RECOVERY PROFILE AND EMERGENCE DELIRIUM FOLLOWING SEVOFLURANE AND ISOFLURANE ANESTHESIA IN CHILDREN POSTED FOR CLEFT LIP SURGERY

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Abstract

This prospective, randomized, double control study was carried out in 84 children aged 2-24months posted for elective cleft lip surgery. **Methods:** Patients were randomally divided into 2 groups of 42 patients each. In **Group A** patients were induced and maintained on sevoflurane while in **Group B** patients were induced with sevoflurane and maintained on isoflurane. Standardized anesthesia technique was used. Recovery milestones and post operative complications were recorded.

Results: Incidence of emergence delirium in sevoflurane group was 11.9% while in isoflurane group is 2.38%. The overall incidence of emergence delirium in the study was 7.14%. There was no significant difference (p >0.05) in the incidence of emergence delirium between the two groups. There was no effect of duration of exposure of sevoflurane and time taken for achievement of recovery milestones while we observed a positive correlation with isoflurane. In sevoflurane the recovery endpoint first reached was limb movement > spontaneous respiration > spontaneous eye opening. In isoflurane group the recovery end point first reached was spontaneous respiration > limb movement = spontaneous eye opening.

Conclusion: our study confirms that the recovery profile of sevoflurane in children less the two years is superior compared to isoflurane.

Keywords: recovery milestones, sevoflurane, isoflurane, cleft lip

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Introduction

Very early on, it became clear that pediatric patients had the needs that were fundamentally different from those of adults thus provision of anesthesia for such patients depends on a clear understanding of their needs and the psychological, anatomical, physiologic, and pharmacologic differences that underlie them[1, 2].

Most children do very well postoperatively and recover quickly from anesthesia and surgery and return to full function faster than adults. But recovery from anesthesia is a time of transition a number of potential complications may occur and require immediate attention in the post anesthesia care unit. (PACU)[3].

Upon emergence from general anesthesia a condition of uncontrollable anxiety and agitation described as Emergence delirium (ED) has been observed[4]. Although emergence agitation is not a new phenomenon in clinical practice, it is of growing interest because its incidence appears to be increasing 24-66% with the widespread use of sevoflurane[5, 6]. The possible causes of emergence delirium range from too rapid return of consciousness in a strange environment, pain (wound, sore throat), a sequelae of a stressful induction, hypoxemia, the child's age (more agitation if <3 years) and temperament, duration of anesthesia (more agitation after short anesthesia) to environmental conditions (physical stimuli noise) may also influence its occurrence[4,7].

Delirium on emergence demands increased nursing care in the PACU, delays reunion with parents and may lead to adverse outcomes in some cases.

Because of the conflicting results in the literature and unavailability of the data from the well controlled studies regarding procedures in the children, we undertook this prospective, randomized double blind study to compare the haemodynamic variations, emergence characteristics and post operative complications with sevoflurane and isoflurane in children less than two years after elective surgery.

Material & Methods

Following Institutional Ethics Committee approval and fully informed parental consent, we studied 84 American Society of Anesthesiology (ASA) physical status I children aged 2-24 months undergoing elective cleft lip surgery under general anesthesia. Exclusion criteria included the need for postoperative ventilation and significant cardiovascular, respiratory or neurological abnormalities and any other congenital abnormality. The study size was ascertained after reviewing the existing data as most of the studies [3,4,8] have taken a sample size of 50, further as the total duration of study was 12 months that include data collection (09 months), compilation and analysis. The total patients that were operated in the abovementioned period were 92 but after eliminating the incompletely filled forms, the investigator finally analyzed the sample of 85 patients. One patient was deliberately excluded to have equal number of patients in both the groups. A scheme of block randomization was undertaken to ensure equality for age and duration of operation between the two groups. Random number tables were used for group allocation and codes were stored in sealed envelopes. Patient characteristics recorded included; weight, height, age and full medical history.

All the patients posted for surgery were given syrup promethazine in the dose of 0.5 mg/kg orally at night and 6 am in the morning on the day of surgery. Standard fasting guidelines for paediatric patients were followed.

