Effects of Fentanyl and Dexmedetomidine Infusion on Tracheal Intubation and Emergence Agitation in Children Anesthetized With Sevoflurane

Samy A. Amr[1] and Mohamed A. Osma[2]

[1]Anesthesiology Department, South Egypt Cancer Institute
[2] Pediatric Surgery Department, Children Hospital, Assiut University, Egypt
saaerfan62@yahoo.com.ph

Abstract: Background: Emergence agitation (EA) is a common side effect after anesthesia with sevoflurane as a sole agent in children. Fentanyl and dexmedetomidine, can be used to facilitate intubation and decrease emergence agitation. This study was designed to evaluate the efficacy of adding either fentanyl or dexmedetomidine on conditions at intubation and on emergence from sevoflurane anesthesia without confounding nitrous oxide or premedication. Methods: This study was approved by Our Clinical Ethical Committee and written consents were obtained from patients prior entry into the study. This study included a total number of (150) patients, ASA physical status I, and their ages range between (2-8years). Patients were randomly allocated to receive either i.v. saline (control group), a bolus dose of fentanyl 2µg/kg followed by a continuous infusion of 1 µg/kg/h (group F), or a bolus dose of dexmedetomidine 0.75 µg/kg followed by a continuous infusion of 0.5 µg/kg/h (group D). Anesthesia was induced with sevoflurane in oxygen and maintained using a predetermined concentration of sevoflurane. Sevoflurane minimum alveolar concentration for tracheal intubation (MAC_{TI}) was assessed. After extubation. Agitation parameters were measured using a five-point scale, agitated children were managed by giving intravenous increments of fentanyl 1 µg/kg. Postoperative fentanyl consumption, incidence of postoperative nausea and vomiting and the time of hospital discharge allowance were recorded. Results: MAC_{TI} value were (2.64%, 1.35% and 1.31%) in control group, group F and group D respectively ($p< 0.05$) with no deference between group F and D. Incidence of postoperative agitation, amount of fentanyl consumption and nausea and vomiting were significantly higher in control group ($P< 0.001$). No significant difference between the three groups in the time of hospital discharge allowance. Conclusion: Adding either fentanyl infusion or dexmedetomidine infusion in a proper doses facilitate tracheal intubation and reduced sevoflurane-related emergence agitation with high safety profile.
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1. Introduction

Pediatric Anesthesiologists often intubate the trachea using only sevoflurane without a neuromuscular blocking agent [1,2]. Sevoflurane is widely used in pediatric anesthesia because of fast and well tolerated inhalation induction, low hepatotoxicity, hemodynamic stability, and rapid emergence from anesthesia [3]. However, the occurrence of emergence agitation in children is the major disadvantage of this volatile anesthetic, with the reported incidence up to 80 % [4]. Rapid emergence and pain sensation have been proposed as possible causes of emergence agitation seen with sevoflurane [5]. However, anxiolytic premedication and effective analgesia do not necessarily prevent emergence agitation and may even cause delayed recovery and hospital discharge or affect the quality of life of the child after discharge [6,7]. Various perioperative pharmacological (analgesics, opioids, benzodiazepines, clonidine and dexmedetomidine) and non-pharmacological techniques were used with the aim of reducing the minimum alveolar concentration for tracheal intubation (MAC_{TI}) and emergence agitation after sevoflurane based anesthesia, with variable results [3,4,8,9]. Previous studies have shown that a bolus of fentanyl i.v. 1 µg/kg or 2.5 ug/kg or nasal 2 µg/kg can reduce the incidence of severe emergence agitation after sevoflurane anesthesia [10-12]. Dexmedetomidine (Precedex® , Abbott laboratories), a short acting $alpha_2$ – agonist, was approved by the U.S. food and Drug Administration (FDA) as an ICU sedative in (1999). It possesses anxiolytic, anesthetic, hypnotic, and analgesic properties, patients receiving dexmedetomidine infusions are easily aroused, yet appear calm and comfortable [13]. However, co-administration of dexmedetomidine with sevoflurane, isoflurane, propofol, alfentanil and midazolam may result in enhancement of sedative, hypnotic, or anesthetic effects [14]. Dexmedetomidine provide sedation and analgesia without respiratory depression. In pediatric patients, it has been demonstrated to provide effective sedation for radiographic procedures because of its sedative and analgesic effect, dexmedetomidine may be useful for the management of emergence agitation [3,15].

