

## Effectiveness of sevoflurane or propofol combined with remifentanil for intubation without muscle relaxants

### *Kas gevşeticiler olmadan remifentanil ile kombine edilen sevofluran veya propofol ile entübasyonun etkinliği*

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#### ABSTRACT

**Objectives:** We aimed to investigate the reliability of the hypothesis that whether sevoflurane-remifentanil could offer equivalent intubation conditions with propofol-remifentanil in the absence of muscle relaxants.

**Materials and methods:** Total of 80 patients of ASA grades I and II scheduled for elective surgery were randomly allocated into two groups. Patients in group I received an infusion of remifentanil 1 mcg/kg/min and inhalation of sevoflurane 8% until the Bispectral index (BIS) being less than 60. Patients in group II received a co-infusion of remifentanil 1 mcg/kg/min and propofol 1 mg/kg/min until BIS is <60. Intubation was attempted when BIS is <60. Intubation conditions were assessed as optimal, good, marginal, and poor using jaw relaxation, vocal cord opening, and limb movement. The heart rate and mean arterial blood pressure (ABP) were recorded before and during the induction, and thereafter, 1, 2 and 5 minutes following intubation. The time for BIS to be <60 was recorded.

**Results:** Optimal intubation conditions were achieved more often in group II than in group I (90% versus 45%,  $p=0.002$ ). The ratio of patients showing optimal or good intubating conditions was 80% in group I and 100% in group II ( $p=0.035$ ). Time required for BIS to be <60 was shorter in group II than in group I ( $47.1\pm 27.2$  sec vs.  $111.9\pm 60.6$  sec,  $p<0.001$ ). In both groups, there was a decrease in heart rate and mean ABP compared to baseline.

**Conclusion:** Under BIS monitorization, propofol-remifentanil combination offered better intubation conditions and shorter anesthesia induction period compared with sevoflurane-remifentanil. *J Clin Exp Invest* 2011;2(2):138-43

**Key words:** Intubating conditions, propofol, remifentanil, sevoflurane, comparison

#### ÖZET

**Amaç:** Bu çalışmada, kas gevşetici kullanılmadığında, sevofluran-remifentanil kombinasyonunun propofol-remifentanil kombinasyonuna eşdeğer düzeyde entübasyon koşulları sağlayabileceği hipotezinin doğruluğunu araştırmayı amaçladık.

**Gereç ve yöntem:** Elektif cerrahi geçirecek ASA I-II grubundan 80 hasta rastgele iki gruba ayrıldı. Grup I'deki hastalara 1 mcg/kg/dk remifentanil infüzyonu ile %8 sevofluran inhalasyonu eş zamanlı olarak uygulandı. Grup II'deki hastalara 1mcg/kg/dk remifentanil ve 1 mg/kg/dk propofol infüzyonu eş zamanlı olarak uygulandı. Bispektral indeks (BİS) değeri 60'ın altına düşer düşmez entübasyon girişimi uygulandı. Entübasyon koşulları çene gevşemesi, vokal kord açıklığı ve ekstremitte hareketi kriterlerine göre optimal, iyi, sınırdan ve zayıf olmak üzere değerlendirildi. Kalp hızı ve ortalama arter basıncı induksiyondan önce, induksiyon boyunca dakikada bir ve entübasyondan 1, 2 ve 5 dk sonra kaydedildi. BİS değerinin 60'ın altına inmesine kadar geçen süre de kaydedildi.

**Bulgular:** Grup II'de (%90) grup I'e (%45) göre daha yüksek oranda hastada optimal entübasyon koşulları elde edildi ( $p=0.002$ ). Başarılı entübasyon koşulları oranı grup I'de %80 iken, grup II'de %100 idi ( $p=0.035$ ). Bispektral indeks değerinin 60'ın altına inmesi için geçen süre grup II'de ( $47.1\pm 27.2$  sn) grup I'e ( $111.9\pm 60.6$  sn) göre daha kısa idi ( $p=0.000$ ). Kalp hızı ve ortalama arter basıncı her iki grupta da bazal değere göre düşüş gösterdi.