In both the groups the children were induced with 50% oxygen and 50% nitrous oxide and incremental concentration of sevoflurane starting from 1% and gradually increasing to 5-6% that is 1% every 6-8 breaths via Jackson Rees Circuit. After securing the intravenous line the patient was administered i.v. fentanyl 2 μg/kg for analgesia and facilitation of endotracheal intubation was done using i.v atracurium 0.5 mg/kg body weight. The study anaesthetic agent was started at the earliest opportunity. Anesthesia was maintained in **Group A** with 66% nitrous oxide in oxygen and sevoflurane while in **Group B** with 66% nitrous oxide in oxygen and isoflurane. All the patients were ventilated to normocapnia using Drager Fabius GS and Jackson Rees circuit according to the patient weight. The end-tidal concentration of the study agent was adjusted to 1-1.5 MAC in oxygen and nitrous oxide. Fresh gas flow was 1.5 litres/minute for all children. At the end of surgery infraorbital nerve block was given in both the groups for analgesia. The

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administration of IV fluids was left to the discretion of the anesthetist. Operation theatre temperature was kept constant around 24°C and surface warming was done.

The nitrous oxide and volatile anesthetic were discontinued simultaneously without tapering with the last surgical stimulus and the patient was allowed to wake up spontaneously with minimal handling. Ventilation with 100% oxygen was continued until the establishment of spontaneous ventilation. The observer blinded to the type of volatile agent used for maintenance of anesthesia timed the patient's emergence events from stoppage of anesthesia to first gross limb movement, eye opening, establishment of regular breathing pattern and extubation

The criteria for transferring the patient from operating room to recovery area were awake, moving all the four limbs, normal oxygen saturation with no need for mandibular support, patent airway and normal respiratory pattern, stable hemodynamics, normothermia and pain free.

During the recovery period and postoperatively the patient was observed for complications like nausea, vomiting, pain, delirium, dysarrhythmia, cyanosis, hypothermia and shivering.

Behaviour was rated on the following four scales; 1 = calm, 2 = not calm but easily calmed, 3 = not easily calmed, moderately agitated or restless, 4 = combative, excited or disoriented. [8] For statistical purposes grades 1, 2 were considered non problematic behaviour, and grades 3 or 4 were considered delirium. The observed delirium was not treated with any drug.

Descriptive statistics (mean, standard deviation, range) were used to summarize patient's demographic data and operative details. The statistical analysis was done using two sample unpaired t test and the correlation r test.

Observations & Results

The two groups were similar in terms of age, weight, sex, duration of study agent and operative time. All the children belonged to ASA grade I. (Table 1) There was no significant hemodynamic changes intraoperatively between the two groups. the recovery milestones in minutes after cessation of anesthesia were significantly shorter for sevoflurane compared with isoflurane. The positive correlation between exposure and time to extubation is apparent for isoflurane in both age groups demonstrating the time sensitive elimination characteristics of isoflurane. In our study we observed that in Group A the earliest recovery milestone achieved was limb movement 174.18 ± 85.08 sec followed by spontaneous eye opening at 295.24 ± 187.98 sec and lastly establishment of spontaneous respiration at 311.48 ± 132.66 sec after which the child was extubated. While in Group B all the recovery parameters reached their endpoint at similar time intervals i.e. spontaneous respiration, limb movement and spontaneous eye opening were observed at 464.12 ± 228.93 sec, 504.42 ± 216.93 and 504.42 ± 201.65 respectively after which the child was

Table I
Demographic Profile & The Operative Details Of The Patients

	Group A	**Group B**
Age in months (Mean ± SD)	9.43 ± 6.89	11.76 ± 7.66
Male: Female	30:12	27:15
Weight in Kg(Mean ± SD)	7.02 ± 1.95	7.83 ± 2.27
Duration of surgery(min) (Mean ± SD)	36.91 ± 9.75	39.52 ± 14.13
Duration of anaesthetic exposure(min) (Mean ± SD)	44.35 ± 11.12	49.71 ± 14.13

II: Time to Reach Recovery Milestones for Patients in Both the Groups(in min)

Parameter (in seconds)	Group A	Group B	P value
Spontaneous respiration (mean ± S.D)	290.52 ± 118.57	483.24 ±237.79	P <0.001
Hip Flexion (mean ± S.D)	168.93 ± 83.37	290.36 ± 209.98	P <0.001
Eye Opening (mean ± S.D)	266.07 ± 161.75	483.21 ± 188.85	P <0.001
Extubation (mean ± S.D)	319.9 ± 120.36	582.9 ± 249.77	P <0.001

extubated.

