Comparison of propofol and fentanyl for the prevention of emergence agitation in children after sevoflurane anesthesia

Bo Eun Moon

Department of Medicine

The Graduate School, Yonsei University

Comparison of propofol and fentanyl for the prevention of emergence agitation in children after sevoflurane anesthesia

Directed by Professor Jeong-Rim Lee

The Master's Thesis
submitted to the Department of Medicine
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the
degree of Master of Medical Science

Bo Eun Moon

June 2012

This certifies that the Master's Thesis
of Bo Eun Moon is approved.

Thesis Supervisor : Jeong-Rim Lee

Kyeong Tae Min

Seung Ho Choi

The Graduate School
Yonsei University

June 2012

ACKNOWLEDGEMENTS

This dissertation could not be fructified without the supports, advices, and encouragements of many people and colleagues. I would like to express my gratitude to those who have contributed to this work in various ways.

First of all, I would like to express sincere gratitude to my academic advisor, Prof. Jeong-Rim Lee, who has provided advices, supports, and encouragements over years. Next, I would like to thank the other members of my dissertation committee, Prof. Kyeong Tae Min and Prof. Seung Ho Choi.

Likewise, I would like to thank Prof. Min Soo Kim and Prof. Hyunzu Kim. They gave me a lot of help and advices throughout the study, especially in experimental techniques and analysis of the results.

I would like to extend my thanks to my residency colleagues, who supported me to concentrate all my effort on the study.

My family always gave me love, support and encouragement, and I would like to thank all of them.

<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Comparison of propofol and fentanyl for the prevention of emergence agitation in children after sevoflurane anesthesia

Bo Eun Moon

Department of Medicine

The Graduate School, Yonsei University

(Directed by Professor Jeong-Rim Lee)

Propofol and fentanyl can be administered at the end of anesthesia to prevent emergence agitation (EA), although the superior efficacy between these agents has not been determined. This study was conducted to compare the preventive effects of EA between propofol and fentanyl administered at the end of sevoflurane anesthesia under the identical clinical conditions.

Two hundred twenty-two children, 18ï 72 months of age, performed

inguinal hernia repair under sevoflurane anesthesia received intravenous propofol 1 mg/kg (group P), fentanyl 1 ㎍/kg (group F) or saline (group S) at the end of anesthesia according to the random allocation. The incidence and severity of EA was evaluated with pediatric anesthesia emergence delirium (PAED) scale and Aonoôs scale. Time to recovery and incidence of nausea/vomiting were assessed.

The mean PAED score was 4.3 in group P and 4.9 in group F (P = 0.682 between two groups), which were lower than 9.0 in group S (P < 0.001). The proportion of patients with Aonoôs scale Ó3 in group P (4.3%) and group F (12.1%) were comparable (adjusted P = 0.297) and lower than that of group S (38.6%) (adjusted P < 0.001). Nausea and vomiting was significantly more frequent in group F than in group P or group S (adjusted P = 0.003 and adjusted P < 0.001).

Small dose of propofol and fentanyl at the end of anesthesia comparably reduced EA. Propofol was better than fentanyl regarding low incidence of vomiting.

Key words: aonoôs scale, emergence agitation, fentanyl, nausea and vomiting, propofol, pediatric anesthesia emergence delirium scale, sevoflurane anesthesia

Comparison of propofol and fentanyl for the prevention of emergence agitation in children after sevoflurane anesthesia

Bo Eun Moon

Department of Medicine

The Graduate School, Yonsei University

(Directed by Professor Jeong-Rim Lee)

I. INTRODUCTION

Emergence agitation (EA) in children during the early stage after sevoflurane anesthesia is a common postoperative problem, with incidence ranging up to 80%.[1,2] It is characterized by behaviors that may include crying, disorientation, excitation, and delirium. Although EA is self-limiting and may not result in permanent sequelae, it should not be taken lightly as 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 prevent EA, such as administrating sedative medication before induction, a change in the maintenance technique of anesthesia, or pharmacological agent administration at the end of anesthesia.[2,5-7]

Among these strategies, the use of pharmacological agents at the end of anesthesia is thought to be the most convenient and easily applicable method in clinical situations since it does not rely on the nature of the anesthetic agents used during induction and maintenance or the duration of anesthesia.[2,8,9] In this perspective, low-dose of propofol (1 mg/kg) or fentanyl (1 μg/kg) has been shown to successfully reduce EA if administered at the end of anesthesia.[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 may influence different variables related to recovery and complications.[1,11] Therefore, we hypothesized that the efficacy of preventing EA and the effect on recovery profiles might be different between propofol and fentanyl under identical clinical conditions.

