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Comparison between Incidence of Emergence Agitation in Pre-school Age Group with that of Older Children undergoing Sevoflurane Anaesthesia

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Abstract

Background: Emergence agitation (EA) is a known fact after general anaesthesia which is observed more in children and that too after sevoflurane anaesthesia. Dexmedetomidine and propofol are both known to reduce EA when used in prophylactic doses. The aim of our study was to compare the incidence of EA in preschool age group (< 5 years) with that of older children (> 5 - 12 years) in both dexmedetomidine and propofol group. *Methods:* Total 100 children having age less than 12 years and belonging to ASA I and II were included in the study. All of them received sevoflurane as inhalational anaesthetic agent. They were randomly divided in to two groups. About 5 minutes before the end of surgery, patients in group A received 0.3 µg/kg dexmedetomidine and group B patients received 1mg/kg propofol. The incidence of EA in both the groups was measured with Aono's four point scale upon arrival in the post anaesthesia care recovery room. The database was analyzed using stata 12, epi-info software and p value of < 0.05 was considered as level of significance. *Results:* The incidences of EA in < 5 years age group in group A and B was 21.05% and 40.91% respectively whereas; it was 3.23% and 21.43% in > 5 -12 years age group. *Conclusion:* The incidences of EA were higher in pre-school (≤ 5 years) age group as compared to older children (> 5 -12 years) age group in both group A and B who received dexmedetomidine at a dose of 0.3 ug/kg and propofol at a dose of 1mg/kg respectively.

Keywords: Emergence Agitation; Sevoflurane; Dexmedetomidine; Propofol; Aono's Four Point Scale.

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Introduction

Invention of inhalational anaesthetic agents helped paediatric anaesthesia to grow and inhalation agents are amongst the mainstays of paediatric anaesthesia, as children are often induced by mask before venous access is obtained [1]. Desired properties of an ideal agent included inherent stability, lack of inflammability in combination with oxygen or nitrous oxide, low blood: gas solubility to allow rapid induction and recovery from anaesthesia as well as rapid control of the anaesthesia depth, lack of irritation to airway passages, minimal respiratory and cardiovascular effects as well as reversible central nervous system (CNS) effects, wide therapeutic index, absence of toxicity or other unwanted effects with normal doses or repeated exposure, and no interaction or toxicity with other drugs [2].

In literatures, the term "emergence agitation" has been used in places of "emergence delirium", "emergence excitement" or "post-anaesthetic excitement" in order to describe an irritable, uncooperative and inconsolable patient upon emergence from anaesthesia [3,4]. It is more common

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with the use of newer volatile anaesthetic agents like sevoflurane [5]. Although in most of the cases, it is self-limiting that develops in the early phase of awakening from anaesthesia. Generally short lasting (5-15 min), but EA can be severe and may result in physical harm to the patient and particularly to surgical sites [3,6].

The exact incidence of EA is difficult to establish, but according to various literatues a more frequent incidence is found in children (12-13%) [7]. Its occurrence after sevoflurane anaesthesia can even go up to 80% [8].

Apart from various non pharmacological methods, numerous pharmacological agents like dexamethasone, opioids, NSAID-analgesics, benzodiazepines, propofol, alpha-2 (α_2) agonists were used in the perioperative period for reducing the occurrence of EA after sevoflurane-based anaesthesia.

Materials and Methodology

This study was conducted at a tertiary teaching centre (medical college) in central India after obtaining approval from the Institutional Ethics Committee. This was a prospective, randomized comparative study. Total 100 children receiving sevoflurane anaesthesia were included in this study after meeting the eligibility criteria's.

Inclusion Criteria

1. American Society of Anesthesiologist's (ASA) physical status I and II patients.
2. Patients aged <12 year of either sex.
3. Patients receiving sevoflurane for induction and maintenance of general anaesthesia.
4. Patients whose parent / guardian gave consent for this study.

Exclusion Criteria

1. Patients receiving any other inhalational general anaesthetic agent other than sevoflurane were excluded.
2. Patients whose parent/guardian did not give consent.
3. Patients who had neurological disease or psychological issues.
4. Patients who were already on treatment with sedatives.

Study Procedure

Pre-anaesthetic check-up (PAC) was done. Baseline Investigations like hemoglobin, complete blood count, blood group were documented. After obtaining PAC fitness, those who were planned for sevoflurane based general anaesthesia were selected for the study.

Parents/guardians were provided with written information consent form before patients were shifted to operation theater. Face to face detail discussion was done regarding the anaesthesia technique and all their queries were solved. Children were fasted for 8 hours prior to surgery. They received oral midazolam 0.5 mg/kg approximately 30 mins before separation from the parents. An electrocardiograph, pulse oximeter and noninvasive blood pressure monitor were attached to the patients after shifting to operating table.

Patients were randomized into two groups, Group A and Group B; each containing 50 patients. Randomization was done by using simple sealed opaque envelope technique. Group A received 0.3 µg/kg dexmedetomidine and group B received 1mg/kg propofol as intravenous infusion over 5 minutes.

