



## Comparison of Propofol and Fentanyl in Prevention of Emergence of Delirium after Sevoflurane Anesthesia

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### Abstract

**Introduction:** The occurrence of emergence agitation in children after sevoflurane anaesthesia is common with an incidence ranging between 10 to 80%.

**Aim:** To study Propofol and Fentanyl in Prevention of Emergence of Delirium after Sevoflurane Anesthesia.

**Material and Methods:** After approval from ethical committee and written informed consent from parents or guardian, 115 children with ASA I and II aged 2 to 6 years, were selected for elective urological surgery, under sevoflurane anaesthesia. Patients were divided into three groups i.e. Group C (Control), Group F (Fentanyl), and Group P (Propofol). All collected data enter into the IBM SPSS 20<sup>th</sup> (statistical parameter of soci 20<sup>th</sup> and analyzed it. Continuous data expressed as mean  $\pm$  sd and non-continuous expressed as in percentages. Anova test, kruskal wallis and chi square (fisher exact) test have been performed to carry out p value at 95% CI. p value <0.05 shows statistically significant.

**Result:** In score 1, child is obtunded with no response to stimulation, in stage 2, child is asleep but responsive to movement or stimulation, in stage 3, child is awake and responsive while score 4 includes crying and in score 5 thrashing behavior that requires restraint. We found highest score in group S that is around 4 compared to group F and group P. The control group children were awake and responsive but most of the children were crying from five minutes onwards and some children had thrashing behavior. Amongst group F and group P, group P is better than group f. Group P children were more sedated compared to group F. After 30 minutes, almost all children were awake and responsive. This emergence of Agitation at 5 min, 10 min, 15 min was significantly higher in Control and Propofol group as compared to Fentanyl and Control (P < 0.01 respectively).

**Conclusion:** We concluded that fentanyl and propofol both have effect on reduction of emergence agitation after sevoflurane anaesthesia but the children of propofol group remains calm and quiet and have significant reduction in emergence delirium than fentanyl at 10 and 15 mins after discontinuation of sevoflurane anaesthesia.

**Keywords:** Propofol; Fentanyl; Sevoflurane; Emergence of Delirium

### Introduction

“We are not anaesthetising the child we are really anaesthetizing the family” That should be the strategy of a paediatric an-

aesthesiologist. The preparation of a paediatric patient and his or her family begins with the visit to out-patient department. Anaesthesiologists play an important role in educating the child and

the parents what they can expect pre, intra and post operatively. To give successful anaesthesia to the neonate and small children as compare to the older child and adult require understanding of differences in anatomy physiology pharmacology and psychology among them.

Sevoflurane is now the choice of inhalational anaesthetic agent for paediatric patient, as it is non pungent, with minimal airway irritation, and its cardiac adverse effects are very minimal like cardiac depression and dysrhythmias [1].

The occurrence of emergence agitation in children after sevoflurane anaesthesia is common with an incidence ranging between 10 to 80%.<sup>2,3</sup> It is characterized by behaviour that can include crying, disorientation, excitation, and delirium. Although EA is self-limiting and might not result in permanent sequelae, it carries the risks of self-injury and is a cause of stress to both caregivers and families [2,3]. Different drugs such as propofol,  $\alpha$ 2-adreno receptor agonists like dexmedetomidine and clonidine, midazolam, fentanyl, and ketamine have been used to allow a smooth emergence from sevoflurane anaesthesia [4].

Propofol is a short acting sedative and hypnotic agent. Generally, it is used in children for its sedative action as well as for induction and maintenance of general anaesthesia.

Fentanyl is a potent opioid receptor agonist with sedative and analgesic effects. It is routinely used in the practice of paediatric perioperative medicine. Some clinical trials have shown that fentanyl can prevent EA after sevoflurane anaesthesia in children [5,6].

## Materials and Methods

After approval from ethical committee and written informed consent from parents or guardian, 115 children with ASAI and II aged 2 to 6 years, were selected for elective urological surgery, under sevoflurane anaesthesia. They were randomly allocated to one of the groups. 10 cases of were excluded from the study because of excessive crying or non-compliance and remaining distributed equally to 3 different groups having 35 in each:

- Group C (Control)
- Group F (Fentanyl)
- Group P (Propofol).

## Exclusion criteria

Children with developmental delay, psychological or neurological disorders, abnormal airway, reactive airway, history of up-

per respiratory tract infection in previous 3 weeks, or who were known to be allergic to any of this study drug were excluded from the study.