The purpose of this randomized double-blind study was to compare the preventive effect on EA between propofol and fentanyl administered at the

end of sevoflurane anesthesia in children undergoing inguinal hernia repair. In addition, characteristics of anesthesia recovery and incidence of adverse effects were also compared.

II. MATERIALS AND METHODS

1. Patient Selection

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 consents were obtained from the parents of all participants. Two hundred twenty-two children, 18-72 months of age, American Society of Anesthesiologists (ASA) class I or II, who were scheduled for ambulatory inguinal hernia repair under general sevoflurane anesthesia, were prospectively included in this study. Children with developmental delay, psychological or neurologic disorders, abnormal airway, reactive airway disease, or history of general anesthesia were excluded. All of the patients were made to fast at least 8 h, with an opportunity to drink clear fluids up to 4 h before the operation.

2. Study Design

The enrolled children were randomly allocated to one of 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 anesthesia process.

The children were not premedicated. Upon arrival at the operating room, patients were monitored by pulse oximetry, capnography, non-invasive arterial blood pressure, and electrocardiography. Anesthesia was induced by inhalation of 8% sevoflurane in oxygen via a face mask with the monitoring of inhaled and exhaled sevoflurane concentrations. During induction, induction quality was briefly evaluated according to a 4-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. Patients presenting with a score of 1 were withdrawn from the study.[5] After loss of consciousness, sevoflurane was adjusted to end-tidal 3-3.5% and maintained for several minutes and an intravenous cannula was inserted. A laryngeal mask airway (LMAÊ , The Laryngeal Mask Company Ltd, UK) was inserted after adequate jaw

relaxation was attained. The LMA size was determined by the manufacturerôs guidelines, which suggests; size 2 for 10-20 kg of body weight, size 2.5 for 20-30 kg and size 3 for 30-50 kg. If LMA insertion failed after three attempts, endotracheal intubation was performed and the patient was withdrawn from the study. After LMA insertion and before the operation, the patients received a caudal block with 1.2 ml/kg of 0.5% lidocaine. Skin incision served as the test of adequate analgesia of the caudal block, and the block was deemed inadequate if the patientôs heart rate increased at skin incision. Only the children with an adequate caudal block were finally included in this study. During the operation, anesthesia was maintained with sevoflurane 2-2.5% in approximately 50% oxygen with a total inflow of 2 L/min. Spontaneous ventilation was maintained in all patients.

About 10 minutes before completion of surgery, anesthesia was maintained with 2% sevoflurane with a total inflow of 6 L/min. At the completion of surgery, the concentration of oxygen was adjusted to 100% while anesthesia was maintained. At the same time, the patient received each study drug (propofol 1 mg/kg, fentanyl 1 ㎍/kg, or saline) over 1 min according to the allocated group. The study drug wrapped in aluminium foil was injected through a three-way stopcock directly connected to an angiocatheter so the attending anesthesiologist and the investigator who collected the data

remained blinded to the agent administered. After regular breathing with adequate tidal volume (> 6 ml/kg) was confirmed, the LMA was removed under anesthetic state and sevoflurane was discontinued immediately after removal; simultaneously, the patient received 100% oxygen via a face mask and was observed for at least five minutes for management of possible respiratory complications such as upper airway obstruction, breath holding, or suspicious laryngospasm. When spontaneous breathing with airway patency was confirmed without assistance and complications were resolved, the patient was transferred to the post-anesthesia care unit (PACU).

Upon arrival at the PACU, the patient was monitored and cared by two nurses. Guardians were not allowed to stay with the patients in the PACU because of the policy of our institute. Three different investigators (one anesthesiologist and two nurses) who were blinded to the allocation of the patient evaluated EA and recovery profiles. First, the anesthesiologist assessed the 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 from sevoflurane anesthesia. 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 anesthetist evaluated the incidence and severity of EA by using the Pediatric Anesthesia

Emergence Delirium (PAED) scale (Table 1).[2,12] In addition, Aonoôs scale (1 = calm; 2 = easily consoled state; 3 = moderate agitation; 4 = severe agitation) and the 5-step Emergence Agitation (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 behavior that requires restraint)[13,14] were also used to assess EA by two nurses independent of the anesthesiologist. Aonoôs scale scores Ó 3, or 5-step EA scale Ó 4 were considered as presence of EA.[2,12,14] If agitation of Aonoôs scale scores Ó 3 persisted for more than five minutes, intravenous propofol 1 mg/kg was used as rescue medication.