Only few studies tested the role of fentanyl and dexmedetomidine infusion in reducing MAC_{TI} and

emergence agitation after sevoflurane. The aim of this study was to investigate the effects of dexmedetomidine infusion on sevoflurane concentrations required for tracheal intubation and on the emergence agitation in children anesthetized using sevoflurane in comparison to fentanyl.

2. Methods:

This was a prospective, randomized, double blind, single center study that was carried out in Assiut University Children Hospital, 150 children (age 2-8 years of ASA I) Who were undergoing elective minor surgery under general anesthesia. The study protocol was approved by the clinical ethical committee and written informed consent was obtained from a parent or a guardian. Patients with airway malformation, clinical evidence of a difficult airway, asthma, or any sign of upper respiratory infection were excluded. Patients taking central nervous system (CNS) depressants or anti seizure medication, or who had CNS disorders including spinal cord dysfunction, developmental delay, or autism, were also excluded.

The required numbers for each group in this study were calculated using power analysis to find a significant difference of $P< 0.05$ ($\alpha = 0.05$) with a power of 95 % (B error = 0.05). This analysis determined 45 patients per group is sufficient.

2.1 General procedure

Patients were fasted for 4-6 h before induction of anesthesia and they did not receive premedication. Routine monitoring was applied, including pulse oximetry, non-invasive arterial blood pressure, and electrocardiography. Body temperature was monitored by a tympanic probe and maintained at 36.8°C using a heating pad. Inspired/end tidal sevoflurane and carbon dioxide concentrations were measured with a multi-gas analyzer pre-calibrated automatically before each use. The end tidal concentration of carbon dioxide was maintained at (34-38) during the study.

Patients were randomly allocated to one of three groups (n= 50 per group) using computer-generated numbers to receive either i.v. saline (control group), a bolus of 2 µg kg fentanyl followed by a continuous infusion of 1 µg/kg/h (group F), or a bolus of 0.75 µg/kg dexmedetomidine followed by a continuous infusion of 0.5 µg/kg/h (group D). Measurement of sevoflurane concentration to prevent coughing on tracheal intubation (MAC_{TI}) was recorded. Anesthesia was induced with 8% sevoflurane in 100% oxygen (6 Ls / min) through a face mask. The concentration of sevoflurane was decreased to the test concentration. After reaching a predetermined value, the end-tidal sevoflurane concentration was kept constant, and the ratio of predetermined end-tidal to inspiratory concentration was maintained at 0.95-1.00% for 5 min (stable status) before the initiation of fentanyl or dexmedetomidine infusion.

When the simulated effect-site concentration of fentanyl or dexmedetomidine increased to its maximum concentration (3 min after establishing stable off end-tidal sevoflurane concentration and starting drug injection), laryngoscopy and tracheal intubation were quickly attempted using a curved blade and an uncuffed suitable size tracheal tube without a neuromuscular blocking agent. Each sevoflurane concentration at which laryngoscopy and tracheal intubation were attempted was chosen by the anesthesiologist in charge of each case (1.5-3.5% in the control group, and 0.75-3% in the fentanyl and dexmedetomidine groups). The step size of sevoflurane was 0.25%. The lowest concentration (1.5%) of sevoflurane in the control group was chosen based on the results of previous study, which determined MAC_{TI} values of sevoflurane alone in children[1]. For the fentanyl and dexmedetomidine, the lowest concentration of sevoflurane was reduced to half that of the control group (0.75%). The highest concentration of sevoflurane in each group was increased to inhibit positive responses in 100% of patients. A single measurement was obtained per patient. Tracheal intubation accomplished without coughing, bucking, or gross purposeful muscular movements was considered smooth as determined by a nurse and a surgeon blinded to sevoflurane concentration and tested drug dose. Patients who moved during laryngoscopy or after tracheal intubation were immediately given 5% sevoflurane. The time for tracheal intubation was defined as the time from discontinuation of face-mask ventilation to connection of the tracheal tube to the anesthesia circuit. Anesthesia was then maintained with sevoflurane in oxygen at 1 L/min and in air at 5 L/min and infusion of the tested drug. The sevoflurane concentration was controlled according to the hemodynamics of each patient to maintain systolic arterial pressure (SAP), heart rate (HR), or both changes within 20% of baseline. Upon completion of surgery , the airway was gently suctioned if necessary, sevoflurane and infused drug were discontinued. Controlled ventilation at the same settings and a total gas flow of 6 L/min of oxygen were continued without attempts to stimulate the patient. Spontaneous respiration was initially assisted and then adequate spontaneous breathing was established. With the return of the cough reflex, patients were allowed to breathe spontaneously. When patients demonstrated complete emergence from anesthesia by displaying a regular respiratory pattern, facial grimacing, and purposeful movement, the trachea was extubated and oxygen at 6 L/min was administered via the mask, then patients were transferred to the PACU.

