



Effect of Dexmedetomidine on Emergence Agitation in Children Undergoing Surgeries using Sevoflurane- Randomized Controlled Observational Study

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Abstract

Background: Emergence agitation is one of the post-operative complication after paediatric surgeries. Its incidence ranging in literature from 10% to 80%¹. Sevoflurane is very commonly used inhalational anaesthetic agent in induction and maintenance of anaesthesia. Incidence of emergence agitation may be high as 67%² when Sevoflurane is used.

Study Design: Randomized controlled observational study

Objective: Aim of this study was to assess the effect of DEXMENDETOMIDINE in prevention of emergence agitation in children (between 6 and 12 yrs of age) after undergoing various surgeries using Sevoflurane as an anaesthetic agent.

Method: This study included 150 patients randomly classified into two groups. Group A underwent surgeries using sevoflurane as sole anaesthetic agent and Group B underwent surgeries using Sevoflurane with Dexmedetomidine intravenously. In Post operative stage all patients were assessed for emergence agitation using PAED³ scale. Those having PAED score equal to or more than 16 were considered agitated.

Result: Dexmedetomidine group had reduced emergence agitation (10.7%).

Keywords: Emergence agitation, objective pain scale, Sevoflurane, Dexmedetomidine.

Introduction

Emergence agitation is described as a state of non-purposeful restlessness and inconsolability that is often accompanied by thrashing, screaming, prolonged crying and disorientation. Sevoflurane is a popular inhalational anaesthetic agents for general anaesthesia in children. It is especially characterized by a lower blood/gas partition coefficient, less irritant to airways, less cardio depressive affects and less toxicity to the liver or

kidney as compared to other inhalational anaesthetic agents. Anesthesiologists prefer these characteristics in paediatric use. However, concern has been raised over its propensity to result in significant excitatory emergence in recovery phase of Sevoflurane anaesthesia. Sevoflurane has been associated with increased emergence agitation and incidence may be high as 67%.

Multiple medications including Ketamine, Propofol, Clonidine and Opioids have been used effectively to prevent EA. However, these medications may increase sedation after an anaesthesia, some cases associated with undesirable side effect such as nausea and vomiting delaying discharge⁴.

Dexmedetomidine, another α_2 adrenergic agonist with a larger ratio of α_2/α_1 activity (1600:1) has been used in Paediatric population. Manna EM, Abdel Haleem AA, Mohammed EA and his colleagues used Dexmedetomidine in paediatric patients receiving Sevoflurane anaesthesia and observed a significant reduction in emergence agitation⁵.

Present study was designed to find out the efficacy of Dexmedetomidine in reducing emergence agitation after Sevoflurane anaesthesia in paediatric patients between 6-12 years of age underwent various surgeries.

Method

This study was conducted in Department of Anesthesiology in RIIMS, Ranchi, after approval from Ethical Committee. This study included 150 patients having inclusion criteria of age between 6 to 12 yrs with absence of mental or developmental delay with physical status ASA Grade I or II. All these patients were scheduled for elective surgeries using Sevoflurane as inhalational anaesthetic agent and written informed consent from parent or guardian. Patients having systemic or psychiatric illness with mental or developmental delay and history of hypersensitivity to drugs used in this study were excluded.

150 patients were divided into two groups by random allocation using closed envelop method by an anaesthesiologist who had no idea about medications used in the study.

Group A - Control Group (n=75)

Group B - Dexmedetomidine Group (n=75)

Along with all routine investigations and thorough pre-anaesthetic evaluation was done a day before