TABLE 1. The Pediatric Anesthesia Emergence Delirium (PAED) Scale

	score
The child makes eye contact with the caregiver	4 = not at all
The childôs 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

The scores of individual items were summed to produce a total Pediatric Anesthesia Emergence Delirium Scale. The severity of emergence agitation increased proportional to the total score.

When the children satisfied the following criteria: fully awake, stable vital signs, patent airway without support and oxygen saturation > 95% under breathing room air, they were transferred to the outpatient recovery room and stayed with their guardian. All patients were to remain in the outpatient recovery room for at least three hours before discharge according to the protocol of our institute. During the whole recovery period, the occurrence of nausea or vomiting was assessed and treated with ondansetron 0.1 mg/kg. The anesthesiologist who assessed PAED scale also recorded the duration of PACU stay, delayed discharge from the outpatient recovery room, adverse events such as somnolence, delayed voiding, and nausea or vomiting.

3. Statistical Analysis

Previous studies reported the prevalence of EA in the presence of effective prevention as approximately 10-20%. According to power analysis, a sample size of 59 patients per group would have 80% power to detect a difference of 20% at a significance level of 5%, based on the assumption that the prevalence of EA in the more effective of the two drugs would be 10%. Finally, 74 patients were required in each group when considering a drop-out rate of 20%. Continuous variables were reported as mean (SD) and were analyzed using the one-way analysis of variance (ANOVA) test with

post hoc multiple comparisons. Categorical data such as the incidence of EA were reported as numbers and percentages and were analyzed using the Chi-square test or Fisher exact test with Bonferroni correction to calculate adjusted P-values.

III. RESULTS

Of 265 patients who were initially assessed, 205 patients successfully completed the study (Fig. 1). There were no significant differences in age, weight, gender or duration of anesthesia among the three groups (Table 2).

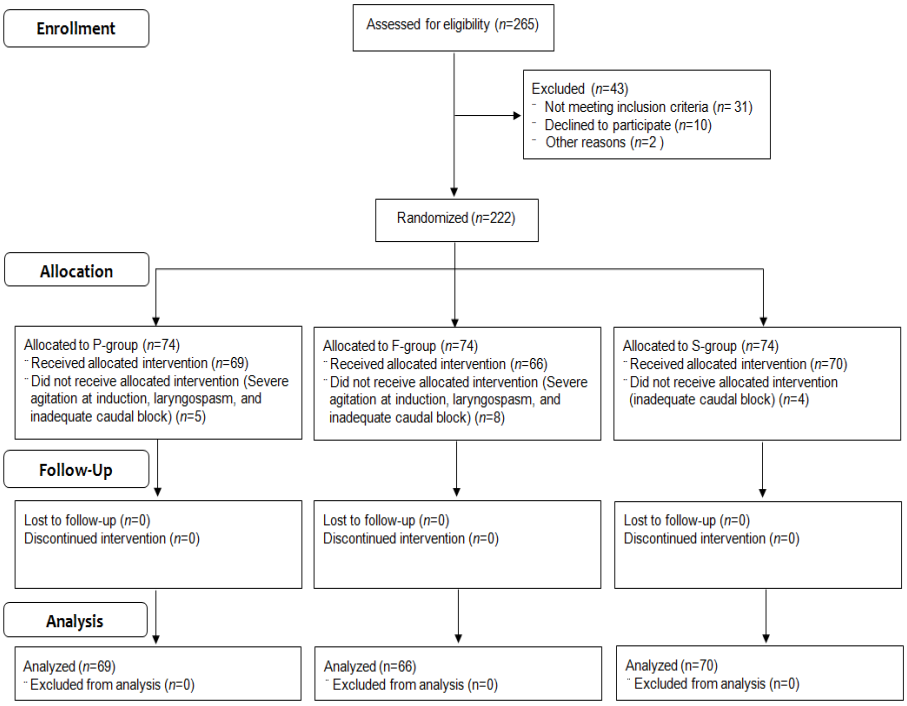

FIGURE 1. Consort flow diagram. P, propofol; F, fentanyl; S, saline.

TABLE 2. Patient characteristics and duration of anesthesia

	Group P (n = 69)	Group F (n = 66)	Group S (n = 70)	P-value
Age (yr)	3.6(1.4)	3.7(1.4)	3.8(1.3)	0.556
Weight (kg)	15.7(3.3)	15.9(3.6)	15.6(3.0)	0.926
Gender (M/F)	52(75)/17 (25)	38(58)/28 (42)	48(69)/22 (31)	0.085
Duration of anesthesia (min)	63.5(14.8)	61.6(11.9)	62.1 (11.9)	0.683

Data are presented as mean (SD) for age, weight, duration of anesthesia, and number of patients (%) per gender.
P, propofol; F, fentanyl; S, saline.

