



REVISTA BRASILEIRA DE ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology
www.sba.com.br



SCIENTIFIC ARTICLE

Comparison of the effects of remifentanil and remifentanil plus lidocaine on intubation conditions in intellectually disabled patients[☆]

Can Eyigor, Esra Cagiran*, Taner Balcioglu, Meltem Uyar

Department of Anaesthesiology, Faculty of Medicine, Ege University, Izmir, Turkey

Received 1 March 2012; accepted 22 March 2013

Available online 7 November 2013

KEYWORDS

Remifentanil;
Lidocaine;
Endotracheal
intubation;
Without
neuromuscular
blockade

Abstract

Background and objectives: This is a prospective, randomized, single-blind study. We aimed to compare the tracheal intubation conditions and hemodynamic responses either remifentanil or a combination of remifentanil and lidocaine with sevoflurane induction in the absence of neuromuscular blocking agents.

Methods: Fifty intellectually disabled, American Society of Anesthesiologists I–II patients who underwent tooth extraction under outpatient general anesthesia were included in this study. Patients were randomized to receive either 2 $\mu\text{g kg}^{-1}$ remifentanil (Group 1, $n=25$) or a combination of 2 $\mu\text{g kg}^{-1}$ remifentanil and 1 mg kg^{-1} lidocaine (Group 2, $n=25$). To evaluate intubation conditions, Helbo-Hansen scoring system was used. In patients who scored 2 points or less in all scorings, intubation conditions were considered acceptable, however if any of the scores was greater than 2, intubation conditions were regarded unacceptable. Mean arterial pressure, heart rate and peripheral oxygen saturation (SpO_2) were recorded at baseline, after opioid administration, before intubation, and at 1, 3, and 5 min after intubation.

Results: Acceptable intubation parameters were achieved in 24 patients in Group 1 (96%) and in 23 patients in Group 2 (92%). In intra-group comparisons, the heart rate and mean arterial pressure values at all-time points in both groups showed a significant decrease compared to baseline values ($p=0.000$)

Conclusion: By the addition of 2 $\mu\text{g/kg}$ remifentanil during sevoflurane induction, successful tracheal intubation can be accomplished without using muscle relaxants in intellectually disabled patients who undergo outpatient dental extraction. Also worth noting, the addition of 1 mg/kg lidocaine to 2 $\mu\text{g/kg}$ remifentanil does not provide any additional improvement in the intubation parameters.

© 2013 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. All rights reserved.

[☆] The study was conducted in Department of Anaesthesiology, Faculty of Medicine, Ege University.

* Corresponding author.

E-mail: esrayuksel73@yahoo.com (E. Cagiran).

PALAVRAS-CHAVE

Remifentanil;
Lidocaína;
Intubação
endotraqueal;
Sem bloqueio
neuromuscular

Comparação dos efeitos de remifentanil e remifentanil + lidocaína em intubação de pacientes intelectualmente deficientes**Resumo**

Justificativa e objetivos: Este é um estudo prospectivo, randômico e duplo-cego. Nosso objetivo foi comparar as condições de intubação endotraqueal e as respostas hemodinâmicas com o uso de remifentanil ou combinação de remifentanil e lidocaína em indução anestésica com sevoflurano sem agentes bloqueadores neuromusculares.

Métodos: Cinquenta pacientes intelectualmente deficientes, estado físico ASA I–II, submetidos à extração dentária sob anestesia geral em ambulatório foram incluídos neste estudo. Os pacientes foram randomizados para receber $2\ \mu\text{g kg}^{-1}$ de remifentanil (Grupo 1, $n=25$) ou uma combinação de $2\ \mu\text{g kg}^{-1}$ de remifentanil e $1\ \text{mg kg}^{-1}$ de lidocaína (Grupo 2, $n=25$). Para avaliar as condições de intubação, o sistema de pontuação de Helbo-Hansen foi usado. Em pacientes com 2 ou menos pontos em todas as pontuações, as condições de intubação foram consideradas aceitáveis, porém, se qualquer uma das pontuações fosse superior a 2, as condições de intubação seriam consideradas inaceitáveis. Pressão arterial média, frequência cardíaca e saturação periférica de oxigênio (SpO_2) foram registradas no início do estudo, após a administração de opiáceos, antes da intubação e nos minutos 1, 3 e 5 após a intubação.