During emergence, patients were observed for respiratory complications such as breath holding,

muscle rigidity, and for arterial desaturation. The time to extubation from discontinuation of anesthesia (extubation time) and the time from the discontinuation of anesthesia till the time of eye opening (defined as the time until the eye opened on verbal command) were recorded.

Agitation parameters were assessed with a five-point emergence agitation scale (Table 1) [8], and measured on admission to the post anesthesia care unite (PACU) and for 6 hours after extubation. Delirium was defined as the agitation score of ≥ 4 for more than five minutes, despite all calming efforts done by the parents [3].

Table 1: Five-point emergence agitation scale

Score	
1	Obtunded with no response to stimuli
2	Asleep, but responsive to movement and stimuli
3	Awake and appropriately responsive
4	Crying and difficult to console
5	Wild thrashing behavior that requires restraint

Table 2: Objective Pain Scale

Observation	Criteria	Points
Blood pressure	± 10% of preoperative value	0
	> 20% of preoperative value	1
	< 30% of preoperative value	2
Crying	Not crying	0
	Crying, but stops with tender, loving care	1
	Crying without stopping, doesn't respond to tender, loving care	2
Movement	None	0
	Restless	1
	Thrashing around	2
Agitation	A sleep or calm	0
	Mild agitation	1
	Hysterical	2

In the PACU, parents were allowed to be with their child. Pain was assessed by objective pain scale (OPS), table 2 [16,17]. Pain and EA were treated with i.v. fentanyl 1 µg/kg with at least 10-minute time interval between each dose, during which time the children were monitored for any signs of respiratory depression, and postoperative fentanyl consumption (µg) was recorded. All Scores and observations were recorded by the anesthesia technician who was unaware of patient group.

The time of hospital discharge allowance was recorded (starting from the time of eye opening). Patients were not allowed to go home unless they fulfilled the discharge criteria [18].

2.2 Data analysis

Patient characateristics and clinical details are provided as mean ± standard deviation. Statistical comparisons among the three groups (control, F and D) were performed using analysis of variance (ANOVA) with the Scheffe test for posthoc analysis . Statistical comparisons within each group were performed using repeated-measures ANOVA, and significance was assessed using the Scheffe test. Sex, ASA physical status, and surgical procedure were analyzed using Fishers exact test .In all cases, values of $p < 0.05$ were considered the minimum level for statistical significance. The preventive sevoflurane concentration against coughing on tracheal intubation was determined using a multiple independent variable logistic regression model.

3. Results

Patients characteristics and clinical trials were similar between groups (Table 3) with no differences in base line (before induction) SBP or HR. Both SBP and HR before intubation decreased significantly below base line values in all three groups with no significant difference between the three groups.

Thereafter, both SBP and HR increased significantly after intubation in control group but no change in group F and group D as compared to base line values. SBP in the group F and D did not significantly increase compared with the value before intubation.

In the group F and D, both SBP and HR immediately after intubation were significantly lower than those values in the control group and no statistical difference between them. Time for tracheal intubation did not exceed 10 s. No patients showed breath - holding, muscle rigidity, vomiting, bradycardia, hypotension or arterial oxygen desaturation necessitating treatment.

Table 3: Patient characteristics and clinical details. Value were presented as the mean (SD) or mean (range).

	Control group (n=45)	Group F (n=47)	Group D (n=48)
Age (year)	4.6± 1.08	4.5±1.12	4.6±1.06
Body weight (kg)	18 ± 3.6	20.4 ± 5.4	19 ± 4.6
Sex (Male/Female)	25/20	28/19	26/22
Procedure			
Inguinal herniorraphy	35	32	37
Hypospadias repair	6	7	5
Plastic surgery	4	8	6
Duration of anesthesia (min)	75.37±15.05	77.35±16.46	76.58±17.65
Duration of surgery (min)	56.47±12.5	58.6±13.7	56.7±14.8
Systolic arterial pressure (mm Hg) SAP			
Baseline before induction	120 (14)	119 (12)	122 (13)
Before intubation	108 (13)$^{+}$	104 (11)$^{+}$	103 (15)$^{+}$
After intubation	129 (14)$^{\#}$	110 (10)*	108 (12)*
Heart rate (beats/min)			
Baseline before induction	120 (18)	119 (16)	122 (24)
Before intubation	102 (22)$^{+}$	99 (23)$^{+}$	96 (24)$^{+}$
After intubation	128 (16)$^{\#}$	105 (25)*	102 (21)*
Range of ET sevoflurane during surgery (%)	2-2.5	2-2.5	2-2.5

* P < 0.05 compared with control group.
+p < 0.05 compared with baseline. # P < 0.05 compared with value before intubation.