The mean values of PAED score in group P [4.3 (3.2)] and group F [4.9 (3.5)] were significantly lower than the value of group S [9.0 (5.3)] ($P < 0.001$), and there was no significant difference between group P and group F ($P = 0.682$). (Fig. 2) Using Aonoôs scale, the incidences of EA in group P (4.3%) and group F (12.1%) were comparable (adjusted $P = 0.297$) and significantly lower than that of group S (38.6%) (adjusted $P < 0.001$). The 5-step EAS also showed that the incidences of EA between group P (33.3%) and group F (27.3%) were similar (adjusted $P > 0.999$) and were significantly lower than that of group S (74.3%) (adjusted $P < 0.001$). The score distributions of Aonoôs scale and the five-step EA scale in each group are shown in Fig. 3.

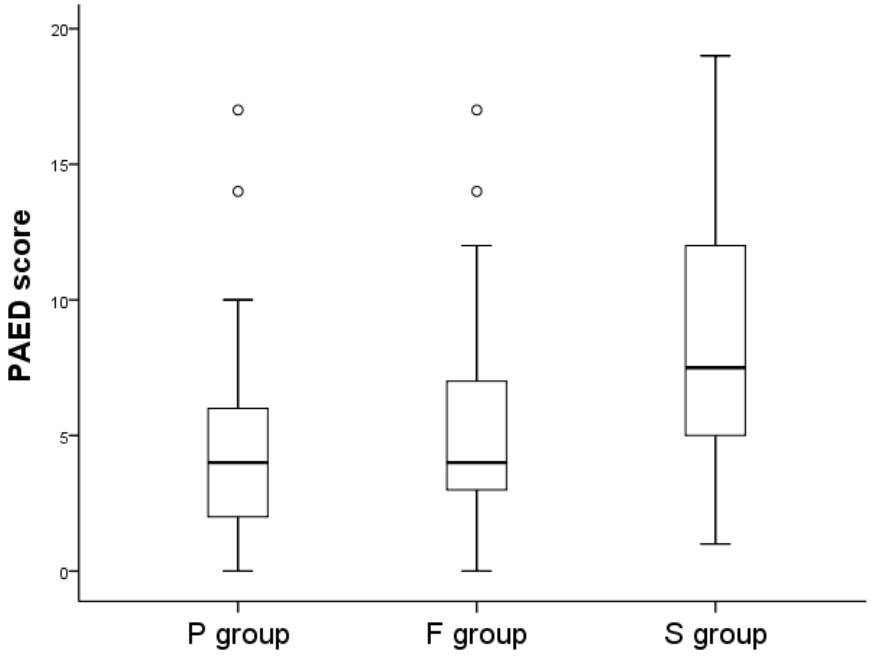

FIGURE 2. The distributions of PAED score. PAED, pediatric anesthesia emergence delirium; P, propofol; F, fentanyl; S, saline. The box contains the median 50 % of the data. The upper edge of the box indicates the 75th percentile of the data set, and the lower edge indicates the 25th percentile. The range of the middle two quartiles is known as the inter-quartile range. The ends of the vertical lines indicate the minimum and maximum data values, unless outliers are present in which case the vertical lines extend to a maximum of 1.5 times the inter-quartile range. Any data not included between the vertical lines should be plotted as an outlier with a circle.

