

## Sevoflurane versus propofol in the induction and maintenance of anaesthesia in children with laryngeal mask airway

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### Abstract

**Objective:** To compare effectiveness of inhalation sevoflurane and intravenous (IV) propofol anaesthesia with the laryngeal mask airway (LMA) in children undergoing surgeries below umbilicus.

**Method:** Sixty premedicated children 3-12 years old with the American Society of Anaesthesiologists physical status of I to II were enrolled and received either induction with sevoflurane 7% by face mask and maintained with a 50% oxygen and 50% nitrous oxide mixture followed by 1.7% sevoflurane or induction with 3 mg/kg propofol IV followed by infusion of 170µg/kg/min with LMA. Demographic data, induction time, number of attempts, LMA insertion, removal and recovery times, haemodynamic parameters, complications, Aldrete score and child's behaviour score were recorded.

**Results:** Demographic data and induction time were similar for the 2 treatment groups. LMA insertion was successful at the first attempt in 93% with sevoflurane and 83% with propofol. LMA insertion, removal and recovery times were significantly longer in the propofol group (1.56±0.22, 5.89±1.23, 12.3±3.09 minutes respectively) than in the sevoflurane group (1.26±0.36, 2.76±0.51, 5.16±1.6 minutes respectively) (P<0.0001). Perioperative minor complications were comparable. Recovery milestones including Aldrete score were significantly higher in group S (9.03) than in group P (7.8) at 5 minutes (P<0.05) and comparable at 15 and 30 minutes. There was a greater incidence of excitatory phenomena with sevoflurane compared with propofol which was statistically significant (P<0.05). Haemodynamics were comparable in both groups.

**Conclusions:** Sevoflurane provided shorter LMA insertion, removal and recovery times than IV propofol in children undergoing minor surgeries below umbilicus with comparable perioperative complications. Agitation was significantly more with sevoflurane.

(Key words: Sevoflurane; laryngeal mask airway; propofol; paediatric)

### Introduction

In paediatric anaesthesia laryngeal mask airway (LMA) has gained widespread acceptance as it provides an effective bridge between face mask and endotracheal tube, thereby providing effective (spontaneous or controlled) ventilation<sup>1</sup>. It is a simple, well tolerated, safe, reusable, cost effective method for airway management in both neonatal and paediatric patients<sup>2,3</sup>. It minimizes stress response and airway resistance<sup>4</sup>.

Satisfactory insertion of LMA after induction of anaesthesia [commencement of giving drugs either intravenous (IV) or inhalational to loss of eyelash reflex] requires sufficient depth of anaesthesia. Various studies have been carried out to find the ideal induction agent for LMA insertion<sup>5,6</sup>. Inhalation induction remains a widely used technique in paediatric anaesthesia<sup>7</sup>. Sevoflurane is a recently introduced halogenated volatile anaesthetic agent. It is an attractive alternative to the currently available anaesthetics and has replaced halothane for inhaled anaesthetic induction in needle phobic paediatric patients<sup>8</sup>. Its low blood gas solubility, non pungent odour and lack of irritation to the airway passages makes it a very useful anaesthetic for rapid induction and recovery from anaesthesia<sup>9,10</sup>. Ability to induce and maintain anaesthesia with one drug, better conditions for LMA insertion, an ability to induce anaesthesia without IV access, thereby facilitating patient turnover in busy ambulatory settings are other advantages<sup>9,10</sup>. It has disadvantages such as more frequent incidence of postoperative nausea and vomiting, agitation and increased pollution of the

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operating room with anaesthetics when compared with IV propofol<sup>11</sup>.