A total of five control group patients, three F-group patients, and two group D patients were excluded from the study because they lost follow up observation. The end tidal sevoflurane concentrations and percentages of patients with smooth tracheal intubation were shown in Table 4. Smooth tracheal intubation was possible in all groups at an end – tidal sevoflurane concentration of 3.50 in the control group, 2.75 in group F and 2.50 in the group D, table 4.

Table 4: Incidence of smooth tracheal intubation

End tidal sevoflarane concentration in each subgroup (Vol%)	Control group (n= 45)	Group F (n = 47)	Group D (n= 48)
0.50		0 % (0/1)	0 % (0/1)
0.75		0 % (0/2)	0 % (0/1)
1.00		25 % (1/4)	33 % (1/3)
1.25		25 % (1/4)	43 % (3/7)
1.50	0 % (0/2)	66 % (4/6)	70 % (7/10)
1.75	0 % (0/2)	72 % (8/11)	80 % (8/10)
2.00	33 % (2/6)	78 % (7/9)	91 % (10/11)
2.25	37 % (3/8)	80 % (4/5)	100 % (2/2)
2.50	44 % (4/9)	100 % (2/2)	100 % (3/3)
2.75	57 % (4/7)	100 % (3/3)	
3.00	71 % (5/7)		
3.25	100 % (2/2)		
3.50	100% (2/2)		

Assessment of emergence agitation: The incidence of postoperative agitation was significantly less in the F group (21%) and D group (25%) compared with the control group (60%). The incidence of postoperative vomiting was significantly less in the treated groups compared with the control group, 42 % (19/45), 17 % (8/47) and 19 % (9/48) for the control group, fentanyl group and dexmedetomidine group respectively (P< 0.001), with no significant different between the treated groups.

Time to eye opening were significantly shorter in control group (mean 10.8 ± 1.5 min) compared with group F (mean 14.6 ± 1.3 min) and group D (mean 15.4 ± 1.6 min), (P< 0.001) . Higher pain scores were recorded in control group compared to group F and group D with no difference between group F and group D. The time of first postoperative analgesic dose was significantly shorter in control group(10.6 ± 2.5 min) compared with the F group (35.4 ± 4.6 min) and D group (32.6 ± 3.8 min)(P<0.001), and also shorter in D group as compared to F group (P<0.002).

Table 5: Comparison between the three groups as regards the time of eye opening, time of first postoperative analgesic dose, time for hospital discharge allowance, incidence of postoperative agitation .

	Control group (n=45)	Group F (n = 47)	Group D (n= 48)
Time to eye opening (min)	10.8 ± 1.5*	14.6 ± 1.3#	15.4 ± 1.6
Time to first postoperative analgesic dose (min)	10.6 ± 2.5 *	35.4 ± 4.6#	32.6 ± 3.8
Time for hospital discharge allowance (min)	291.6±25.6	292.7±26.7	298.7±26.4
Postoperative agitation	60 %*	21%	25%
Postoperative fentanyl consumption (mcg)	18.9±8.7*	4.06±5.8	5.6±6.9
Incidence of postoperative nausea and vomiting	42 %*	17 %	19 %

*Significant compared to the other group. # Significant compared to group D

4. Discussion

Emergence agitation is a frequent side effect of sevoflurane anesthesia in children with a reported incidence of up to 80%, and remain a significant post-anesthetic problem that interferes with children's recovery, and challenges the PACU staff in terms of assessment and treatment [4]. The cause of agitation after sevoflurane anesthesia is still unknown, the incidence of this excitatory behavior seems to be reduced by the perioperative use of sedative and analgesic drugs. Although there is no evidence that this adverse effect, affects long term outcome , it is a source of dissatisfaction for parents.

There is no well established prophylaxis or treatment , although the incidence of this excitatory behavior seems to reduced by preoperative use of sedative and analgesic drugs. Fentanyl and dexmedetomidine were expected to both facilitate intubation and decrease emergence agitation .