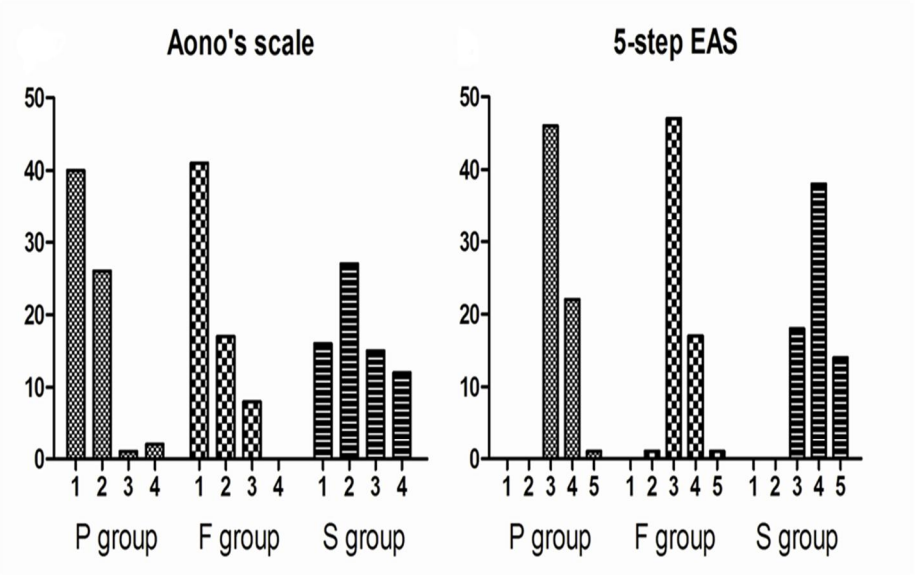

Figure 3. The distributions of scores according to Aonoôs scale and 5-step EAS. EAS, emergence agitation scale; P, propofol; F, fentanyl; S, saline. Aonoôs scale (1 = calm, 2 = easily consoled state, 3 = moderate agitation, 4 = severe agitation) and 5-step Emergence Agitation scale (1 = obtunded with no response to stimulation, 2 = asleep but responsive to movement or stimulation, 3 = awake and responsive, 4 = crying, 5 = thrashing behavior that requires restraint).

The time for awakening and duration of stay in the PACU are shown in Table 3. The time for awakening of group P and group F was comparable (P = 0.394) and significantly longer than that of the group S (P < 0.001), but only the children in group F stayed longer in the PACU than the children in group S (P < 0.001). All children were discharged after 3 hr admission in the outpatient recovery room.

TABLE 3. Comparison of time for awakening and PACU duration among the three groups

	Group P (n = 69)	Group F (n = 66)	Group S (n = 70)
Time to awakening (min)	27.7 (8.5)*	30.5 (12.3)*	17.6 (11.9)*
PACU duration (min)*	37.1(8.7)Àÿ	40.4 (11.5)¶,ÿ	33.4(10.3)¶,À

PACU, post-anesthesia care unit; P, propofol; F, fentanyl; S, saline; Time for awakening, time period from administration of study agent to emergence; PACU duration, time period from admission to discharge of PACU.

*The time for awakening of both the P and F groups was comparable (P = 0.394) and significantly longer than that of the S group (P < 0.001).

¶The PACU duration of the F group was significantly longer than that of the S group (P < 0.001).

ÀThere were no significant differences of the PACU duration between the P and S groups (P = 0.108).

ÿThere were no significant differences of the PACU duration between the P and F groups (P = 0.194).

The incidences of complications are shown in Table 4. Two children in group P and four children in group F required jaw thrust for maintaining upper airway patency, and two children (one from each group P and F) presented with suspicious laryngospasm, which was resolved by continuous positive pressure ventilation. Propofol as rescue medication of EA was more frequently used in group S compared to the other two groups (adjusted P <

0.001). The incidence of nausea or vomiting was significantly higher in group F than in group P and group S, with 24.3% of children in group F requiring antiemetic medication (adjusted P = 0.003 and adjusted P < 0.001).

TABLE 4. Incidence of complications and use of rescue medications during the postoperative period

	Group P (n = 69)	Group F (n = 66)	Group S (n = 70)
Airway obstruction	2 (2.9)	4 (6.0)	0 (0)
Laryngospasm	1 (1)	1 (2)	0 (0)
Nausea or vomiting	4 (5.8)[À]	17 (25.8)[À]	2 (2.9)[À]
Delayed voiding	0	0	1 (1.4)
Rescue medication			
Propofol use	1 (1.4)[¶]	0 (0)[¶]	17 (24.3)[¶]
Ondansetron use	4 (5.8)[À]	17 (25.8)[À]	2 (2.9)[À]

Data are presented as number of patients.

There were no significant differences in incidences of airway obstruction, laryngospasm and delayed voiding among three groups.

[À]The incidence of nausea or vomiting and the use of ondansetron in group F were significantly higher than those in group P and group S (adjusted P = 0.003 and adjusted P < 0.001).

[¶]The incidence of rescue propofol use in group S was significantly higher than those in the other two groups (adjusted P < 0.001).

P, propofol; F, fentanyl; S, saline.

IV. DISCUSSION

This study revealed that the administration of either propofol 1 mg/kg or fentanyl 1 ㎍/kg at the end of sevoflurane anesthesia had a comparable effect on reducing EA compared to saline, and the patients who had received propofol had less incidence of vomiting compared to those who received fentanyl.