On arrival in operation theatre, intravenous cannula insertion and monitoring like pulse oximetry (SPO<sub>2</sub>), ECG and noninvasive blood pressure (NIBP), temperature, EtCO<sub>2</sub> were applied under inhalation anaesthesia of sevoflurane in oxygen via face mask.

Child was induced with IV thiopentone 4 - 5 mg/kg followed by suxamethonium 2 mg/kg administration. Laryngoscopy and tracheal intubation were done with appropriate size of portex endotracheal tube and maintenance of anaesthesia done with sevoflurane 1.5 - 2.5% in 50% oxygen and 50% nitrous oxide. For controlled ventilation, injection atracurium was given in a dose of 0.5 mg/kg bolus followed 0.1 mg/kg as according to peripheral nerve stimulator (PNS). Intra operatively hemodynamic monitoring were recorded every 5 mins. Intravenous fluid was given according to Holliday-segard nomogram. Analgesia was given in the form of rectum paracetamol suppositories in a dose of 45 mg/kg.

Before 5 minutes of completion of surgery, sevoflurane anaesthesia was discontinued with the same time the concentration of oxygen was adjusted to 100%. At the same time, subjects received intravenous propofol 1 mg kg<sup>-1</sup> or fentanyl 1 mg kg<sup>-1</sup>, or saline slowly by the doctor who was not knowing the drug. Reversal in the form of intravenous glycopyrrolate 0.008 mg/kg and neostigmine 0.05 mg/kg was given according to PNS.

After regular breathing with adequate tidal volume was confirmed, the endotracheal tube was removed. Time of eye opening was noted from discontinuation of sevoflurane anaesthesia. The five step EA scale (Cravero scale) were used to assess the Emergence agitation at interval of 5, 10 and 15 minutes respectively.

Subjects were observed for at least 30 mins for the management of possible respiratory complications such as upper airway obstruction, breath holding, or suspicious laryngospasm. Consciousness defined as crying or eye opening in response to verbal command or light touch every 15 mins from the arrival at the recovery room. Subjects were to remain in the recovery room for at least 3 - 4 hrs before discharge.

If there any occurrence of nausea or vomiting that was assessed and treated with ondansetron 0.1 mg/kg.

**Paediatric emergence behaviour score (Cravero scale)**

- Obtunded with no response to stimulation: 1
- Asleep but responsive to movement or stimulation: 2
- Awake and responsive: 3
- Crying (for > 3 min): 4
- Thrashing behaviour that requires restraint: 5.

We have observed the patient for 30 mins after for Emergence Agitation. After 15 mins of observation the child who was having score 4 and 5 have received inj. Pentazocin 0.3 mg/kg to make the child calm and quiet. We were also watchful for other side effects like nausea, vomiting, somnolence etc. children having nausea and vomiting were given inj. Ondansetron ---/kg. The children were kept in recovery room and for 4 - 6 hours and discharge directly from recovery room.

For sample size calculation, Cravero score at 5 min from sevoflurane discontinuation has been considered. Mean Of Group-S was 4.01, Group-F was 2.46 and Group-P mean was 2.30 where 0.69 standard deviation have been considered at  $\alpha = 0.05$  and power 80%. According to this, in each group, 33 sample size is appropriate in each group. Considering some drop outs we have selected 35 patients in each group.

All collected data enter into the IBM SPSS 20<sup>th</sup> (statistical parameter of soci 20<sup>th</sup> and analysed it. Continuous data expressed as mean  $\pm$  sd and non-continuous expressed as in percentages. Anova test, kruskal wallis and chi square (fisher exact) test have been performed to carry out p value at 95% CI. p value <0.05 shows statistically significant.

**Results**

(Table 1)

Variables	Group C	Group F	Group P	P value
Age (months)	56 $\pm$ 29.95	60.40 $\pm$ 32.73	66.34 $\pm$ 36.46	0.62 (NS)**
Weight (Kg)	15.59 $\pm$ 4.07	14.63 $\pm$ 4.30	14.93 $\pm$ 4.69	0.66 (NS)**
Sex (M\F)	29/6	27/8	28/7	0.83 (NS)**

**Table 1:** Demographic data.

In our study, there is no significant difference in age, sex and weight in between the three groups. As shown in table 1, in all the groups mean age is around 5-6 years with non-significant p value. Minimum age in all groups were 2 years while maximum age was 6

years. Mean weight in all the groups were around 15 kg. The minimum weight of the patients in group S group F and group P is 4 kg. As we have done studies in patient of urological procedures most of the patients were from male gender in all the groups. The gender differentiation between the three groups were almost equal.

