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# Comparison of propofol and fentanyl administered at the end of anaesthesia for prevention of emergence agitation after sevoflurane anaesthesia in children

M.-S. Kim, B.-E. Moon, H. Kim and J.-R. Lee*

Department of Anaesthesiology and Pain Medicine, Anaesthesia and Pain Research Institute, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea

* Corresponding author. E-mail: leejeongrim@gmail.com

## Editor's key points

- Emergence agitation is common in children after sevoflurane anaesthesia.
- This prospective randomized trial compared the use of propofol or fentanyl administered at the end of anaesthesia in reducing emergence agitation.
- Both propofol and fentanyl reduced emergence agitation, but fentanyl was associated with more postoperative nausea and vomiting.

**Background.** Propofol and fentanyl can be administered at the end of sevoflurane anaesthesia to decrease the incidence and severity of emergence agitation (EA), although it has not been determined which agent has superior efficacy. The purpose of this study was to compare the effects of propofol and fentanyl on EA.

**Methods.** In this prospective, randomized, double-blind study, 222 children, 18–72 months of age, undergoing sevoflurane anaesthesia were randomly assigned to one of the three groups receiving either propofol 1 mg $kg^{-1}$ (Group P), fentanyl 1 μg $kg^{-1}$ (Group F), or saline (Group S) at the end of anaesthesia. The incidence and severity of EA were evaluated with the paediatric anaesthesia emergence delirium (PAED) scale. Time to recovery and incidence of nausea/vomiting were assessed.

**Results.** The mean PAED score was 4.3 in Group P and 4.9 in Group F ($P=0.682$), which were lower than 9.0 in Group S ($P<0.001$). Nausea and vomiting were significantly more frequent in Group F than Groups P and S (adjusted $P=0.003$ and adjusted $P<0.001$). Group F had also longer stay in the post-anaesthesia care unit (PACU) than Group S ($P<0.001$), while Group P did not. However, the differences in PACU stays between the P and F groups were considered clinically insignificant.

**Conclusion.** Small doses of propofol or fentanyl at the end of sevoflurane anaesthesia comparably reduced EA. Propofol was better than fentanyl due to a lower incidence of nausea and vomiting.

**Keywords:** anaesthetics i.v., propofol; anaesthetics volatile, sevoflurane; analgesics opioid, fentanyl; recovery, postoperative

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Emergence agitation (EA) in children early after sevoflurane anaesthesia is a common postoperative problem, with incidence ranging up to 80%.[1 2] 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.[3 4]

Different strategies have been suggested to decrease the incidence and severity of EA, such as administrating sedative medication before induction, a change in the maintenance technique of anaesthesia, or pharmacological agent administration at the end of anaesthesia.[2 5–7] Among these strategies, the use of pharmacological agents at the end of anaesthesia is thought to be the most convenient and easily applicable method in clinical situations, since it does not rely on the nature of the anaesthetic agents used during induction and maintenance or the duration of anaesthesia.[2 8 9] From this perspective, low doses of propofol or fentanyl (1 mg $kg^{-1}$ or 1 μg $kg^{-1}$, respectively) have been shown to successfully reduce EA if administered at the end of anaesthesia.[1 2 10] However, these studies were carried out independently under different conditions with various assessment tools, and the therapeutic efficacies of these two drugs have not been directly compared. In addition, their different molecular mechanisms could influence different variables related to recovery and complications.[1 11] Therefore, we hypothesized that the effects of decreasing the incidence and severity of EA and recovery profiles are different between propofol and fentanyl under comparable clinical conditions.

The purpose of this randomized double-blinded study was to compare the effects of propofol and fentanyl administered at the end of sevoflurane anaesthesia on EA in children undergoing inguinal hernia repair. In addition, characteristics of anaesthesia recovery and incidence of adverse effects were compared.

## Methods

This study was approved by the institutional review board of Severance Hospital, Yonsei University Health system (ref: 4-2010-0536), and was registered with ClinicalTrials.gov (ref: NCT01506622). Written informed consent was obtained from the parents of all participants. Two hundred and twenty-two children, 18–72 months of age, ASA class I or II, who were undergoing ambulatory inguinal hernia repair under general sevoflurane anaesthesia, were prospectively included in this study. Children with developmental delay, psychological or neurological disorders, abnormal airway, reactive airway disease, or history of general anaesthesia were excluded. All patients fasted at least 8 h, with an opportunity to drink clear fluids up to 4 h before operation.