Various agents have been investigated with the aim of reducing the occurrence of EA, with variable outcomes. A recent meta-analysis demonstrated that propofol, fentanyl, Ŭ$_2$-adrenergic receptor agonist and ketamine have a prophylactic effect.[8] However, the relative efficacy of one drug over others was not clear. Particularly regarding the drugs administered at the end of anesthesia, only two recent studies were conducted with the aim of comparing two or three drugs. Chen J et al. compared the concurrent use of midazolam, propofol, or ketamine with fentanyl just after discontinuing sevoflurane anesthesia in children who underwent cataract surgery and showed that propofol or midazolam in combination with fentanyl were both effective in reducing EA.[15] However, the effect of propofol or midazolam on EA is additive or synergistic with fentanyl because fentanyl is thought to prevent EA independent of its analgesic effect.[10,16] Kim et al. also compared propofol and midazolam in patients

undergoing strabismus surgery. They similarly found that propofol and midazolam decreased the incidence of EA by about 40%, but the final incidence of EA in the prophylactic groups was 40%, which is higher than 15ï 20% of Chenôs study.[17] Furthermore, both of these studies compared the effect of propofol and midazolam on EA only in patients undergoing ophthalmologic surgery. More comparative studies need to be conducted with additional combinations of drugs and in diverse clinical situations. Hence, we compared propofol and fentanyl, which are most commonly studied in the field of EA, in patients undergoing inguinal hernia repair.

Propofol is frequently used in children for induction and maintenance of general anesthesia.[18,19] Because of the pharmacokinetic properties of propofol, anesthesia maintenance rather than induction provides a smoother recovery profile in children compared with that of sevoflurane.[6,8,20] However, propofol-based anesthesia requires sophisticated infusion pumps with software algorithms for target controlled infusion (TCI), and it is difficult to monitor continuous administration of intravenous agents in patients.[21] Moreover, induction is commonly achieved without intravascular assess in pediatric anesthesia.[22] Fortunately, several studies have suggested that a single administration of 1 mg/kg of propofol at the discontinuation of anesthesia is effective in reducing EA without delay of discharge from the PACU in children receiving sevoflurane for induction and maintenance of

anesthesia.[1 2] In the above studies, children underwent strabismus surgery or MRI scanning. Fentanyl provides another option to be provided at discontinuation of anesthesia. One previous study evaluated the effect of fentanyl on EA with a dose smaller than that used for induction (1 μg/kg) in children after sevoflurane anesthesia 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] Therefore, although the analgesic properties of fentanyl play a role in the prevention of EA, supplementation of sevoflurane anesthesia with a small dose of fentanyl can also be considered even in the absence of substantial postoperative pain. The present study conducted for comparing the efficacies of these two drugs in preventing EA under the same clinical condition which kind of study have not been previously performed. As our result, there were no differences in efficacy between propofol and fentanyl with regard to EA prevention after sevoflurane anesthesia in identical clinical conditions.

Drug selection for a specific purpose is based not only on efficacy, but also on possible complications or side effects. We found that the incidence of nausea or vomiting of the fentanyl group was about 26%, which was much higher than that of group P, despite the comparable efficacies of the two drugs in preventing EA. In a previous study conducted to estimate the mean effective dose of fentanyl required for reduction of EA, postoperative

vomiting also occurred in 75% of patients.[23] Although the incidence of postoperative vomiting of the present study did not lead to delayed discharge because all patients remained in the outpatient recovery room for at least three hours according to the policy of our institute, the risk of emesis should be considered when fentanyl is used for prophylaxis of EA. Another concern for using propofol and fentanyl at the end of anesthesia is the possibility of delayed emergence. Both propofol and fentanyl delayed the time taken for awakening more than 10 min than placebo. However, the children in group P and group F were transferred to the outpatient recovery room from the PACU after 10 min upon their awakening whereas the children in group S took more than 15 min for discharge from the PACU. Therefore, slightly delayed awakening after propofol or fentanyl administration may not lead to clinically significant delayed discharge from the PACU.

Although EA after sevoflurane anesthesia can occur in pain-free patients, postoperative pain is also a well-known cause of postoperative distress and agitation in children. In consequence, the effects of anesthetic techniques on EA should ideally be investigated in the absence of postsurgical pain.[10,24,25] In our study, a caudal block for postoperative analgesia could exclude any contribution of postoperative pain to the occurrence of EA. Some previous studies proposed that a preoperative caudal block in children following

sevoflurane anesthesia is effective in preventing EA, and that the incidence of EA in patients with caudal block varied from 4.5 % to 26 %:[22,24] The lower incidence of EA in previous studies than that of group S in the present study might be due to the use of midazolam as premedication and parental presence in the PACU which were not used in our study.[22,24]

A reliable scale or scoring system to assess whether EA is present should be used for the objective comparison of two drugs. However, the incidence of EA varies widely depending on the evaluation tools, and each scale has limitations to assess EA.[8,14] Thus, we used the three commonly used scales, and propofol and fentanyl showed comparable effectiveness on prevention of EA by all three scales.