Propofol has replaced IV sodium thiopental and is the currently used IV agent of choice for induction and maintenance in outpatient, short surgical procedures because of its favourable recovery profile and low incidence of side effects like pain on injection and greater respiratory depression<sup>12,13</sup>. Propofol is in the essential drug list of India, while sevoflurane is not. Both agents are available in tertiary care hospitals. Propofol costs 160-200 Indian rupees per hour, while sevoflurane costs 300-350 Indian rupees per hour as we have to use high flow with Jackson Rees system and we do not have circle absorber for paediatric patients. The cost of sevoflurane can be reduced with circle absorber. To deliver sevoflurane we need to have a special vaporizer. To our knowledge there have been few studies comparing the clinical efficacy of sevoflurane and propofol in children with LMA<sup>5,14</sup>. Outcome assessment cannot be blinded as one drug is given IV and the other is inhaled. We hypothesized sevoflurane would provide better anaesthesia and a shorter recovery time.

## Objectives

This randomized prospective study was designed to compare the effectiveness of propofol and sevoflurane anaesthesia with LMA for children undergoing minor surgeries below umbilicus.

## Method

*Sample size calculation:* Power analysis was performed to compare the effect of sevoflurane with propofol on the basis of LMA insertion, removal and recovery times. This analysis was based on two samples with statistical significance of 0.05 and 80% power. The sample size required to detect the standard difference of 0.81 are approximately 62 (31 in each group). Thus the power analysis indicated that the minimum number of patients in each group should be 30.

Sixty children aged 3-12 years with American Society of Anaesthesiologists (ASA) physical status of class I – II scheduled for minor surgery below the umbilicus participated in this randomized, prospective study approved by the Institute of Kidney Diseases and Research Centre (IKDRC) and Institute of Transplantation Sciences (ITS) Review Board. Informed written consent was obtained from all parents.

Exclusion criteria included ASA III – IV, patients with oropharyngeal pathology, at risk of aspiration or hypersensitivity to halogenated anaesthetic agents or propofol.

The children fasted from solids for 6 hours and from clear liquids for 2 hours before anaesthesia. Preoperative anxiety was reduced with oral midazolam 0.5mg/kg one hour before induction. Standard monitoring like electrocardiogram, pulse oximeter, capnograph and noninvasive blood pressure were applied and baseline vital parameters were recorded. After establishing an IV line, injection glycopyrrolate 4µg/kg and injection fentanyl 2µg/kg IV 10 minutes prior to induction were given. Then children were divided randomly into 2 groups to receive either propofol or sevoflurane. Children in propofol group (group P) received induction with 3mg/kg propofol IV over 30 seconds. Lidocaine 1% 10mg was mixed with bolus dose of propofol. During induction when child moved additional boluses of 1mg/kg of propofol were given. Children in sevoflurane group (group S) had inhalational induction with sevoflurane 7% in nitrous oxide 50% and oxygen 50% on face mask at a total gas flow of 6 litres per minute. The sevoflurane concentration was increased to 1% when movement occurred. The induction time was noted from the start of drug administration to the loss of eyelash reflex. The LMA was inserted when the jaw was relaxed and the eyelash reflex was absent. The insertion and fixation technique, size selection and cuff volume were according to manufacturer's instructions. LMA insertion time (start of induction to successful placement of LMA) was noted. Ease of insertion, coughing, gagging, laryngospasm, airway obstruction and patient movement were noted. Successful placement of LMA, judged by capnography, chest wall movement and number of attempts, were noted. A failed attempt was defined as removal of the device from the mouth. Anaesthesia was maintained with 50% oxygen and 50% nitrous oxide, 6 L/min flow rate and in group S, 1.7% sevoflurane and in group P, propofol infusion of 170µg/kg/min with spontaneous breathing. Injection fentanyl 1µg/kg was repeated if surgery lasted for more than 60 minutes. During LMA insertion episodes of gastric distention, regurgitation, aspiration, bronchospasm and apnoea were noted. Vital parameters were recorded at baseline, at induction, after insertion of LMA, at 2, 5, 10, 15 minutes and then every 15 minutes till complete recovery from anaesthesia. At the end of the procedure, the infusion of propofol or sevoflurane was discontinued and 100% oxygen was given. Total duration of surgery (incision to dressing) and