The enrolled children were randomly allocated to one of the three groups to receive either propofol (Group P), fentanyl (Group F), or saline (Group S) in a double-blinded fashion according to random number sequences generated by an Internet site program (http://www.random.org/). The agents used for this study were prepared in a 2 ml syringe wrapped in aluminium foil by an investigator who was not involved in the anaesthesia process.

Subjects were not premedicated. Upon arrival at the operating theatre, subjects were monitored by pulse oximetry, capnography, non-invasive arterial pressure, and electrocardiography. Anaesthesia was induced by inhalation of 8% sevoflurane in oxygen via a face mask with monitoring of inhaled and exhaled sevoflurane concentrations. Induction quality was briefly evaluated according to a four-point scale: 1, crying, needs restraint; 2, moderate fear and reassured with difficulty; 3, slight fear but can be reassured easily; and 4, asleep or calm or awake and co-operative, accepting the mask.[5] Subjects presenting with a score of 1 were withdrawn from the study. After the loss of consciousness, sevoflurane was adjusted to end-tidal 3–3.5% and maintained for several minutes and an i.v. cannula was inserted. A laryngeal mask airway (LMA$^{TM}$, The Laryngeal Mask Company Ltd, UK) was inserted after adequate jaw relaxation was attained. LMA size, according to the manufacturer's guidelines, was size 2 for 10–20 kg body weight, size 2.5 for 20–30 kg, and size 3 for 30–50 kg. If LMA insertion failed after three attempts, tracheal intubation was performed and the subject was withdrawn from the study. After LMA insertion and before operation, the subjects received a caudal block with 1.2 ml kg$^{-1}$ of 0.5% lidocaine. Skin incision served as the test of adequate analgesia of the caudal block, and the block was deemed inadequate if heart rate increased >20% within 60 s of skin incision. Only subjects with an adequate caudal block were included in this study. During the operation, anaesthesia was maintained with sevoflurane 2–2.5% in ~50% oxygen with a total inflow of 2 litre min$^{-1}$. Spontaneous ventilation was maintained in all subjects.

About 10 min before completion of surgery, anaesthesia was maintained with 2% sevoflurane with a total inflow of 6 litre min$^{-1}$. At the completion of surgery, the concentration of oxygen was adjusted to 100% while anaesthesia was maintained. At the same time, subjects received propofol 1 mg kg$^{-1}$, fentanyl 1 μg kg$^{-1}$, or saline over 1 min according to the allocated group. The study drug wrapped in foil was injected through a three-way stopcock directly connected to an angiocatheter, so the attending anaesthesiologist and the investigator who collected the data remained blinded to the agent administered. After regular breathing with adequate tidal volume (>6 ml kg$^{-1}$) was confirmed, the LMA was removed under anaesthesia. Sevoflurane was discontinued immediately after removal, 100% oxygen via a face mask was given, and subjects were observed for at least 5 min for the management of possible respiratory complications such as upper airway obstruction, breath holding, or suspicious laryngospasm. When spontaneous breathing with airway patency without assistance was confirmed and complications were resolved, subjects were transferred to the post-anaesthesia care unit (PACU).

Upon arrival at the PACU, subjects were monitored and cared for by two nurses. Guardians were not allowed to stay in the PACU because of the policy of our institute. Three different investigators (one anaesthetist and two nurses) who were blinded to subject allocation evaluated EA and recovery. First, the anaesthetist assessed recovery of consciousness defined as crying or eye opening in response to verbal command or light touch every 5 min from the arrival at the PACU, and recorded the time taken to recover consciousness. The degree of agitation was evaluated and recorded upon awakening and every 5 min thereafter during the first 30 min, and the highest-recorded value was used for evaluation. The anaesthetist evaluated the incidence and severity of EA using the paediatric anaesthesia emergence delirium (PAED) scale (Table 1).[2 12] In addition, Aono's scale (1, calm; 2, easily consoled state; 3, moderate agitation; 4, severe agitation) and the five-step EA scale (1, obtunded with no response to stimulation; 2, asleep but responsive to movement or stimulation; 3, awake and responsive; 4, crying; 5, thrashing behaviour that requires restraint)[13 14] were used to assess EA by two

**Table 1** The PAED scale. The scores of individual items are summed to produce a total PAED score. The severity of EA increased proportional to the total score

| | Score |
|---|---|
| The child makes eye contact with the caregiver | 4=not at all |
| The child's actions are purposeful | 3=just a little |
| The children is aware of the surroundings | 2=quite a bit |
| | 1=very much |
| | 0=extremely |
| The child is restless | 0=not at all |
| The child is inconsolable | 1=just a little |
| | 2=quite a bit |
| | 3=very much |
| | 4=extremely |