surgery. Patients were advised for 6-8hrs of fasting before surgery and Intravenous line was secured in operation theatre. On arrival in operation theatre monitors were attached and baseline parameters were recorded - H/R, BP, SPO₂, ECG and Respiratory rate. Premedication with Glycopyrrolate (.004 mg/kg) I.V, Ranitidine (0.45 mg/kg) I.V. and Ondansetron 0.15 mg/kg I.V. given. Anaesthesia was induced with 4% Sevoflurane. After induction of anaesthesia endotracheal intubation was done with 0.5 mg/kg Atracurium I.V. and patient was put on mechanical ventilation. All patients in both groups were given Fentanyl 2 μ g/kg I.V for analgesia. After induction of anaesthesia patients in group B were given loading dose of Dexmedetomidine 0.5 μ g/kg I.V. over 10 minutes slowly then at the rate of 0.2 μ g/kg/hr I.V. intraoperatively till 5 minutes after extubation. Patients in Group A were given 10 ml Normal Saline I/V over 10 minutes. Anaesthesia in both groups were maintained with 1% to 2% end tidal Sevoflurane, 66% nitrous oxide in oxygen and Atracurium 0.1 mg/kg I.V. Concentration of Sevoflurane was adjusted to maintain adequate depth of anaesthesia which was assessed by measuring heart rate, blood pressure and respiratory rate. Intra operative monitoring included ECG, NIBP, respiratory rate and pulse oximetry. For analgesia, Fentanyl was given at 0.25 μ g/kg I.V. during surgery. At the end of surgery anaesthetic agents were discontinued. Effect of Neuromuscular blocking agents were reversed with administration of neostigmine (0.05 mg/kg) and glycopyrrolate 0.2 mg for each 1 mg of neostigmine intravenously. Extubated in awake condition after proper suctioning. Patients were observed for emergence agitation, pain, analgesia if needed along with heart rate, oxygen saturation and blood pressure in post-operative period in operation theatre and in PACU at intervals of 10 minutes till patients shifted toward or ICU. Emergence agitation was assessed with the help of Paediatric anaesthesia emergence delirium scale (PAED).

Paediatric anesthesia emergence delirium scale (PAED)³

Clinical Status	Not at all	Just a little	Quite a bit	Very much	Extremely
1. The child makes eye contact with care givers	4	3	2	1	0
2. The child's actions are purposeful	4	3	2	1	0
Clinical Status	Not at all	Just a little	Quite a bit	Very much	Extremely
3. The child is aware of his/her surroundings`	4	3	2	1	0
4. The child is restless	0	1	2	3	4
5. The child is inconsolable	0	1	2	3	4

If total score is equal to or greater than 16, patient is considered as a case of post operative emergence delirium. If emergence agitation was

present (PAED score equal to or greater than 16), patient was treated with Midazolam (0.1 mg/kg) I.V.

Pain was assessed by objective pain scale.

Objective Pain Scale⁶

Parameter	Finding	Point
Systolic blood pressure	Increase <20% of preoperative blood pressure	0
	Increase 20-30% of preoperative blood pressure	1
	Increase >30% of preoperative blood pressure	2
Crying	Not crying	0
	Responds to age-appropriate nurturing (tender loving care)	1
	Does not respond to nurturing	2
	Thrashing (moving wildly)	2
	Rigid (stiff)	2
Agitation	Asleep or calm	0
	Can be comforted to lessen the agitation (mild)	1
	Cannot be comforted (hysterical)	2
Complains of pain	Asleep	0
	States no pain	0
	Cannot localize	1
	Localize pain	2

If objective pain score was equal to or more than 4 then Fentanyl was given 0.25µg/kg intravenously postoperatively.

Data were statistically described in terms of mean ± standard deviation (±SD), median and range or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's t test for independent samples. For comparing categorical data, Chi square (X²) test was performed. P Values less than 0.05 were considered statistically significant. All statistical calculations were done using Statistical package for social science.

Result

Demographically patients in both groups were comparable to each other which is obvious from table below:

Table No. 01

Item	Group-A(n=75)	Group-B(n=75)	P-value
Age(yrs)	8.98±2.10	8.92±2.05	0.234
Sex(M:F)	39/36	41/34	0.162
Weight(kg.)	20.82±4.33	20.85±3.53	0.764

P value < 0.05 => Significant; P value > 0.05 => Insignificant

Other intraoperative were also comparable to each other in Group A and Group B.

