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LETTER TO THE EDITOR

Comparison of incidence of emergence delirium in pediatric patients with three different techniques of general anesthesia using sevoflurane and propofol: a randomized controlled trial

Dear Editor,

In 1960, Eckenhoff first identified Emergence Delirium (ED), also known as Emergence Agitation (EA), a phenomenon observed at the time of recovery from General Anesthesia (GA).[1] It is characterized by a dissociative state of consciousness, causing behavioral disturbances. Incidence of ED in the general population ranges from 5% to 30%, but its incidence varies from 2% to 80% in the pediatric population, more so in children in the age group of 2—8 years. The cause of ED appears to be multifactorial in origin. Use of volatile anesthetics, prolonged duration and type of surgery, pain, and rapid emergence are some factors known to increase its incidence.

There is literature suggesting the influence of GA techniques in the incidence of ED. Total Intravenous Anesthesia (TIVA) is proven to have the least ED incidence than other methods. However, TIVA carries certain disadvantages like requiring intravenous (IV) access for administration, infusion pumps designed to deliver TIVA and their high cost, known allergies to propofol, etc.[2] The use of only inhalation technique is also not free from disadvantages like difficulty in administration by mask, the need of higher concentration of agents, operation theatre environment pollution, high cost, higher incidence of malignant hyperthermia in susceptible individuals, and increased incidence of ED in pediatrics.[3] We studied the technique of combination of inhalational and intravenous agents to overcome the disadvantages of both the techniques and take advantage of their benefits. Our study aimed to find and compare the incidence of ED in pediatric patients of 2 to 10 years of age while using three different anesthetic techniques with sevoflurane and/or propofol.

We conducted the study after approval from the Institute's Ethical Committee AIIMS Jodhpur and registered under the Clinical Trial Registry India (CTRI/2018/05/014064) before enrolling the patients. This was a parallel, double-blinded, randomized, controlled trial. Seventy-five pediatric patients of ages 2 to 10 years, American Society of Anesthesiologists (ASA) physical status I and II, scheduled for elective laparoscopic surgery of 1—4 hours duration under GA were enrolled. Patients who did not give consent, assigned for elective surgery under regional anesthesia, with hepatic impairment and renal insufficiency, with active upper respiratory tract infection, with a history of previous psychiatric or congenital neurological disease, on drugs like antipsychotic drugs, antiepileptics which would influence the outcome were excluded from the study. The patients were divided into three groups of 25 each by a computer-generated random number table, and allocation concealment was done by Sequential Numbered Opaque Sealed Envelope as:

Group A, anesthesia was induced with oxygen (FiO_2 0.50), air, and sevoflurane (increasing concentration up to 8%) via face mask and was maintained with sevoflurane (1—1.2 MAC).

Group B, anesthesia was induced with a bolus injection of 3 $mg.kg^{-1}$ propofol and was maintained with sevoflurane, oxygen (FiO_2 0.50), and air.[4]

Group C, anesthesia was induced with a bolus injection of 3 $mg.kg^{-1}$ propofol and was maintained with oxygen (FiO_2 0.50), air, and continuous infusion of 100—400 $mcg.kg^{-1}.min^{-1}$ propofol.[5]

Premedication was given to the patient as per the Institute's protocol with IV midazolam (20 $mcg.kg^{-1}$) 30 minutes before surgery. After adequate preoxygenation with 100% oxygen, 0.25 $mg.kg^{-1}$ IV lidocaine and 2 $mcg.kg^{-1}$ fentanyl were given to all patients during anesthesia induction. The attending anesthesiologist was given a sealed envelope with instructions for including the patients in different study groups.

After adequate mask ventilation, a standard dose of a muscle relaxant atracurium was administered and patients were intubated. Supplementary doses of fentanyl (1 $mcg.kg^{-1}$) were given every hour from the initial dose until the completion of the procedure or the patient's requirement as assessed by the attending anesthesiologist for all the patients. In addition, all patients received IV paracetamol 10—15 $mg.kg^{-1}$ before extubating. Neuromuscular blockade was reversed with standard doses of IV neostigmine and glycopyrrolate.

Emergence reactions and severity of pain at extubation and in PACU were recorded at intervals of 5 min for 20 minutes by another anesthesiologist as per the PAED scale & FLACC scale respectively, who was blinded to the technique

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Table 1 Comparison of number and percentage of children with ED and pain at emergence in the three groups of children undergoing different techniques of GA.

		Groups			
		A	B	C	*p*-value
Emergence Delirium n (%)	Absent	14 (56)	21 (84)	23 (92)	0.006
	Present	11 (44)	4 (16)	2 (8)	

ED, Emergence Delirium; GA, General Anesthesia; Groups: A, Anesthesia induced and maintained with sevoflurane; B, Anesthesia induced with propofol and maintained with sevoflurane; and C, TIVA.

used for anesthesia. The PAED score of > 12 was considered as ED, and a FLACC score of > 4 was considered as moderate pain and requiring intervention.

The cumulative incidence of ED was 44%, 16%, and 8% in groups A, B, and C, respectively (Table 1). The mean age of children presenting with ED was found to be less than 4 years, and 87% of ED patients experienced pain. By using time-to-event analysis, as compared to Group A, a significantly lower risk of ED was seen in Group B ($p = 0.003$) and Group C ($p < 0.001$). No difference was seen in groups B and C ($p = 0.133$).

Many studies suggest that ED following sevoflurane and desflurane is probably due to rapid emergence from anesthesia by these agents due to their low blood solubility or due to pain at emergence. The reason could also be the rapidity of induction by sevoflurane, leading to biochemical, physiological, or structural changes in the brain cells, which later manifest as delirium in the postoperative period.[3]

ED not only increases duration of PACU stay but also can cause physical, mental, and psychological trauma to the patient as well as to the parents. There is increased occupancy of PACU beds and resource utilization in the form of drug usage and the number of nursing staff for monitoring and restraining patients.

Though the incidence of ED in Group B is 8% higher than in Group C, the difference is not statistically significant. On the other hand, the incidence of ED in Group B is 18% lower than in Group A, and this difference is statistically significant. Group C, i.e. TIVA, carries certain disadvantages like requiring IV access for administration, infusion pumps designed to deliver TIVA and their high cost, known allergies to propofol, etc. preclude its use. Thus, the combination technique may be recommended over TIVA.

Conflicts of interest

The authors declare no conflicts of interest.

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