Resultados: Parâmetros aceitáveis de intubação foram obtidos em 24 pacientes do Grupo 1 (96%) e em 23 pacientes do Grupo 2 (92%). Nas comparações intragrupo, os valores da frequência cardíaca e pressão arterial média em todos os momentos em ambos os grupos mostraram uma redução significativa em relação aos valores basais ($p=0.000$).

Conclusão: Com a adição de remifentanil ($2\ \mu\text{g/kg}$) durante a indução com sevoflurano, pode-se obter intubação endotraqueal bem-sucedida sem o uso de relaxantes musculares em pacientes intelectualmente deficientes que se submetem à extração dentária em ambulatório. Também é digno de nota que a adição de lidocaína ($1\ \text{mg/kg}$) a remifentanil ($2\ \mu\text{g/kg}$) não apresenta qualquer melhora adicional dos parâmetros de intubação.

© 2013 Sociedade Brasileira de Anestesiologia. Publicado por Elsevier Editora Ltda. Todos os direitos reservados.

Introduction

Tracheal intubation is usually facilitated with a muscle relaxant that is administered following anesthesia induction. During intubation, anesthesia should be deep enough to inhibit the reflex activity and complete muscle relaxation should be accomplished.¹ The use of hypnotics and opioids at induction doses can be sufficient for tracheal intubation without the need for muscle relaxants, where use of a muscle relaxant is not preferred as is the case for day surgery patients, short surgical procedures, motor neuron disease and drug allergy.^{2,3}

Tracheal intubation without muscle relaxants may be a life-saving measure to maintain spontaneous respiration in patients with difficult airways. According to the previous medical literature, intubation can be carried out without the use of a muscle relaxant.^{4–6} Sevoflurane, a nonirritating inhalational anesthetic agent with low blood/gas solubility, has also been used for intubation without neuromuscular blocking agents, either alone or in combination with remifentanil.^{7,8}

In addition, one may improve tracheal intubating conditions through the use of additional drugs, such as remifentanil and lidocaine, which may potentiate depression of the laryngeal reflexes.^{4,9}

The aim of the present study was to compare the effects of remifentanil and remifentanil plus lidocaine using sevoflurane induction without muscle relaxants on tracheal

intubating conditions in intellectually disabled patients admitted for outpatient dental treatment.

Materials and methods

The present study was designed as a prospective, randomized, and single-blind study. The study was approved by the ethics committee, and written informed consents were obtained from the parents and guardians of the patients.

Fifty intellectually disabled American Society of Anesthesiologists (ASA) I and II patients, who were scheduled for dental surgery requiring general anesthesia, were included in the study. Patients with ASA physical status III or higher, an expectance of difficult intubation, limited head and neck movement, reactive airway disease, gastroesophageal reflux, renal or hepatic impairment, allergies to any of the study drugs were excluded from the study. Mallampati classification¹⁰ of airway anatomy higher than class II, mouth opening $<3\ \text{cm}$, sternomental distance $<12.5\ \text{cm}$, tiromental distance $<6\ \text{cm}$, Cormack–Lehane classification¹¹ higher than grade II, and body mass index ≥ 30 ¹² were considered as the indicators of difficult intubation.

Standard intraoperative monitoring included electrocardiography, pulse oximetry, respiratory rate and noninvasive blood pressure measurements (Datex-Ohmeda, Helsinki, Finland). Capnography, and inspired and end-tidal partial pressures of sevoflurane and O_2 were also monitored. A face mask with a semi-closed anesthetic circuit was primed with

Table 1 Intubating condition scores^a

	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Limb movement	None	Slight	Moderate	Severe

^a Devised by Helbo-Hansen Raulo and Trap-Andersen.

4% sevoflurane in 100% O₂. Then, anesthesia was induced using this mask for 2 min, where a fresh flow of gas at 5 L min⁻¹ was supplied to the circuit. Once an adequate level of anesthesia was achieved, an intravenous (IV) line was established and 0.01 mg kg⁻¹ atropine was given. After baseline measurements, the patients were randomly allocated to one of two groups on the basis of a computer-generated random table. Patients in Group 1 (*n* = 25) received 2 μg kg⁻¹ remifentanyl + 5 mL saline whereas Group 2 (*n* = 25) received 2 μg kg⁻¹ remifentanyl + 1 mg kg⁻¹ lidocaine. Tracheal intubation was performed 90 s after remifentanyl administration by a single, experienced anesthesiologist. Intubation was performed and assessed by an anesthesiologist who was blinded to the remifentanyl dose used.