duration of anaesthesia (start of anaesthesia until removal of LMA) were noted. Patients were observed for recovery and recovery time (time from completion of surgery to achievement of Aldrete score of 9) was noted. LMA was removed when the patient was fully awake. LMA removal time (time from discontinuation of anaesthesia to LMA removal) was noted. LMA was checked for presence of blood or foreign material, displacement from pharynx, gastric distention and persistent leak. Fall of oxygen saturation <90% any time during anaesthesia was also documented. Postoperative complications like coughing, laryngospasm, sore throat, nausea and vomiting and excitatory phenomena (agitation) were noted. Patients were transferred to recovery room when they had a patent airway and normal oxygen saturation without need for mandibular support. Hudson oxygen mask was applied. Before start of procedure paracetamol suppository (20-30mg/kg) was inserted for postoperative analgesia. Recovery

was assessed with the Aldrete score at 5, 15 and 30 minutes following LMA removal.

*Statistical analysis:* Statistical analysis was performed using Statistical Package of Social Sciences (SPSS) version 12. Continuous data are described as mean  $\pm$  SD (standard deviation) and categorical variables are given as number (%). Continuous variables were compared using independent two sample t-test and Mann-Whitney U-test as appropriate. Categorical variables were compared using Chi-square test and Fisher exact test. P-values <0.05 were considered to be statistically significant.

## Results

Demographic data, duration of surgery and anaesthesia, type of surgery and induction time performed were similar for the two treatment groups (table 1).

**Table 1**

***Demographic data, duration of surgery & anaesthesia, induction time & type of surgery for the treatment groups***

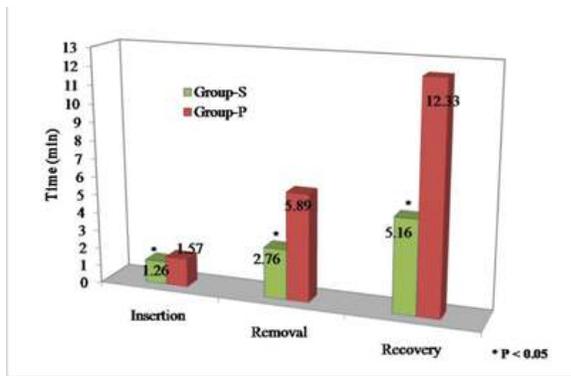
	<b>Group-P</b>	<b>Group-S</b>	<b>P-value</b>
Age (years)	5.25 $\pm$ 2.63	5.38 $\pm$ 2.46	0.841
Gender (M : F)	25:5	20:10	0.136
Weight (kg)	14.96 $\pm$ 4.7	15.43 $\pm$ 4.12	0.685
Total surgery time (minutes)	71.16 $\pm$ 17.98	67 $\pm$ 13.8	0.318
Total anaesthesia time (minutes)	76 $\pm$ 17.87	72.76 $\pm$ 13.53	0.431
Induction time (seconds)	45.77	45.57	
<i>Types of Surgery</i>			
Ureteroscopic lithotripsy (URS)	10	17	0.069
Posterior urethral valve fulguration	08	04	0.197
Herniotomy	02	01	0.554
Percutaneous cystolithotripsy (PCCL)	03	03	--
Others	07	05	0.519

\* Values are expressed as mean  $\pm$  SD

LMA insertion was successful in all enrolled children and adequate ventilation was achieved in all. It was successful at the first attempt in 28/30 (93%) with sevoflurane and 25/30 (83%) with propofol. The LMA insertion, removal and recovery times were significantly longer in the propofol group (1.56 $\pm$  0.22, 5.89 $\pm$ 1.23, 12.3 $\pm$ 3.09 minutes respectively) than in the sevoflurane group (1.26 $\pm$ 0.36, 2.76 $\pm$ 0.51, 5.16 $\pm$ 1.6 minutes respectively) (P<0.0001) (Figure 1).

