketamine (group A).

Thus it shows that Ketamine (Group A) was comparatively better in maintaining the haemodynamic stability in form of blood pressure after induction of anaesthesia as compared to Sevoflurane (Group B). Our study is comparable with the studies carried by Sungur Ulke et al.[2] Rohit S. Loomba et al.[10] Blumberg D, et al.[11] Malik M et al.[12] Hasija S. et al.[1] Eis S, Kramer et al.[13] Milan K S et al.[14]

In this study the baseline mean SPO_2% was comparable in both the groups. There was no significant difference observed between the groups at any time interval later on. A R Tavakollian et al.[8] Sungur Ulke et al.[2]

In our study we observed that no significant side effects or complications were found in any of the study groups. The results of our study showed that 13% patients in ketamine group and 3% patients in sevoflurane group reported with nausea and vomiting ($p = 0.350$). As per various articles both sevoflurane[15] and ketamine[16] are associated with postoperative nausea and vomiting (PONV). Although this PONV can be successfully managed through anaesthesia modification (use of air rather than N_2O) and/or antiemetic administration.

The other finding of our study was excessive salivation. 13% patients in ketamine group reported with increased salivation whereas only 3% patients in sevoflurane group had salivation ($P= 0.350$) this was statistically insignificant. Study done by Sungur et al[2] showed that excessive salivation occurs in 4 children (16%) in ketamine group. In a study Lin and Durieux showed that most common side effects of ketamine were increased salivation and emergence reactions.[17]

Respiratory events (breath holding, coughing and hiccup) occurred more frequently in sevoflurane group in 3 (10%) patients whereas none of patients in ketamine group reported this. We observed mostly breath holding, Coughing and hiccup were observed rarely. But this was not statistically significant ($P=0.236$). Severe respiratory events such as bronchospasm or arterial desaturation did not occur in our study. Respiratory side effects of sevoflurane were debated in a multicentric study by Kataria et al.[18] Similar results were obtained by Sungur ulke et al.[2]

Inicidence of emergence agitation (EA) in our study was not observed. Similarly Sungur et al[2] did not observe any emergence reactions in their study. A study conducted by David Costi et al.[19] they studied the effects of sevoflurane and other general anaesthetic agents with regard to risk of emergence agitation in children. They found that children has less risk of emergence agitation with ketamine as compared to sevoflurane.

Thus our study shows that ketamine induction is a safe choice in paediatric patients undergoing cardiac surgery and when compared to sevoflurane, ketamine provides more stable haemodynamic condition for induction of anaesthesia. Sevoflurane cause decreased in blood pressure, So sevoflurane should be used with caution in this group of surgical population. Moreover ketamine and sevoflurane when compared with regards to adverse effects both are safe as no major side effects were reported in our study.

CONCLUSION

Ketamine is a safe and effective induction agent with better haemodynamic stability as compared to sevoflurane in paediatric patients undergoing cardiac surgery under general anesthesia. It is also devoid of major side effects.

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