The quality of intubation was graded by an independent anesthesiologist using the scoring system devised by Helbo-Hansen Raulo and Trap-Andersen¹³ (Table 1).

- Ease of laryngoscopy
- Position of vocal cords
- Degree of coughing
- Jaw relaxation
- Limb movement

Intubating conditions were deemed acceptable if a patient had ≤2 points in all categories or unacceptable if the patient had >2 points in any single category.

Mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation (SpO₂) were recorded at baseline, after opioid administration, before intubation, and at 1, 3, and 5 min following intubation. Side effects associated with remifentanyl use including muscle rigidity, hypotension, bradycardia and arterial oxygen desaturation below 91% were recorded and treated accordingly. Hypotension (MAP < 25% from baseline) was managed with 5–10 mg ephedrine IV and bradycardia (HR < 50 beat/min) was treated with 0.5 mg atropine.

Statistical analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) for Windows (version 13.0; SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean. Variables with normal distribution were analyzed using the Student's *t*-test while non-normally distributed variables were analyzed using the Mann-Whitney rank sum test. Categorical data were analyzed using the Fisher's exact test. Hemodynamic responses were analyzed

Table 2 Patient characteristics.

	Group 1 ^a	Group 2 ^a
Age (years)	17.88 ± 7.1	21.20 ± 7.1
Weight (kg)	50.44 ± 18.1	58.76 ± 12.5
Gender (M/F)	13/12	11/14

^a Values are presented as mean ± SD.

using the repeated measures analysis of variance (ANOVA). A value *p* < 0.05 was considered statistically significant.

Results

Each group contained 25 patients. Demographic variables were similar in both groups (*p* > 0.05) (Table 2).

According to the Helbo-Hansen scoring system, there was no significant difference between the groups in terms of jaw relaxation (*p* = 0.57), ease of laryngoscopy (*p* = 0.31), vocal cord position (*p* = 0.09), degree of coughing (*p* = 0.14) and limb movement (*p* = 0.42). One patient in Group 1 scored 3 points for jaw relaxation. One patient in Group 2 scored 4 points for jaw relaxation and 3 points for the position of vocal cords, while another patient scored 3 points for vocal cord position.

Intubation was successful in all patients, and no further intervention was necessary. According to the Helbo-Hansen scoring system, acceptable intubating conditions were achieved in 24 patients in Group 1 (96%) and 23 patients in Group 2 (92%) (Fig. 1).

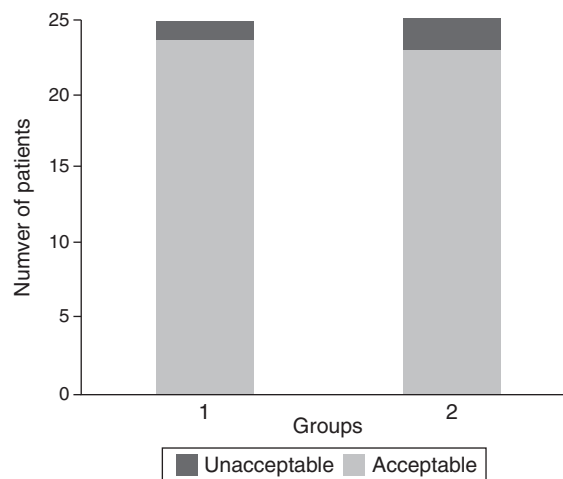


Figure 1 Overall intubating conditions of two groups.