During LMA insertion no episodes of gastric distention, regurgitation, aspiration or bronchospasm occurred. Apnoea occurred in both groups which were comparable. Recovery milestones, including

Aldrete score, were higher in group S (9.3) than group P (7.5) at 5 minutes which was statistically significant suggesting delayed recovery in group P and comparable at 15 and 30 minutes (table 2).



**Figure 1: LMA insertion, removal and recovery times in the propofol and sevoflurane groups**

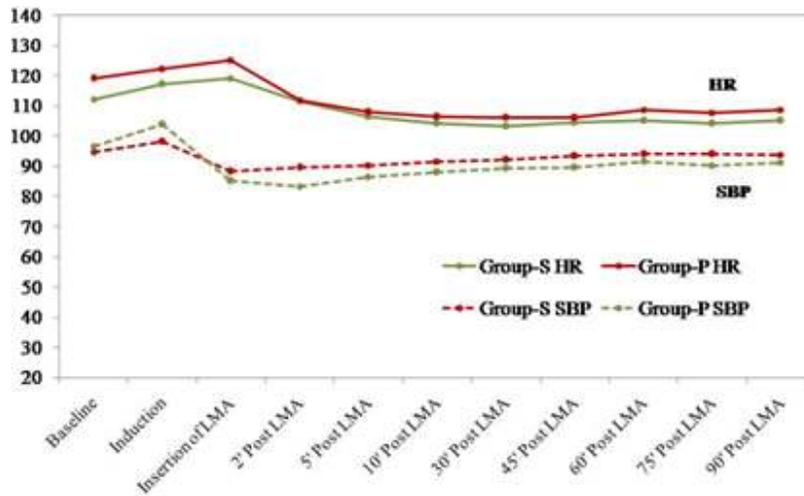
During maintenance, four patients in group P moved, which was statistically insignificant. During recovery, child's behavioural score was significant as propofol group patients were asleep in the immediate postoperative period while 13% children in sevoflurane group were agitated. Thus, there was a significantly greater incidence of excitatory phenomenon with sevoflurane compared with propofol (table 2). Postoperative problems did not differ between groups.

**Table 2**  
**Side effects during induction, maintenance & recovery score for the two treatment groups**

	Group-P (n=30)	Group-S (n=30)	P-value
<b>Induction period</b>			
Coughing	0 (0%)	1 (3.33%)	0.313
Laryngospasm	0 (0%)	0 (0%)	-
Apnea	5 (16.6%)	2 (6.66%)	0.228
Patients movement	5 (16.6%)	1 (3.33%)	0.085
vomiting	0 (0%)	0 (0%)	-
<b>Maintenance period</b>			
LMA displacement	0 (0%)	0 (0%)	-
Gastric distention	0 (0%)	0 (0%)	-
Persistent leak	0 (0%)	0 (0%)	-
<b>Recovery Period</b>			
Coughing	0 (0%)	0 (0%)	-
Laryngospasm	0 (0%)	2 (6.66%)	0.150
Blood on LMA	3 (10%)	2 (6.66%)	0.640
Nausea/Vomiting	0 (0%)	2 (6.66%)	0.150
Agitation	0 (0%)	4 (13.3%)	<b>0.038</b>
Desaturation	0 (0%)	0 (0%)	-
<b>Aldrete score</b>			
	<b>Group-P</b>	<b>Group-S</b>	<b>P-value</b>
5 min	7.5 ± 0.51	9.26 ± 0.52	<b>&lt; 0.0001</b>
15 min	9.56 ± 0.85	9.57 ± 0.72	0.961
30 min	10.57 ± 0.85	10.43 ± 0.82	0.518

Peri-operative systolic arterial blood pressure (SAP) and heart rate (HR) were similar for each group during induction and maintenance of anaesthesia

except that the fall in systolic blood pressure was more at 2 minutes post LMA insertion in propofol group which is statistically insignificant (figure 2).



HR- Heart rate per/min, SBP-Systolic Blood pressure in mmHg,  $p > 0.05$

**Figure 2: HR and SBP at baseline, induction & after LMA insertion in the two treatment groups**  
**Discussion**

Sevoflurane and propofol are popular agents for induction and maintenance of general anaesthesia with LMA to reduce morbidity with endotracheal tube in children.