In this study fentanyl infusion as a bolus of 2ug/kg followed by a continuous infusion of 1 µg/kg/h and dexmedetomidine 0.75 µg/kg followed by a continuous infusion of 0.5 µg/kg/h provided improved conditions for both intubation and emergence.

The MAC_{TI} value for sevoflurane determined previously by Katoh et al in adults was 3.55 vol % [19], it is higher than that observed in children.

This difference might be explained by the difference in type of surgery or tracheal tube, which is cuffed in adults, but not in this study of children. In the present study the MAC_{TI} for sevoflurane determined (2.7%) which is slightly more than that previous value (2.49%) reported by Inomata et al[9], but nearly similar to previous value (2.69 %) which had been reported by Inomata et al[1]. However we used the step size in the MAC_{TI} determination 0.25% to obtain more detailed data , compared with 0.5% in their study.

The frequency of postoperative agitation observed in a previous study [12] , after a single bolus dose of fentanyl at 2.5 µg/kg was 36% where frequencies in this study were 21% in F group and 25% in D group. Two other studies have reported that, a single bolus dose of fentanyl (1 µg/kg in one study [10], and 2 µg/kg in the other [11], reduce the incidence of severe emergence agitation after sevoflurane anesthesia. However, in those studies and in a previous study [12], using fentanyl 2.5 µg/kg , patients received adjuvant drugs (nitrous oxide or midazolam in addition to sevoflurane. Numerous drugs, including benzodazepines, barbiturates and opiods contribute to behavioural disturbances after general anesthesia [20]. The use of premedication, such as oral midazolam 0.5 mg/kg and i.v. clonidine 2 µg/kg , decrease the amount of emergence agitation . Administration of these adjuvant drugs impedes assessment of side-effects or incidence of agitation emergence caused solely by sevoflurane (control group) [21,22]. Although the use of fentanyl or dexmedetomidine was likely to decrease HR and SAP , no patients required treatment for these effects in this study. The difference in incidences of agitation and vomiting between this study and a previous study might partially depend on the period of observation (six hours in this study and 15 min in one study [9] and 24 h in the other study [12].

Several studies have reported emergence agitation in patients anesthetized with sevoflurane even when no pain was present [10,23,24]. Other than surgical pain, airway irritation caused by tracheal intubation could lead to behavioral manifestations, including emergence agitation, emergence time in this study was significantly increased in the treated group ($P<0.001$), and in group D more than group F ($P<0.01$). Rapid awakening in an unfamiliar room thus might not be the main cause of emergence agitation.

Inadequate pain relief may be the cause of agitation, particularly after short surgical procedures for which peak effects of analgesics may be delayed until the child is completely a wake [7, 25]. Fentanyl given either i.v. 2.5 µg/kg or intranasal 2ug/kg also decreased EA [11, 12]. Galinkin et al [11], observed that the use of intranasal fentanyl 2 µg//kg administered after induction of anesthesia reduced the incidence of agitation after sevoflurane anesthesia from 23% to 2% without increasing the discharge times [11].

Also Inomata et al [9], concluded that fentanyl infusion consisting of a bolus dose of 2 mcg/kg followed by a continuous infusion of 1 mcg/kg/h facilitates tracheal intubation and smooth emergence in children anaesthetized using sevoflurane. Similarly; caudal block using clonidine has seen to be effective [26].

The difference in incidences of agitation and vomiting between this study and a previous study [12] might partially depend on the period of observation, type of surgery and difference in the doses of fentanyl and dexmedetomidine used in our study. It has been postulated that rapid awakening after the use of the insoluble anesthetics, such as sevoflurane, may initiate EA [27]. However, recovery from propofol anesthesia, which is also rapid, is smooth and pleasant in comparison to sevoflurane [24].

It is becoming increasingly clear that sevoflurane-related EA is probably an intrinsic characteristic of the anesthetic itself, having central nervous effects different from other volatile anesthetics, particularly in younger children [5]. Epileptiform activity has been reported during the use of sevoflurane anesthesia in non-epileptic patients. This could be caused by rapid change in sevoflurane concentration at the target site in the brain where the γ-aminobutric acid-ergic properties of sevoflurane would induce changes in the balance between neuronal synaptic inhibition and excitation [28].

Data on the possible role of premedication in reducing EA were conflicting. Preoperative administration of 0.5 mg/kg midazolam orally, for 15 minutes before induction, in children undergoing bilateral ear tube insertion reduced the incidence of EA with sevoflurane (from 66.7% to 39.3%) [21]. Also Khattab et al [29] concluded that adding a low dose of oral ketamine to midazolam based oral premedication reduced sevoflurane-related emergence agitation to 37% in preschool children undergoing dental surgery without delaying discharge. However similar studies using oral midazolam premedication in comparison to other drugs failed to show an improved incidence of EA following sevoflurane anesthesia [26,30].