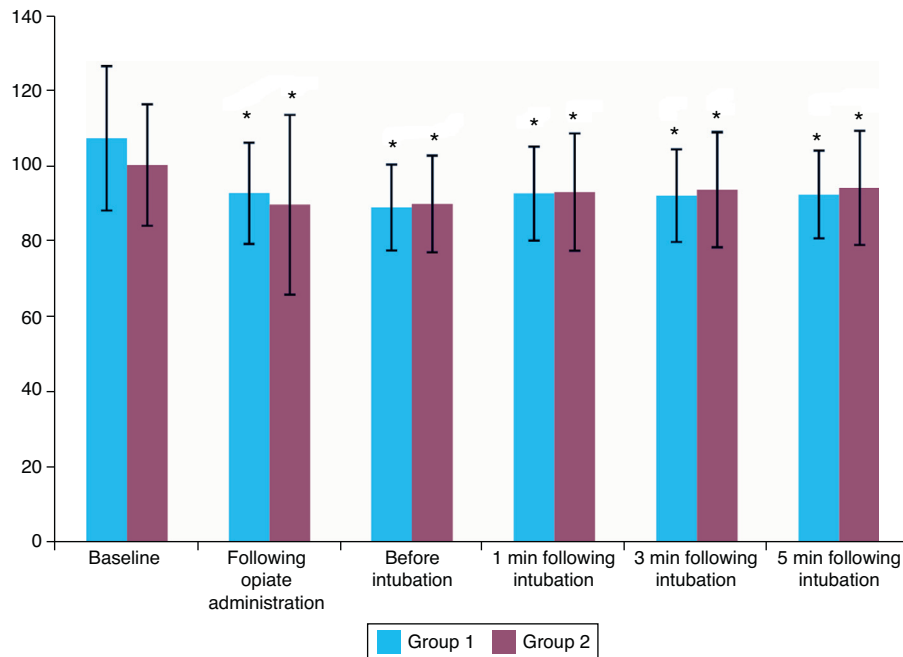


Figure 2 Mean (SD) changes in heart rate (HR), observations: baseline; following opiate administration; before intubation; 1, 3, 5 min following intubation. * $p=0.000$ compared with baseline value.

The mean basal HR was 107.84 ± 19.2 /min in Group 1 and 100.72 ± 16.2 /min in Group 2, and there was no significant difference between the groups ($p=0.16$). The MAP at baseline was significantly lower in Group 2 than that in Group 1 ($p=0.002$). In intra-group comparisons, the HR and MAP values at all-time points in both groups showed a significant decrease compared to baseline values ($p=0.000$).

Cardiovascular responses to induction and intubation are shown in Figs. 2 and 3.

No patient had clinically significant bradycardia, hypotension, rigidity or hypoxemia. However, 1 patient in Group 2 developed laryngeal spasm for a short time.

Discussion

In the present study, we found that, when used with sevoflurane, both remifentanyl and remifentanyl lidocaine combination secured acceptable intubating conditions in mentally retarded patients undergoing outpatient dental treatment when muscle relaxants were not used during intubation.

The risk of an unexpectedly difficult intubation is considerably higher in mentally retarded patients due to inadequate airway examination before anesthesia and the presence of possible anatomical deformities.¹⁴ Machotta and

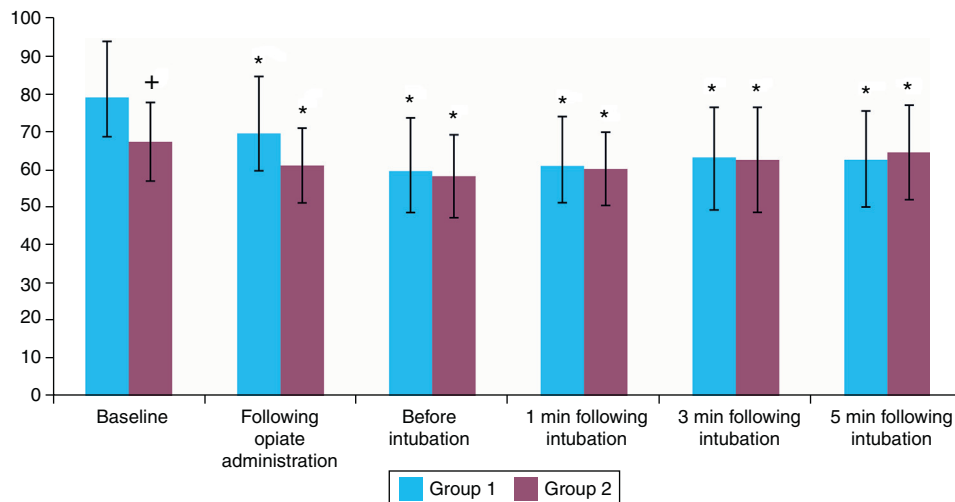


Figure 3 Mean (SD) changes in mean arterial pressure (MAP), observations: baseline; following opiate administration; before intubation; 1, 3, 5 min following intubation. * $p=0.000$ significant differences from baseline. + $p<0.05$ significant difference between groups.

Hoeve¹⁵ successfully performed intubation without muscle relaxants using sevoflurane and remifentanyl in mentally retarded children with Marshall–Smith syndrome. Similarly, Nakazawa and coworkers¹⁶ presented an 11-year-old patient with Down's syndrome to whom they successfully performed tracheal intubation without using a muscle relaxant despite the risk of a difficult intubation estimated during pre-anesthesia examination. In the present study, we did not encounter difficult intubating conditions in any of our mentally retarded cases and all patients were successfully intubated.