Children needed higher induction dose of propofol, which may be explained by a large central volume of distribution of the drug and a greater cardiac output per kilogram body weight which should result in a lower peak concentration of propofol in the blood perfusing the brain after bolus injection<sup>15</sup>. Thus we used 3mg/kg of propofol for induction and 170 µg/kg/min propofol infusion<sup>14,16</sup>. For sevoflurane our dose regimen was similar to those used in previous studies<sup>17</sup>. In the present study, induction was equally fast in both study groups, which is similar to other studies<sup>11,18</sup> as sevoflurane has low blood-gas partition coefficient. Overall success rate for LMA insertion was 100% in both groups, but the average number of attempts for LMA insertion in our study was 1.10 for group S and 1.24 for group P without a statistically significant difference. In contrast, other studies noted less number of attempts with group P compared to group S<sup>19</sup>. This may be because conditions for LMA insertion were reached earlier with sevoflurane as circuit is primed and propofol induction dose should be re-evaluated. Another possible explanation for the difference could be that equipotent doses of both drugs could not be determined.

In the present study, mean LMA insertion, removal and recovery times were significantly shorter with group S than group P, a finding that is consistent with

two previous studies<sup>5,14</sup>. Aldrete score was higher at 5 minutes in group S. This suggested recovery from anaesthesia was slower with propofol than with sevoflurane. This may be due to rapid wash in and out of sevoflurane in children as they have greater alveolar ventilation, greater cardiac output directed to the vessel rich group, lower tissue and blood solubility, while propofol is redistributed causing longer recovery. Perioperative haemodynamic variables were similar in both groups, since both decrease systemic vascular resistance. The transient increase in heart rate during induction and insertion of LMA in both groups in this study, although modest in magnitude, is in contrast with two published reports, where heart rate was significantly lower in group P<sup>5,20</sup>. Various studies proved both sevoflurane and propofol to be anaesthetics which maintain mean arterial pressure and heart rate close to pre-induction values<sup>21,22</sup>.

The anaesthetic agent might have major effects on the pattern of potentially harmful defensive airway reflexes. Laryngospasm occurred more frequently during sevoflurane anaesthesia, whereas cough and expiration reflexes occurred more often during propofol anaesthesia<sup>23</sup>. In contrast to this study we noted less adverse events during LMA insertion, as both agents depress laryngeal reflexes adequately with the doses we used. Coughing during induction in group S may be attributed to inadequate depth of anaesthesia. In our study incidence of apnoea was higher during induction in group P (16.7%) than in group S (6.7%) but this was statistically insignificant. None of the patients had hypoxaemia during induction because manual ventilation with 100%

oxygen before LMA insertion was done in all the patients. In agreement to other studies we noted lesser incidence of nausea and vomiting with propofol as propofol itself has got antiemetic properties, and two patient had vomiting in group S<sup>11,20</sup>. This may be a function of the initial high concentration of sevoflurane or it may be caused by air and gases, which may be swallowed into the stomach during induction. Four patients developed agitation in group S compared to none in group P, which is statistically significant. Agitation following sevoflurane anaesthesia has an incidence of 10-40% being highest in preschool children, which may be related to earlier perception of pain and preoperative anxiety<sup>24,25</sup>. Keeping this trend our figure for agitation is 13.3%. The aetiology of agitation is currently unknown. Recent hypotheses emphasizing rapid emergence associated with new anaesthetic agents such as sevoflurane and desflurane may create a dissociative state i.e. children awaken with altered cognitive perception or involvement of the serotonergic system. Agitation can be prevented by pain prevention, with the drugs like propofol, ketamine, and  $\alpha_2$ -AR agonists<sup>26</sup>.