On comparing the incidence of postoperative complications, in both the groups, it was found that the incidence of delirium was higher 5 (11.9%) in Group A, as compared to 1(2.4%) in Group B. The overall incidence of emergence delirium in the study was 7.3%. The behaviour assessment score in all the patients were 2, 3. No drug was given but the child was not disturbed and the parental comfort was enough to abort the event. The incidence of laryngospasm was 2(4.8%) in Group B, while in Group A 1(2.38%) had laryngospasm. All the three patients had a fall in saturation upto 90% and were managed with100% oxygen with bag and mask. No other respiratory complications like coughing, breath-holding and respiratory depression were observed in either group. The incidence of shivering was higher 2 (4.8%) in Group B, as compared to Group A 1(2.4%). There was no incidence of nausea, vomiting and hypothermia in both the groups. Normocapnia was maintained in both the groups.

Discussion

We conducted the study in children undergoing elective repair of cleft lip as it is a common procedure conducted in infants and young children worldwide[9].

There is no clear definition of emergence delirium and often it has been used interchangeably with emergence agitation. The two have been defined independently by Sikich and Lerman who defined emergence delirium (ED) as "a disturbance in a child's awareness of attention to his/her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behaviour in the immediate postanesthesia period". While emergence agitation is a state of mild restlessness and mental distress that unlike delirium does not always suggest a significant change in behaviour[5,10].

Possible causes of emergence agitation may include hypoxemia, metabolic disturbances, pain and effects of drugs. Social backgrounds and preschool age are confounding factors for post anaesthetic agitation[8,11,12].

In our study all the subjects were healthy and received adequate fluid therapy and there was no oxygen

desaturation during the study period. Another problem is the differentiation between agitated behaviour resulting either from pain or from emergence delirium. To exclude pain as a relevant factor for agitation we introduce rectal suppositories of diclofenac sodium soon after intubation. Thus the incidence of delirium observed after sevoflurane anesthesia was not considered to be due to pain, hypoxia or metabolic disturbances. In a study conducted in Asian children Bong et al suggested that Asian children are raised in authoritarian household usually more compliant on induction. It is known that compliance on induction correlates negatively with emergence delirium[11]. This observation may also apply in our subjects who were of Asian origin.

When analyzing emergence delirium in children after general anesthesia, measurement of agitation and comparison of studies may be difficult as there is no consistent definition and measurement scale for emergence delirium or agitation. In this study we used an extremely easy behaviour scale[8].

Some authors have postulated that two unique intrinsic characteristics of sevoflurane might account for development of emergence delirium. First, that sevoflurane exerts an irritating side effect in the central nervous system and second although sevoflurane degradation products appear to cause no organ damage themselves, data are lacking on their possible interactions with other types of medications[13]. Epileptiform activity has been reported during the use of sevoflurane anesthesia in patients with no medical history of seizures[14,15]. The incidence of post operative agitation ranges from 10 to 50% but may be as high as 80% in paediatric patients[14]. With sevoflurane incidence of emergence delirium as high as 50% has been reported[16].

In our study the overall incidence of emergence delirium was 7.14%. This is in sharp contrast to the study conducted by Valley RD et al[17] who recorded an overall incidence of 32%. The reason for the differences in the incidence of emergence delirium between our results and their studies could be different age groups.