General anaesthesia was induced with sevoflurane with nitrous oxide in oxygen via a face mask. Intravenous cannula was inserted under sevoflurane anaesthesia. Ondansetron 0.15 mg/kg I.V., glycopyrolate 6 mcg/kg I.V., fentanyl 2 mcg/kg IV administered intravenously. Patients were intubated with endotracheal tubes after giving atracurium 0.6 mg/kg I.V and were provided controlled ventilation. Anaesthesia was maintained with 50% nitrous oxide in oxygen, supplemented by an end-tidal concentration of 2-3% sevoflurane to keep an end-tidal carbon-dioxide of 35±5 mm hg. Top-up of muscle relaxant was given as needed in between. All patients received 15 mg/kg paracetamol I.V. slowly approximately 15 minutes before the completion of surgery for control of post-operative pain.

Approximately about 5 minutes before the end of the surgery, patients in group A received 0.3 µg/kg dexmedetomidine diluted in 10 ml of 0.9% normal saline and group B patients received 1mg/kg propofol. Experimental drugs were administered as continuous intravenous infusion over last 5 minutes of surgery through syringe pump following which sevoflurane was stopped simultaneously along with end of surgery.

To avoid bias, EA was assessed upon arrival to post anaesthesia recovery room by an independent

anaesthesiologist who was not present inside the operation theatre during surgeries and was not aware about what drugs the patients received.

The incidence of emergence agitation was evaluated using Aono's four point scale [9,10]; scores of one and two were considered as absence of emergence agitation and scores of three and four were considered as presence of it.

Table 1: Aono's four point scale [9,10]

Calm	1
Not calm but could be easily calmed	2
Moderately agitated or restless	3
Combative, excited or disoriented	4

Any peri operative adverse events like laryngospasm, bronchospasm, hypotension, bradycardia, cardiac arrhythmia, anaphylaxis, oxygen desaturation episodes, vomiting were recorded if were present in any of the study subjects.

Statistical Analysis

All the data were entered into the microsoft excel database from paper pro-forma. During the data entry, data were checked for any error or missing data. After resolution of all issues, the database was analyzed using stata 12, epi-info software and p value of < 0.05 was considered as level of significance. Following analyses were performed.

- Results were expressed as the number, percentages, mean±standard deviation as appropriate and statistical analysis was performed for each group.
- Comparison of numerical variables between the study groups was done using Student's t test for independent samples. For comparing categorical data, Chi square (X^2) test was performed. Fisher's exact test was used instead when the expected frequency was less than 5.
- p value < 0.05 was considered statistically significant.

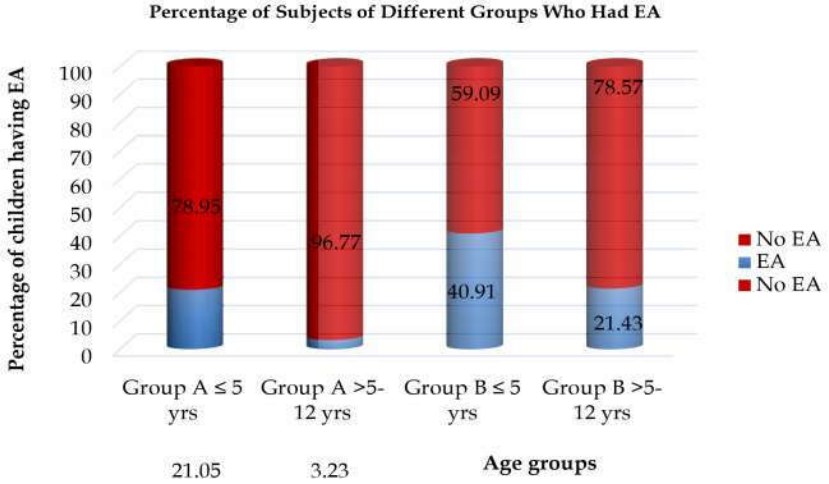
Results

Two studied groups were comparable to each other in respect to patient's characteristics like age, sex, weight, ASA status, types of surgeries as well as duration of surgery and anaesthesia.

Table 2 and graph 1 show the comparison of age group of the subjects who had emergence agitation. Here, it is seen that the incidence of EA is much higher in ≤ 5 yrs age-group as compared to > 5 – 12 years age group (21.05 % versus 3.23% in Group A and 40.91% versus 21.43% in Group B).