It is possible that the incidence of agitation may be reduced by progressive weaning rather than abrupt cessation at the end of surgery and using drugs preoperatively to reduce anxiety. Inadequate analgesia appears to be an unlikely cause of agitation in our study as pain was adequately taken care of with perioperative analgesia.

## Conclusions

- Sevoflurane at the doses used in this study provided shorter LMA insertion and removal times than intravenous propofol in children undergoing surgeries below the umbilicus.
- Faster recovery was seen with sevoflurane but agitation was more common with use of this agent.
- Sevoflurane appears to be a useful alternative to propofol for induction and maintenance of general anaesthesia in children with LMA.

## References

1. Bortone L, Ingelmo PM, De Ninno G, et al. Randomized controlled trial comparing the laryngeal tube and the laryngeal mask in

paediatric patients. *Pediatric Anesthesia* 2006; **16**: 251-7.

<http://dx.doi.org/10.1111/j.14609592.2005.01756.x>

2. Lerman J. Sevoflurane in paediatric anaesthesia. *Anesthesia & Analgesia* 1995; **81**(Suppl. 6):S4-S10.  
<http://dx.doi.org/10.1097/00000539-199512001-00002>
3. Fredman B, Nathanson MH, Smith I, et al. Sevoflurane for outpatient anesthesia: A comparison with propofol. *Anesthesia and Analgesia* 1995; **81**:823-8.  
<http://dx.doi.org/10.1097/00000539-199510000-00028>
4. Pennant JH, White PF. The laryngeal mask airway. Its uses in anaesthesiology. *Anesthesiology* 1993; **79**(1):144-63.  
<http://dx.doi.org/10.1097/00000542-199307000-00021>
5. Lopez Gil M, Brimacombe J, Clar B. Sevoflurane vs. propofol for induction and maintenance of anaesthesia with the laryngeal mask airway in children. *Pediatric Anesthesia* 1999; **9**: 485-90.  
<http://dx.doi.org/10.1046/j.14609592.1999.00404.x>
6. Mary EM, Donal JB, Patrick S. Propofol or sevoflurane for laryngeal mask airway insertion. *Canadian Journal of Anesthesia* 1999; **46**(4):322-6.  
<http://dx.doi.org/10.1007/BF03013222>
7. Lerman J, Jöhr M. Inhalational anesthesia vs. total intravenous anesthesia (TIVA) for paediatric anesthesia. *Pediatric Anesthesia* 2009; **19**(5): 521-34.  
<http://dx.doi.org/10.1111/j.14609592.2009.02962.x>
8. Ibraheem NM, Ibraheem HA, Morabaa EL, Hasan L, Hofny K, Ismael E. Sevoflurane versus halothane for induction and maintenance of anaesthesia in children while breathing spontaneously via a laryngeal mask airway (LMA). *El-Minia Medical Bulletin* 2003; **14**: 273-86.