Emergence time and hospital discharge time in this study were prolonged in fentanyl group and dexmedetomidine group than the control group and no significant difference in time for hospital discharge allowance (min) between F group and D group.

A relationship between opioid and sedative status has recently been reported [31]. The hypothalamic hypocretin / orexin system regulates arousal and maintenance of the waking state. Hypocretin neurons are depressed by opioids which inhibit the hypocretin system by directly acting on the cell body and by indirectly reducing the excitatory synaptic tone through a presynaptic mechanism.

These findings suggest that the low frequency of EA in patients receiving fentanyl might be influenced by the hypocretin system. However, a recent meta analysis reported that the analgesic properties of opioids do not seem to play a role in prophylactic effects against EA [32]. The result of our study showed that, The use of dexmedetomidine 0.75 ug/kg to be followed by infusion 0.5 µg/kg/h intraoperative reduced the incidence of EA after sevoflurane anesthesia and reduce postoperative pain score.

Kulka et al [4], demonstrated the role of clonidine in decreasing EA because of its sedative and analgesic effects, from 72% to 10% in a clonidine treated group undergoing circumcision.

Intravenous dexmedetomidine has similar action to clonidine and in our study when administered as a bolus followed by infusion , results in a reduction of postoperative agitation after sevoflurane anesthesia from 60% in the control group to 25% in D group. The time for postoperative analgesic dose was significantly shorter in control group compared with the other tow groups, this means easily appearance of pain or discomfort after rapid recovery from sevoflurane anesthesia alone . So the use of either fentanyl or dexmedetmidine during sevoflurane anesthesia not only decrease postoperative agitation but also give satisfactory pain relief and decrease postoperative analgesia requirement.

Abeer et al [33], demonstrated that the use of dexmedetomidine whether iv or intranasal resulted in optimization of the intraoperative hemodynamic stability, lower incidence of EA and better post operative pain scores, and improvement in the quality of the perioperative circumstances in such sensitive and risky population (pediatric patients).

Kulka et al[4], in his study of 2 µg/kg clonidine, reported a decrease in EA without delay in patient discharge. However Lankinen et al [34], found that clonidine at 1.5 µg/kg could not prevent agitation.

Ibacache et al [35], observed that clonidine at 3 µg/kg decreased the incidence of agitation after sevoflurane anesthesia but the small dose 1mcg/kg failed to prevent agitation.

Multiple factors may be the causes of postoperative EA as shorter time for awakening , young age , sevoflurane anesthesia, waking up in a strange environment, and psychological immaturity, have also been considered possible risk factors [10,34]

To our knowledge, this is the first study to compare dose related effects of continuously infused dexmedetomidine versus fentanyl on emergence agitation in children without using nitrous oxide or premedication.

Some limitations need to be considered for the present study as we enrolled patients undergoing several types of surgeries , further study should be performed in patients doing the same surgeries. There is much debate about the reliability and validity of the tool used to measure emergence agitation in young children. Although the Pediatric Anesthesia Emergence Delirium (PAED) scale, which developed in 2004 [25], appears to be the most reliable tool for the measurement of EA; yet it was difficult for us to train the observers to apply it. Therefore we used the simpler and rapidly applicable (Five-point scale) [8]. Cravero et al.,[10], reported a high incidence of agitation using a different method without a validated agitation scale. The agitation score can be determined as the highest score in an instant or the score that lasted the longest. So future studies on agitation should consider both the score and the period (e.g. area under the curve). In conclusion , we assessed the effects of continuous infusion of fentanyl or dexmedetomidine on sevoflurane concentrations required for tracheal intubation and on conditions at emergence after surgery in children. Both fentanyl and dexmedetomidine produce comparable smooth intubation and calm emergence in children anesthetized with sevoflurane without any difference in hospital discharge time.

Further studies are needed to demonstrate the effect of different doses of fentanyl and dexmedetomidine during different types of surgery in pediatric population and find the optimum dose for controlling EA with high safety profile and cost effectiveness of dexmedetomidine remain to be considered and or resolved in future studies.

Corresponding author
Samy A. Amr
Anesthesiology Department, South Egypt Cancer Institute
saaerfan62@yahoo.com.ph

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