In our study all the subjects were premedicated with promethazine the night before and in the morning before the surgery and then received fentanyl and nitrous oxide intraoperatively and also the study agent

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was discontinued and the child with the last surgical stimulus and the child was allowed to awaken with minimal handling. The trachea was extubated after return of spontaneous regular respiration. All these are confounding factors which may have contributed to low incidence of emergence delirium in both groups.

While the latter gave post operative analgesia but no premedication or intraoperative opiod was administered. The addition of a small dose of fentanyl to inhaled sevoflurane anesthesia decreases the incidence of emergence agitation, independent of pain control effects as proven in a study conducted by Cravero JP et al[18].

Unlike our study, in which we noticed a highly significant difference in the recovery milestones, Valley RD et al and Meyer RR et al[17,19] observed no significant difference in the recovery milestones. In our opinion there is a methodological difference between two studies. Valley RD et al in their study reversed the neuromuscular block in the last 20 min of the surgery and allowed the child to breathe spontaneously. At the end of surgery nitrous oxide was discontinued and the inhalational agent isoflurane or sevoflurane was adjusted to provide an end tidal concentration of 1.5 MAC. The endotracheal cuffed tube was then removed while the child was still deep. They then recorded the time from tracheal extubation to spontaneous eye opening[17]. While in a study conducted by Meyer RR they induced the patient with thiopentone 8-10mg/kg, mivacurium 0.3mg/kg and alfentanil 10-20 µg/kg. For maintenance they used either sevoflurane or isoflurane in 40% oxygen and 60%air and an age-adjusted MAC in the range 0.7-1.3. No additional opiod was given. At the end of surgery the halogenated agent was discontinued and the child was extubated after showing purposeful movements[19].

In our study since the children were premedicated with promethazine, opiod analgesia was used intraoperatively, rectal suppository of diclofenac sodium was effective in preventing post operative pain and extubating the child with minimal handling may have contributed to prolonged recovery profile.

In our study we extubated children when they were fully awake, which may account for the 4% incidence of laryngospasm in Group B same as reported by Pounder et al[20]. They suggested that the use of isoflurane is associated with more coughing and airway obstruction than with the use of halothane in children who were awake when the trachea is extubated. If the trachea is extubated, while the children are deeply sedated then there is no difference between the two agents. Pandit et al reported that the increase in airway irritability seen with isoflurane may be less of a problem on emergence, than on induction[21].

In our study there was statistically significant difference in the time taken to achieve recovery endpoints when comparing sevoflurane with isoflurane which some clinicians may not consider clinically significant . Children who were extubated while breathing sevoflurane reached an arousable state more quickly than those breathing isoflurane. Based on the different blood gas partition coefficient for sevoflurane (0.65) versus isoflurane (1.4), a more rapid emergence is expected with sevoflurane[22].

We have observed a positive correlation between the duration of anaesthetic exposure and the emergence times with isoflurane, which was not present with sevoflurane. Patients receiving isoflurane showed progressive lengthening of times to attain early recovery endpoints with increasing duration of isoflurane exposure. A theoretical explanation has been provided by Campbell C et al, using the pharmacokinetic model. It would appear that emergence from anesthesia under the condition of the study has much greater dependence on the relative solubilities of the two volatile agents in blood and is less influenced by their affinity for tissues. Indeed inspite of similar tissue /blood partition coefficients, accumulating the depots of anaesthetics especially in the vessel rich tissues over time have minimal effect on emergence from sevoflurane while prolonging that from isoflurane[23].

Elimination of a volatile agent is dependent on the alveolar ventilation, and while the young child breathing spontaneously may have greater ventilatory depression than older children because of increased sensitivity to central nervous system depressants; the ratio of alveolar ventilation to functional residual capacity is much greater[24]. This latter property results in a more rapid exchange in alveolar gas, and therefore a faster elimination of the inhalational agent.

Conclusion: Volatile anaesthetics have their own unique advantages and disadvantages. The new era of

inhalational anaesthetics with low blood gas partition coefficients have proved to be beneficial in paediatric anesthesia due to rapid induction and emergence. From our study we can say that lower incidence of emergence delirium and early recovery milestones with sevoflurane has helped in early extubation of our patients.

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