We note that general application of our results requires several considerations. First, the incidence of EA is different depending on the type of surgery and is known to be higher in otorhinolaryngologic or ophthalmologic procedures,[26] suggesting that the shown efficacy of propofol and fentanyl in the present study may be modified in different types of surgical procedures. Second, the 3 hr stay at the outpatient recovery room, which is the routine protocol of our institute, may have failed to discriminate the difference of discharge time among the three groups.

V. CONCLUSION

In summary, the use of either propofol or fentanyl at the discontinuation of sevoflurane anesthesia was effective to reduce the incidence of EA, and propofol may be preferable regarding the lower incidence of vomiting.

REFERENCES

1. Abu-Shahwan I. Effect of propofol on emergence behavior in children after sevoflurane general anesthesia. Paediatr Anaesth 2008;18:55-9.
2. Aouad MT, Yazbeck-Karam VG, Nasr VG, El-Khatib MF, Kanazi GE, Bleik JH. A single dose of propofol at the end of surgery for the prevention of emergence agitation in children undergoing strabismus surgery during sevoflurane anesthesia. Anesthesiology 2007;107:733-8.
3. Kuratani N, Oi Y. Greater incidence of emergence agitation in children after sevoflurane anesthesia as compared with halothane: a meta-analysis of randomized controlled trials. Anesthesiology 2008;109:225-32.
4. Galinkin JL, Fazi LM, Cuy RM, et al. Use of intranasal fentanyl in children undergoing myringotomy and tube placement during halothane and sevoflurane anesthesia. Anesthesiology 2000;93:1378-83.
5. Koner O, Ture H, Mercan A, Menda F, Sozubir S. Effects of hydroxyzinemidazolam premedication on sevoflurane-induced paediatric emergence agitation: a prospective randomised clinical trial. Eur J Anaesthesiol 2011;28:640-5.
6. Uezono S, Goto T, Terui K, et al. Emergence agitation after sevoflurane versus propofol in pediatric patients. Anesth Analg 2000; 91: 563-6.
7. Kim JY, Chang YJ, Lee JY, Park HY, Kwak HJ. Post-induction alfentanil reduces sevoflurane-associated emergence agitation in children undergoing an adenotonsillectomy. Acta Anaesthesiol Scand 2009;53:678-81.
8. Dahmani S, Stany I, Brasher C, et al. Pharmacological prevention of

sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies. Br J Anaesth 2010;104:216-23.

9. Abu-Shahwan I, Chowdary K. Ketamine is effective in decreasing the incidence of emergence agitation in children undergoing dental repair under sevoflurane general anesthesia. Paediatr Anaesth 2007;17:846-50.
10. Cravero JP, Beach M, Thyr B, Whalen K. The effect of small dose fentanyl on the emergence characteristics of pediatric patients after sevoflurane anesthesia without surgery. Anesth Analg 2003;97:364-7.
11. Hung WT, Chen CC, Liou CM, Tsai WY. The effects of low-dose fentanyl on emergence agitation and quality of life in patients with moderate developmental disabilities. J Clin Anesth 2005;17:494-8.
12. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology 2004;100:1138-45.
13. Cravero J, Surgenor S, Whalen K. Emergence agitation in paediatric patients after sevoflurane anaesthesia and no surgery: a comparison with halothane. Paediatr Anaesth 2000;10:419-24.
14. Bajwa SA, Costi D, Cyna AM. A comparison of emergence delirium scales following general anesthesia in children. Paediatr Anaesth 2010;20:704-11.
15. Chen J, Li W, Hu X, Wang D. Emergence agitation after cataract surgery in children: a comparison of midazolam, propofol and ketamine. Paediatr Anaesth 2010;20:873-9.
16. Cohen IT, Finkel JC, Hannallah RS, Hummer KA, Patel KM. The effect of fentanyl on the emergence characteristics after desflurane or sevoflurane anesthesia in children. Anesth Analg 2002;94:1178-81.
17. Kim YH, Yoon SZ, Lim HJ, Yoon SM. Prophylactic use of midazolam or propofol at the end of surgery may reduce the incidence of emergence agitation after sevoflurane anaesthesia. Anaesth Intensive Care 2011;39:904-8.