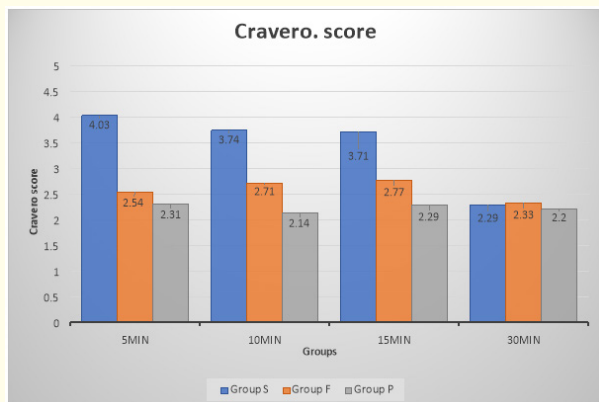
Variables	Group S	Group F	Group P	P value
Anesthesia time	128.34 $\pm$ 59.68 min	129.28 $\pm$ 50.63 min	135.22 $\pm$ 60.19 min	0.67 (NS)**

**Table 2:** Anesthesia time.

Mean duration of anaesthesia in all three groups was around two to two and half hours. We have included various urological surgeries like hypospadias repair, open and laparoscopic pyeloplasty, nephrectomy, percutaneous nephrolithotripsy, orchidopexy, ureteric reimplant. The shortest duration of anaesthesia was in a case of percutaneous nephrolithotripsy (45 mins) while longest duration found in open ureteric reimplant (4 hrs 25 mins).

Variables	Group C	Group F	Group P	P value
5 min	4.03 $\pm$ 0.70	2.54 $\pm$ 0.70	2.31 $\pm$ 0.47	<0.01**
10 min	3.74 $\pm$ 0.70	2.71 $\pm$ 0.57	2.14 $\pm$ 0.35	<0.01**
15 min	3.71 $\pm$ 0.67	2.77 $\pm$ 0.80	2.29 $\pm$ 0.57	<0.01**
30 min	2.29 $\pm$ 0.49	2.33 $\pm$ 0.43	2.20 $\pm$ 0.41	<0.68

**Table 3:** Emergence agitation score (Cravero score).



Graph 1: Cravero score.

In score 1, child is obtunded with no response to stimulation, in stage 2, child is asleep but responsive to movement or stimulation, in stage 3, child is awake and responsive while score 4 includes crying and in score 5 thrashing behaviour that requires restraint. We found highest score in group S that is around 4 compared to group F and group P. The control group children were awake and responsive but most of the children were crying from five minutes onwards and some children had thrashing behaviour. Amongst group F and group P, group P is better than group f. Group P children were more sedated compared to group F. After 30 minutes, almost all children were awake and responsive. This emergence of Agitation at 5min, 10min, 15min was significantly higher in Control and Ferouptanyl group as compared to Control and Propofol ( $P < 0.01$  respectively).

### Discussion

Many scales have been proposed that evaluate the incidence and severity of Emergence Delirium and variety of scales are used in clinical practice and research purposes. Agitation due to pain is a significant confounding factor for the evaluation of the presence or measurement of the degree of Emergence delirium. There are so many scales for EA assessment like Bajwa scale, Watcha scale, Aono scale, PAED scale, Cravero scale etc. We selected Cravero scale in our study.

The Cravero scale has five steps from obtunded and unresponsive to wild thrashing behaviour requiring restraint. A score of  $\geq 4$

i.e. from crying and difficult to console to wild thrashing for a 5 or more than 5 minute duration despite active calming efforts is regarded as indicative of Emergence Delirium (ED). PAED scale is validated but is difficult to use in routine clinical practice [1].

SAMY A. AMR and MOHAMED A. OSMAN had used the five point scale (Cravero scale) as it is simpler and rapidly applicable in their study to observe the effects of Fentanyl and Dexmedetomidine infusion on tracheal Intubation and Emergence Agitation in children anesthetized with sevoflurane. It appears to be the most reliable tool for the measurement of EA [7].

Joseph Cravero had studied the comparisons of sevoflurane and halothane in Emergence agitation in 32 children. They have used the five step Cravero scale for assessment of emergence agitation and they found high incidence and threshold for emergence agitation with sevoflurane compare to halothane (33% vs 0%  $P = 0.010$ ) [8].