The improvement in intubating conditions, in case of remifentanyl use in combination with sevoflurane induction without neuromuscular blocking drugs, may be due to the analgesic effects of these drugs.^{4,6} Cros et al.¹⁷ suggested that opioids might block afferent nerve impulses resulting from stimulation of the pharynx, larynx and trachea during intubation and cuff inflation. In a study by Joo et al.,⁷ the authors reported good to optimal conditions for tracheal intubation in 89% and 100% of their patients when $1 \mu\text{g kg}^{-1}$ and $2 \mu\text{g kg}^{-1}$ remifentanyl, respectively, was used. In their study, where Weber et al.¹⁸ used $1 \mu\text{g kg}^{-1}$ of remifentanyl with 4% end-tidal sevoflurane concentration, all of the children included in the study had acceptable (excellent or good) intubating conditions. Woods et al.^{19,20} achieved good or ideal intubating conditions in 80–90% of the patients with $2 \mu\text{g kg}^{-1}$ of remifentanyl. In agreement with the literature, we achieved acceptable (excellent or good) intubating conditions in 96% of the patients in Group 1 and in 92% of the patients in Group 2, when we used $2 \mu\text{g kg}^{-1}$ of remifentanyl with 4% sevoflurane without a muscle relaxant for intubation. Intubation was completed successfully in all patients without the need for any other intervention.

The use of remifentanyl for tracheal intubation without muscle relaxants, has been reported to cause hypotension, in many studies.^{16,21} Batra et al.²¹ observed hypotension with $2 \mu\text{g kg}^{-1}$ and $3 \mu\text{g kg}^{-1}$ of remifentanyl administration. Similar results were reported by Joo et al.⁷ with $2 \mu\text{g kg}^{-1}$ of remifentanyl. However, in both studies low blood pressure values were within the clinically acceptable range and did not require treatment. In the present study, in agreement with the literature, hypotension developed after $2 \mu\text{g kg}^{-1}$ of remifentanyl, but blood pressure measurements were within clinically acceptable limits and none of the patients needed treatment. Lidocaine is known to be involved in the suppression of airway reflexes. While numerous studies reported improvement in intubating conditions with lidocaine,^{9,22,23} there are also studies with conflicting results.^{24,25} Munholland and colleagues²⁴ designed a double-blind study to compare the intubating conditions with 2.5 mg kg^{-1} of propofol or a similar volume of isotonic saline after intravenous lignocaine pretreatment, and found no significant difference between the groups. Similar findings were observed in a study by Grange et al.²⁵ who also found no significant difference between the effects of lignocaine and alfentanil pre-treatment on orotracheal intubation conditions following induction with propofol, but without the use of muscle relaxants. Several studies also examined the effectiveness of intravenous lidocaine to suppress the cough reflex.^{26,27} In our study, lidocaine offered no additional benefit on cough reflex. In our study, lidocaine, when given with remifentanyl, did not improve the tracheal intubating

conditions when a muscle relaxant was not used. Most plausible explanation of the failure of lidocaine to improve the intubating conditions may be the fact that acceptable intubating conditions were achieved in as high as 96% of the patients, even when only remifentanyl was used.