9. Paris ST, Cafferkey M, Tarling M, Hancock P, Yate PM, Flynn PJ. Comparison of sevoflurane and halothane for outpatient dental anaesthesia in children *British Journal of Anaesthesia* 1997; **79** (3): 280-4.  
<http://dx.doi.org/10.1093/bja/79.3.280>
10. Sarner JB, Levine M, Davis PJ, et al. Clinical characteristics of sevoflurane in children: A comparison with halothane. *Anesthesiology* 1995; **82**:38-46.  
<http://dx.doi.org/10.1097/0000542-199501000-00006>
11. Joo HS, Perks W. Sevoflurane versus propofol for anaesthetic induction a meta-analysis. *Anesthesia and Analgesia* 2000; **91**:213-9.  
<http://dx.doi.org/10.1213/0000539-200007000-00040>
12. Tesniere A, Servin F. Intravenous techniques in ambulatory anesthesia. *Anesthesiology Clinics of North America* 2003; **21**:273-88.  
[http://dx.doi.org/10.1016/S0889-8537\(02\)00081-0](http://dx.doi.org/10.1016/S0889-8537(02)00081-0)
13. Thwaites A, Edmonds S, Smith I. Inhalation induction with sevoflurane: a double-blind comparison with propofol. *British Journal of Anaesthesia* 1997; **78**(4): 356-611.  
<http://dx.doi.org/10.1093/bja/78.4.356>
14. Iclal Ozdemir Kol Open-Label, prospective, randomized comparison of propofol and sevoflurane for laryngeal mask anaesthesia for magnetic resonance imaging in paediatric patients. *Clinical Therapeutics* 2008; **30**(1):1.
15. Martlew RA, Meakin G, Wadsworth R, Sharples A, Baker RD. Dose of propofol for laryngeal mask airway insertion in children: effect of premedication with midazolam. *British Journal of Anaesthesia* 1996; **76**:308-9.  
<http://dx.doi.org/10.1093/bja/76.2.308>
16. Usher AG, Kearney RA, Tsui BC. Propofol total intravenous anaesthesia for MRI in children. *Paediatric Anaesthesia* 2005; **15**: 23-8.  
<http://dx.doi.org/10.1111/j.14609592.2004.01390.x>
17. Keller C, Sparr HJ, Brimacombe J. Positive pressure ventilation with the laryngeal mask airway in non-paralysed patients: comparison of sevoflurane and propofol maintenance techniques. *British Journal of Anaesthesia* 1998; **80**: 332-6.  
<http://dx.doi.org/10.1093/bja/80.3.332>
18. Lian KT, Mark YHC, Tat LL. Comparison of sevoflurane with propofol for laryngeal mask airway insertion in adults *Anesthesia & Analgesia* 1999; **88**: 908-12.  
<http://dx.doi.org/10.1213/0000539-199904000-00041>
19. Priya V, Divatia JV, Dasgupta D. A comparison of propofol versus sevoflurane for laryngeal mask airway insertion. *Indian Journal of Anaesthesia* 2002; **46** (1):31-4.
20. Jun L, Pung G, Hong C. Comparison of LMA insertion conditions with sevoflurane inhalational and propofol TCI anaesthesia. *Anesthesiology* 2008; **109**: A777.
21. Wiesner G, Schwurzer S, Horauf K, Hobbahn J. Emergence times, haemodynamics and adverse effects of sevoflurane and isoflurane: an open, randomized cooperative phase III study. *Anaesthetist* 1994; **43**: 587-93.  
<http://dx.doi.org/10.1007/s001010050097>
22. Marshall CA, Jones RM, Bajorek PK, Cashman JN. Recovery characteristics using isoflurane or propofol for maintenance of anaesthesia: a double-blind controlled trial. *Anaesthesia* 1992; **47**: 461-6.  
<http://dx.doi.org/10.1111/j.13652044.1992.tb02265.x>
23. Oberer C, von Ungem-Sternberg BS, Frei FJ, Erb TO. Respiratory reflex responses of the larynx differ between sevoflurane and propofol in paediatric patients. *Anaesthesiology* 2005; **105**: 1142-8.  
<http://dx.doi.org/10.1097/0000542-200512000-00007>
24. Dalens BJ, Pinard AM, Letourneau DR, Albert N T, Truchon RJ. Prevention of emergence agitation after sevoflurane anesthesia for paediatric cerebral magnetic resonance imaging by small doses of ketamine or nalbuphine administered just before discontinuing

- anaesthesia. *Anesthesia and Analgesia* 2006; **102**: 1056-61  
<http://dx.doi.org/10.1213/01.ane.0000200282.38041.1f>
25. Kain ZN, Caldwell-Andrews AA, Maranets I, et al. Preoperative anxiety and emergence delirium and postoperative maladaptive behaviours. *Anesthesia and Analgesia* 2004; **99**:1648-54.  
<http://dx.doi.org/10.1213/01.ANE.0000136471.36680.97>
26. Dahmani S, Stany I, Brasher C, Lejeune C, Bruneau B, Wood C, et al. Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies *British Journal of Anaesthesia* 2010; **104** :216-23.  
<http://dx.doi.org/10.1093/bja/aep376>