Table No. 02

Intra Operative Parameters	Group A(n=75)	Group B(n=75)
Mean Duration Of Anaesthesia(mins)	82.64±27.24	83.37±25.18
Mean duration Of Surgery(mins)	70.86±24.91	71.84±22.99
Mean ET Sevoflurane(%)	1.90±0.576	1.93±0.426
Mean SPO2(%)	98.70%	98.60%
Mean Heart Rate(Per min.)	98.9	98.6
Mean Blood Pressure(mm of mercury)	74.1	73.6

Table 03 Incidence of Post Anaesthetic Emergence Delirium (PAED)

Group	Incidence	%age
Group-A (N = 75)	34	45.3%
Group-B (N = 75)	8	10.7%
P Value	0.03	

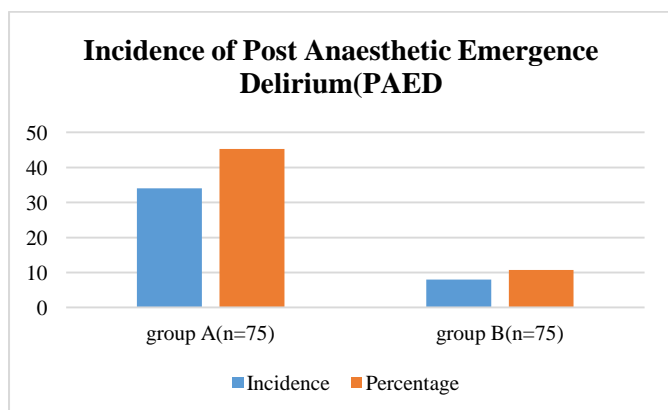


Figure No. 01

The incidence of emergence agitation was 34 patients (45.2%) in group A and 8 patients (10.7%) in group B, the comparison was statistically significant between the two groups (P<0.05). This observation clearly shows that incidence of emergence agitation was higher in group A in comparison to group B. Patients with emergence delirium were treated properly with midazolam 0.1 mg/kg intravenously if PAED score was equal to 16 or greater than 16.

Observation for pain score in post-operative Period

The number of patients requiring analgesia was higher in group A than in group B. In Group A, all patients required Fentanyl at the dose of 0.25 µg/kg in post-operative stage for analgesia. In group B, only 4 patients required analgesia in post-operative period.

There was significant difference in requirement of Fentanyl as analgesia in postoperative period between the two groups. The total dose of Fentanyl was 30.36±9.46µg in group A and 1.37±5.85µg in group B patient.

There was no significant side effects of the drug used in the study. 8% patients in group A and 10.6% in group B developed bradycardia. 6.6% in group A and 5.3% in group B developed hypotension. These effects were transient. Bradycardia was treated with atropine and hypotension was treated with mephentermine intravenously.

Discussion

Emergence agitation as a state of dissociation of consciousness in which the child is irritable, uncooperative, uncompromising, incoherent, and inconsolably crying, moaning, kicking, thrashing. Typically, such children do not recognize familiar objects or people. Such restless recovery from anaesthesia is undesirable. It may cause injury to the patient and to the surgical site and may also lead to accidental removal of intravenous catheters, drains etc. Additional doses of sedatives and/or analgesics may have to be administered to calm the child which may lead to delayed discharge.

Present study was done to assess the effect of Dexmedetomidine in preventing emergence agitation after using Sevoflurane as sole anaesthetic agent during surgery in the age group of 6 to 12 years. All patients undergone elective surgery after written informed consent of parents or guardian. After approval from Institutional Ethical Committee of RIIMS, Ranchi, 150

patients were selected and divided into two groups.

Group A - Control Group

Group B - Dexmedetomidine Group in normal saline bolus intravenously slowly at the dose of 0.5 µg/kg after induction of anaesthesia over 10 minutes. Intraoperatively same drug was given at the dose of 0.2 µg/kg per hour by infusion syringe. All patients were induced by using Sevoflurane as sole anaesthetic agent. Sevoflurane, 66% Nitrous oxide in oxygen, Atracurium 0.1mg/kg I.V were used during maintenance of anaesthesia.

There was fall in heart rate in both groups after induction of anaesthesia. This was statistically not significant. The decrease in heart rate below 80 bpm was in 6 patients of group A and 8 patients of group B. Patients were treated with Atropine in the dose of 0.02 mg/kg.

The mean arterial pressure decreased after induction in both groups but this fall in mean arterial blood pressure was statistically not significant. The decrease in mean arterial blood pressure below 50mmHg was in 5 patients of group A and 4 patients of group B and patients were treated with small dose of Mephentermine and bolus of I.V. fluids.

Mean oxygen saturation at the time of induction of anaesthesia and during maintenance was 99.06±0.79% in group A and 98.98±0.91% was in group B patient. This was statistically not significant.