In conclusion, we found that both remifentanyl and remifentanyl + lidocaine under sevoflurane induction provided acceptable intubating conditions in mentally retarded patients who had outpatient dental extraction when a muscle relaxant was not used during intubation. In our faculty of dentistry, the rate of mentally retarded patients is less than that of the general population. Thus, the number of patients was limited in the present study. The present study may constitute an example of the design of further studies with higher patient numbers.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Glass PS, Gan TJ, Howell S. A review of the pharmacokinetics and pharmacodynamics of remifentanyl. *Anesth Analg.* 1999;89:7–14.
2. Stevens JB, Wheatley LD. Tracheal intubation in ambulatory surgery patients: using remifentanyl and propofol without muscle relaxants. *Anesth Analg.* 1998;86:45–9.
3. Kavac L. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. *J Clin Anesth.* 1996;8:63–79.
4. Min SK, Kwak YL, Park SY, et al. The optimal dose of remifentanyl for intubation during sevoflurane induction without neuromuscular blockade in children. *Anaesthesia.* 2007;62:446–50.
5. Ithnin F, Lim Y, Shah M, et al. Tracheal intubating conditions using propofol and remifentanyl target-controlled infusion: a comparison of remifentanyl EC50 for Glidescope and Macintosh. *Eur J Anaesthesiol.* 2009;26:223–8.
6. He L, Wang X, Zhang XF, et al. Effects of different doses of remifentanyl on the end-tidal concentration of sevoflurane required for tracheal intubation in children. *Anaesthesia.* 2009;64:850–5.
7. Joo HS, Perks WJ, Belo SE. Sevoflurane with remifentanyl allows rapid tracheal intubation without neuromuscular blocking agents. *Can J Anaesth.* 2001;48:646–50.
8. Sztark F, Chopin F, Bonnet A, et al. Concentration of remifentanyl needed for tracheal intubation with sevoflurane at 1 MAC in adult patients. *Eur J Anaesthesiol.* 2005;22:919–24.
9. Aouad MT, Sayyid SS, Zalaket MI, et al. Intravenous lidocaine as adjuvant to sevoflurane anesthesia for endotracheal intubation in children. *Anesth Analg.* 2003;96:1325–7.
10. Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J.* 1985;32:429–34.
11. Cormack RS. Cormack–Lehane classification revisited. *Br J Anaesth.* 2010;105:867–8.
12. Juvin PH, Lavaut E, Dupont H, et al. Difficult tracheal intubation is more common in obese than in lean patients. *Anesth Analg.* 2003;97:595–600.
13. Helbo-Hansen S, Ravlo O, Trap-Andersen S. The influence of alfentanil on the intubating condition after priming with vecuronium. *Acta Anaesthesiol Scand.* 1988;32:41–4.
14. Ghezzi EM, Chávez EM, Ship JA. General anesthesia protocol for the dental patient: emphasis for older adults. *Spec Care Dentist.* 2000;20:81–92.

15. Machotta A, Hoeve H. Airway management and fiberoptic tracheal intubation via the laryngeal mask in a child with Marshall-Smith syndrome. *Paediatr Anaesth.* 2008;18:341-2.
16. Nakazawa K, Ikeda D, Ishikawa S, et al. A case of difficult airway due to lingual tonsillar hypertrophy in a patient with Down's syndrome. *Anesth Analg.* 2003;97:704-5.
17. Cros AM, Lopez C, Kandel T, et al. Determination of sevoflurane alveolar concentration for tracheal intubation with remifentanyl, and no muscle relaxant. *Anaesthesia.* 2000;55:965-9.
18. Weber F, Füssel U, Gruber M, et al. The use of remifentanyl for intubation in paediatric patients during sevoflurane anaesthesia guided by Bispectral Index (BIS) monitoring. *Anaesthesia.* 2003;58:749-55.
19. Woods AW, Grant S, Harten J, et al. Tracheal intubating conditions after induction with propofol, remifentanyl and lignocaine. *Eur J Anaesthesiol.* 1998;16:714-8.
20. Woods A, Grant S, Davidson A. Duration of apnoea with two different intubating doses of remifentanyl. *Eur J Anaesthesiol.* 1999;16:634-7.
21. Batra YK, Al Qattan AR, Ali SS, et al. Assessment of tracheal intubating conditions in children using remifentanyl and propofol without muscle relaxant. *Paediatr Anaesth.* 2004;14:452-6.
22. Warner LO, Balch DR, Davidson PJ. Is intravenous lidocaine an effective adjuvant for endotracheal intubation in children undergoing induction of anesthesia with halothane nitrous oxide? *J Clin Anesth.* 1997;9:270-4.
23. Davidson JAH, Gillespie JA. Tracheal intubation after induction of anaesthesia with propofol, alfentanil and IV lignocaine. *Br J Anaesth.* 1993;70:163-6.
24. Mulholland D, Carlisle RJ. Intubation with propofol augmented with intravenous lignocaine. *Anaesthesia.* 1991;46:312-3.
25. Grange CS, Suresh D, Meikle R, et al. Intubation with propofol: evaluation of pretreatment with alfentanil or lignocaine. *Eur J Anaesthesiol.* 1993;10:9-12.
26. Poulton TJ, James 3rd FM. Cough suppression by lidocaine. *Anesthesiology.* 1979;50:470-2.
27. Steinhaus JE, Gaskin L. A study of intravenous lidocaine as a suppressant of cough reflex. *Anesthesiology.* 1963;24:285-90.