18. Varveris DA, Morton NS. Target controlled infusion of propofol for induction and maintenance of anaesthesia using the paedfusor: an open pilot study. Paediatr Anaesth 2002;12:589-93.
19. Roberts FL, Dixon J, Lewis GT, Tackley RM, Prys-Roberts C. Induction and maintenance of propofol anaesthesia. A manual infusion scheme. Anaesthesia 1988;43 Suppl:14-7.
20. Cohen IT, Drewsen S, Hannallah RS. Propofol or midazolam do not reduce the incidence of emergence agitation associated with desflurane anaesthesia in children undergoing adenotonsillectomy. Paediatr Anaesth 2002;12:604-9.
21. Mani V, Morton NS. Overview of total intravenous anesthesia in children. Paediatr Anaesth 2010;20:211-22.
22. Weldon BC, Bell M, Craddock T. The effect of caudal analgesia on emergence agitation in children after sevoflurane versus halothane anesthesia. Anesth Analg 2004;98:321-6.
23. Cohen IT, Hannallah RS, Hummer KA. The incidence of emergence agitation associated with desflurane anesthesia in children is reduced by fentanyl. Anesth Analg 2001;93:88-91.
24. Aouad MT, Kanazi GE, Siddik-Sayyid SM, Gerges FJ, Rizk LB, Baraka AS. Preoperative caudal block prevents emergence agitation in children following sevoflurane anesthesia. Acta Anaesthesiol Scand 2005;49:300-4.
25. Yasui Y, Masaki E, Kato F. Sevoflurane directly excites locus coeruleus neurons of rats Anesthesiology 2007;107:992-1002.
26. Voepel-Lewis T, Malviya S, Tait AR. A prospective cohort study of emergence agitation in the pediatric postanesthesia care unit. Anesth Analg 2003;96:1625-30.

ABSTRACT (IN KOREAN)

소아 환자에서 세보플루란 마취 후 발생하는 각성시 흥분을 줄이기 위한 약제로서 프로포폴과 펜타닐의 효과 비교

<지도교수 이정림>

연세대학교 대학원 의학과

문 보 은

세보플루란은 현재 임상에서 사용하는 마취제 중 빠른 흡수와 빠른 배출이 가능하여 소아환자의 마취 유도 및 유지에 유용하게 사용되고 있다. 하지만 많은 수의 환자에서 회복 중 ó각성시 흥분ô이라 불리는 증상이 발생하여 문제가 되고 있다. 이러한 각성시 흥분 증상은 프로포폴과 펜타닐을 수술 종료 직전에 투여하였을 때 감소시킬 수 있다. 하지만 어떤 약제가 더 효과적으로 감소시키는지에 대한 비교 연구는 아직 없다. 따라서 본 연구는 같은 조건에서 프로포폴과 펜타닐을 투여하였을 경우 두 약제간의 각성 시 흥분 증상에 대한 예방 효과를 비교 하고자 하였다.

만 18개월-72개월의 서혜부 탈장 교정수술을 받는 환자 222명을

대상으로 무작위로 프로포폴 투여군 (P군), 펜타닐 투여군(F군), 생리 식염수 투여군(S군)으로 분류하여 세보플루란 마취 후 회복실에서 PAED 등급법과 Aono 등급법을 이용하여 각성 시 흥분의 발생여부를 측정하고 마취에서 회복되기까지의 시간 및 오심, 구토 등의 부작용 발생여부를 측정하였다.

평균 PAED 점수는 P 그룹에선 4.3점, F그룹에선 4.9점으로 두 그룹간에 의미 있는 차이가 없었으나 S그룹에서는 9점으로 ($P < 0.001$), 약제를 투여한 경우 각성 시 흥분 증상의 발생률이 낮았다. 또한 Aono 등급법 3등급 이상인 경우 각성 시 흥분이 발생했다고 판단하는데 P그룹에서는 4.3%, F그룹에서는 12.1%로 ($P = 0.297$) 두 군간에 발생률에는 큰 차이가 없었으나 S그룹과 비교 시 38.6%로 ($P < 0.001$) 약제를 투여한 군에 비해 발생률이 의미 있게 증가되었음을 볼 수 있었다. 오심, 구토 등의 부작용은 F그룹이 P그룹($P = 0.003$)과 S그룹($P < 0.001$)에 비해 의미 있게 증가되었음을 볼 수 있었다.

본 연구를 통해 프로포폴과 펜타닐 모두 수술 종료 직전에 소량 투여하는 것이 각성 시 흥분을 줄이는데 효과적이지만 프로포폴이 오심, 구토 등의 부작용 발생이 더 적으므로 임상에서 효과적으로 쓰일 수 있음을 알 수 있다.

핵심되는 말: 각성시 흥분, 프로포폴, 펜타닐, 세보플루란 마취, Aono 등급법, PAED 등급법, 오심, 구토