Post anaesthetic emergence delirium (PAED) was assessed by PAED score. PAED score more than 16 or equal to 16 were considered a case of post anaesthetic emergence delirium. Incidence of emergence delirium in this study was higher in group A patients. In group A incidence of emergence delirium was 45.2% and in group B it was 10.7%. Since the p value (0.03) was less than 0.05, it was statistically significant. Patients with emergence delirium were treated with Midazolam 0.1 mg/kg intravenously slowly.

Findings of the present study was corroborative with earlier studies done by Meng QT and colleagues in 2012⁷ found Dexmedetomidine to be

effective in reducing Sevoflurane induced emergence agitation in paediatric patients posted for tonsillectomy. The study was conducted in 120 ASA 1 and 11 patients aged 5-14 years. All the patients received intravenous Midazolam at a dose of 0.4 mg/kg intravenously as premedication. They were randomized into three groups. Group I was the control group. The second group received a loading dose of Dexmedetomidine at 0.5 µg /kg over 10 minutes followed by an infusion of 0.2 µg /kg /hour throughout surgery. Group 3 received Dexmedetomidine at a loading dose of 1 µg /kg over 10 minutes followed by an infusion of 0.4 µg/kg/hour throughout surgery. They found that there was significant decrease in the incidence of emergence agitation in group 3 (p<0.05). They concluded that the higher dose of Dexmedetomidine used is a better choice in children undergoing tonsillectomy.

“Rescue” medications include analgesics, benzodiazepines and hypnotics. Fentanyl intravenously 1-2µg/kg, propofol iv 0.5-1 mg/kg, and midazolam iv 0.02-0.1 mg/kg have all been used for the treatment of Emergence Agitation. A single bolus dose of dexmedetomidine 0.5µg/kg was also found to be effective for treatment of Emergence Agitation’

Mauricio E Ibacache et al conducted their study in 2004⁸ in 90 children posted for superficial lower abdominal and genital surgeries under Sevoflurane anaesthesia. They were randomized into three groups. The first group was the control group, the second group received Dexmedetomidine at a dose of 0.15 µg /kg and the third group received Dexmedetomidine at a dose of 0.30 µg/kg intravenously. All the study drugs and placebo were infused after induction of anaesthesia, over a period of 10 minutes. The incidence of emergence agitation was 37%, 17% and 10% in the three groups respectively. They concluded that Dexmedetomidine in a dose of 0.3 µg/kg significantly reduced Sevoflurane induced emergence agitation in children with no adverse effects. Thus, we can conclude that 0.5 µg/kg of dexmedetomidine given prophylactically was

effective in prevention of emergence agitation after sevoflurane anaesthesia in paediatric patients.

Patients were observed for pain after extubation in operation theatre and in PACU. This observation was based on objective pain scale. Objective pain scale equal to or above than 4 were considered for analgesia.

For analgesia patients with objective pain score 4 or more than 4 were given Fentanyl at the dose of 0.25µg/kg intravenously slowly. Requirement of fentanyl was repeated after 10 minutes if patients were not responding.

There was significant difference in the Fentanyl dose during the post-anaesthesia care unit between the two groups. The total dose of Fentanyl was lower in group B(1.37µg/kg) than group A(30.36µg/kg) which was statistically significant.

There was no significant side effects of the drug used in the study. In group A, 8% patients and 10.6% in group B developed bradycardia. In group A, 6.6% and 5.3% in Group B developed hypotension. These effects were transient. Bradycardia was corrected by atropine and hypotension was corrected by mephentermine intravenously.

In this study there was higher incidence of emergence agitation in those patients who were not given Dexmedetomidine. Dexmedetomidine reduced emergence agitation in children underwent surgery with Sevoflurane as an anaesthetic agent. Dexmedetomidine did not produce longer stay in PACU after completion of surgery. This drug reduced the dose of Fentanyl for analgesia in postoperative stage. There was no adverse effect of Dexmedetomidine in this study.

Conclusion

In this study, it was found that Dexmedetomidine is effective in reducing the incidence of emergence agitation after Sevoflurane anaesthesia and was not associated with any significant adverse effect. The post-operative pain scores are significantly lower in the patients receiving

Dexmedetomidine. There is no significant haemodynamic changes because of Dexmedetomidine.

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