In our study Emergence agitation was assessed at 5, 10, 15 and 30 minutes after discontinuation of sevoflurane anaesthesia. We found less Emergence Agitation in group F and group P compare to control group S at 5, 10, 15 minutes. In control group, the children having Emergence Agitation score  $\geq 4$  were given intravenous pentazocine 0.3 mg/kg to make them calm and comfortable. At 30 minutes interval the children of all the groups were awake and responding to verbal command. The Cravero scale at 30 mins interval is non-significant in all the groups and it was between 2 and 3. The emergence agitation at 5 minutes in group f was  $2.54 \pm 0.70$  and group p was  $2.31 \pm 0.47$  at 5 minutes which is non-significant ( $P = 0.11$ ). While at 10 and 15 mins, Cravero scale in group P was ( $2.14 \pm 0.36$ ) and ( $2.29 \pm 0.57$ ) and in group f was ( $2.71 \pm 0.57$ ) and ( $2.77 \pm 0.81$ ) which were significant between two groups. This suggest that EA is less at 10 and 15 mins in propofol group than fentanyl group.

Several previous meta-analysis indicated that fentanyl can reduce the incidence of EA under sevoflurane anaesthesia in children, whereas the meta-analysis by Dahmiani, *et al.* state that intravenous fentanyl failed to prevent ED [4]. In sub group analysis of Fenmei Shi, in 16 different studies found that both intravenous and intranasal fentanyl showed to be effective in decreased the incidence of Emergence Agitation [9]. The reason for this conflicting result may be due to inclusion of only two studies in the meta-analysis by

Dahmiani, *et al.* to observe the effects of Fentanyl on Emergence Agitation in 1362 Children under Sevoflurane Anesthesia. They found that administration of fentanyl decreased the incidences of Emergence Agitation and postoperative pain [8].

Cravero JP, *et al.* evaluated the effect of fentanyl on EA with a dose smaller than that used for induction (1 mg/kg) in children after sevoflurane anaesthesia without surgery; the incidence of EA was decreased independent of its analgesic effects, and the time to achieve hospital discharge criteria was not prolonged [10].

Ashraf Arafat abdelhalim studied the effect of ketamine versus fentanyl on the incidence of emergence agitation after sevoflurane anaesthesia in 120 paediatric patients. In their study incidence of EA was significantly low in ketamine group and fentanyl group (15% and 17.5% respectively) compared to control group (42.5%) with no significant difference between group K and group F [11].

Chen and colleagues compared the use of midazolam, propofol, or ketamine with fentanyl just after discontinuing sevoflurane anaesthesia in 120 children who underwent cataract surgery and showed that propofol or midazolam in combination with fentanyl were both effective in reducing EA. They found The PAED scale (Recovery mental state) showed a significant advantage for midazolam-fentanyl [5 (2 - 15)] and propofol-fentanyl [6 (3 - 15)] versus ketamine-fentanyl [10 (3 - 20)] ( $P < 0.05$ ) [12].

Marie T Aoud used propofol at the end of surgery for prevention of emergence agitation in children after strabismus surgery during sevoflurane anaesthesia. They found PAED scale significantly lower in propofol group compared with the saline group ( $98.9 \pm 3.9$  vs.  $11.5 \pm 4.5$ ;  $p = 0.004$ ) without delaying discharging from the post anaesthesia care unit [3].

YH Kim and colleagues also compared propofol and midazolam in 101 children undergoing strabismus surgery [12]. They found that decreased the incidence of EA in midazolam group 42.9% (15/35) and in propofol group 48.4% (15/31) compared to saline group 74.3% (26/35). That means saline group had 15 to 20% higher emergence agitation than other two groups [13].

Ibrahim Abu-Shahwan studied the effect of propofol (1 mg/kg) on emergence agitation after sevoflurane anaesthesia in 42 children. They found occurrence of EA was diagnosed in the propofol group was 4.8% while in placebo group 26.8%.  $P < 0.05$  [14].

The efficacy of propofol is dependent on the timing of administration. Due to the rapid pharmacokinetics of propofol, a bolus of 1 mg/kg given at the end of the procedure or continuous infusion used during maintenance of anaesthesia results in increased concentrations during emergence resulting in a decreased incidence of ED [15-17].

MS Kim, *et al.* compared the fentanyl and propofol for prevention of emergence agitation after sevoflurane anaesthesia in children. They found PAED score was significantly reduce in group P and group F compare to control group. Group F have longer stay in the post anaesthesia care unit than group S and group P.

## Conclusion

We concluded that fentanyl and propofol both have effect on reduction of emergence agitation after sevoflurane anaesthesia but the children of propofol group remains calm and quiet and have significant reduction in emergence delirium than fentanyl at 10 and 15 mins after discontinuation of sevoflurane anaesthesia.

## Conflict of Interest

Nil.

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