Table 2: Age-Group comparison of study subjects who had Emergence Agitation

Age Groups	Group A(n=50)			Group B(n=50)		
	Study subjects	Positive for EA	Percentage of EA	Study subjects	Positive for EA	Percentage of EA
≤ 5 Years	19	4	21.05 %	22	9	40.91 %
> 5-12 Years	31	1	3.23 %	28	6	21.43 %



Graph 1: Percentage of subjects in different age group who had Emergence Agitation

Table 3: Comparison of emergence agitation in different age groups in the form of 2 x 2 contingency table

Group	Emergence agitation	≤ 5 years	> 5 – 12 years	P Value (< 0.05 is significant)
Group A	Present	4	1	0.1244
	Absent	15	30	(Not significant)
Group B	Present	9	6	0.2381
	Absent	13	22	(Not significant)

Table 3 shows the comparison of emergence agitation in different age groups in both group A and B; where we can find that there were no statistically significant differences of emergence agitation between ≤ 5 years and > 5 -12 years age groups in any of the study groups; ie; dexmedetomidine (group A) or propofol (group B).

Perioperatively no serious adverse events such as laryngospasm, bronchospasm, bradycardia, hypotension, cardiac arrhythmia, anaphylaxis, oxygen desaturation episodes were recorded in any of the study subjects.

Discussion

With development in paediatric anaesthesia, poorly soluble newer inhalational agents like sevoflurane and desflurane came into routine anaesthesia practice. In today's era, sevoflurane is preferred anaesthetic agent for induction and maintenance in paediatric anaesthesia due to its properties like low pungency, non-irritant to airways and a low blood : gas partition coefficient [11]. It can be rapidly and conveniently administered without discomfort, and its low solubility facilitates precise control over the depth of anaesthesia and a rapid and smooth induction and emergence from general anaesthesia.

Eckenhoff et al. [12] first described emergence agitation (EA) in the early 1960's and it is considered as landmark study in this context. EA which results in self injury, poor surgical outcome, parental dissatisfaction, increase in hospital stay with enhanced nursing cost is a known morbidity after sevoflurane anaesthesia [13].

No single aetiology has been determined to explain this phenomenon. But recently a number of studies have examined various patients, anaesthetics and surgical factors that may increase the incidence of EA.

The highest incidence of EA has been seen in children between 2 and 5 years of age [9,14]. Aono compared preschool children to older school age children (6–10 years) receiving sevoflurane anaesthesia and found a markedly increased incidence of EA in the younger age group [9]. In a few studies, the authors have mentioned the role of brain maturation on delirium, with some relating EA susceptibility in children to the development of the hippocampus and cholinergic function [15,16]. Further, a study by Martini showed that neurotransmitter levels in paediatric brains were analogous to levels in brains that had undergone normal age-related changes. Diminished levels of acetyl-choline, dopamine, norepinephrine and aminobutyric acid were neuro-physiological findings characteristic of both the geriatric and paediatric populations [15]. Disturbance to these neurotransmitters have been implicated as precipitating factors for delirium in a significant number of studies.

We have observed in our study that in both the groups incidences of EA were higher in ≤ 5 years age group as compared to > 5-12 years age group which was 21.05% versus 3.23% in dexmedetomidine group and 40.91 % versus 21.43% in propofol group (Table 2 and Graph 1). Although from statistical point of view, there were no significant difference between the two age groups

Aono et al. [9] similarly found in their study that highest incidences of EA seen in less than 5 years age group children. They hypothesized that psychological immaturity, poor ability to cope up with sudden awakening in a strange environment coupled with the rapid recovery potential of sevoflurane caused the greater incidences of EA in the preschool age group.

Although in our study, clinically the incidences of EA were higher in pre-school age group children; but when we compared it statistically, we found that there was no significant statistical difference of EA between ≤ 5 years and > 5 -12 years age group children in any of the group A or B (Table 3).

Post-operative pain is considered as one of the possible risk factors for EA [15]. Pain was not a confounding factor in our study as we have administered I.V. paracetamol at a dose of 15 mg/kg for control of post-operative pain in both the groups.

One limitation of our study was that we did not have a control group and hence could not estimate incidence of EA in patients where no prophylactic drug was used. Amongst many pharmacological agents, dexmedetomidine [17,18] and propofol [19,20] both being evaluated in various studies for the prevention of EA and they have proven safety profile and efficacy. So, we assume that if we had a control group, the incidences of EA in both preschool and older children would had been even higher than what we found in dexmedetomidine or propofol group.

Since last half a century, EA has been studied and reported in the literatures [12]. However, there are still many questions that needs to be answered. Obviously, further trials are required to discover the underlying causes of EA and to determine which factors might help, predict and potentially prevent it [8]. To reduce emergence agitation, it is advisable to identify children at risk and take preventive measures, such as reducing preoperative anxiety, removing postoperative pain, providing a quiet, stress-free environment for recovery, allow parent/guardian to remain in the recovery room if feasible.

Conclusions

From our study, we can conclude that clinically the incidences of emergence agitation were higher in pre-school age group as compared to older children who received sevoflurane anaesthesia; although statistically this difference was insignificant.

Key Message

Since last half a century, EA has been studied and reported in the literatures. It is an important issue in paediatric anaesthesia and is associated with parental dissatisfaction, increased nursing cost. It delays discharge and affects the surgical outcome adversely. To reduce emergence agitation, it is advisable to identify children at risk and take preventive measures.

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