**Sonuç:** Bispektral indeks monitorizasyonu eşliğinde, propofol-remifentanil kombinasyonu sevofluran-remifentanil kombinasyonuna göre daha iyi entübasyon koşulları sağlamış ve anestezi induksiyonu süresini kısaltmıştır. *Klin Deneysel Ar Derg* 2011;2(2):138-43

**Anahtar kelimeler:** Entübasyon, kas gevşemesi, propofol, remifentanil, sevofluran

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## INTRODUCTION

After induction of anesthesia, tracheal intubation is commonly facilitated by use of muscle relaxants. The concept of intubation without muscle relaxants finds its place in the situations where there is contraindication to both depolarizing (hyperkalemia, burns, plasma cholinesterase deficiency, penetrating eye injury) and nondepolarizing (myopathies, and known allergic reactions) neuromuscular blocking agents. It is also advantageous in cases where intubation is necessary but neuromuscular block is not required to facilitate surgical access.<sup>1,2</sup>

With an appropriate drug choice, the trachea can be successfully intubated without the use of muscle relaxants. Acceptable intubation conditions are obtained with propofol accompanied by an opioid such as fentanyl, alfentanil, sufentanil or remifentanil.<sup>1,4</sup> On the other hand, high concentrations of sevoflurane is frequently used for intubation without muscle relaxants, mostly in children.<sup>5-7</sup> It has been also used in adults alone or in combination with nitrous oxide for intubation without muscle relaxants.<sup>8</sup> Joo et al.<sup>9</sup> used sevoflurane-remifentanil combination for intubation without muscle relaxants in adults. Proposed advantages of sevoflurane inhalational induction include lack of pain with drug injection and confirmation that the patient can be ventilated as anesthesia is induced.<sup>9</sup>

In this study, we aimed to investigate the reliability of the hypothesis that whether sevoflurane-remifentanil combination could offer equivalent intubation conditions with propofol-remifentanil combination in the absence of muscle relaxants.

## MATERIALS AND METHODS

After obtaining approval from Institutional Ethics Committee and written informed consent from the patients, 80 patients of ASA grades I and II scheduled for elective surgery in Süleyman Demirel University hospital were included in the study. Patients with anticipated difficult intubation, increased risk of regurgitation, history of cardiorespiratory illness and known sensitivity to the drugs used were excluded from the study. Diazepam 10 mg po was used

for premedication 2 hours prior to surgery. In the operating room, the baseline heart rate, and mean arterial pressure levels were recorded. Before induction of anesthesia, the patients inhaled oxygen for 5 minutes (fresh gas flow 6 L/min) from a face mask connected to a semiclosed breathing circuit. The patients were randomly allocated into two groups by computer-generated table of random numbers.

Patients in group I received an infusion of remifentanil 1 mcg/kg/min accompanied by a simultaneous inhalation of sevoflurane 8% (fresh gas flow was maintained at 6 L/min-1 oxygen, sevoflurane vaporizer was advanced at 8% setting to provide maximum sevoflurane delivery, the anesthetic circuit was filled with the anesthetic gas and the patient was asked to breathe normally through the face mask) until Bispectral index (BIS) becomes smaller than 60 during the induction of anesthesia. The patient was told that the anesthetic agent has a definite odor but would not be unpleasant to breathe.

Patients in group II received a co-infusion of remifentanil 1 mcg/kg/min and propofol 1 mg/kg/min via two different venous access until BIS score becomes smaller than 60 during the induction of anesthesia.

As soon as BIS becomes smaller than 60, intubation was attempted by an experienced anaesthetist using a Macintosh 3 laryngoscope blade and an endotracheal tube 7.0 mm (for women) or 8.0 mm (for men).

The primary variables measured were conditions for tracheal intubation and time for BIS to be <60. Secondary variables measured included: 1- heart rate, blood pressure, end-tidal CO<sub>2</sub>, end-tidal sevoflurane concentration (for group 1) at first, second and third minutes of the induction; 2- degree of muscle rigidity during mask ventilation; 3- coughing after intubation and after the inflation of endotracheal tube cuff; and 4- postoperative sore throat.

Conditions for tracheal intubation were assessed according to jaw relaxation, vocal cord position, and limb movement (Table 1). Hypoxemia was defined as SpO<sub>2</sub> < 90%.

**Table 1.** Criteria for grading intubating conditions.

Intubating conditions	Optimal	Good	Marginal	Poor
Jaw relaxation	Fully relaxed	Partially relaxed	Moderately stiff	Severely stiff
Vocal cord opening	Open	Moving	Closing	Closed
Limb movement	None	Slight	Moderate	Severe

Degree of muscle rigidity during mask ventilation was graded as: none-completely relaxed if no resistance to mask ventilation was felt; mild-mildly rigid if rigidity was felt by the operator but did not affect manual ventilation; moderate-moderately rigid if ventilation was affected but ventilation was still possible; severe-fully rigid if muscle rigidity made positive pressure ventilation difficult.

Coughing at the intubation and after the cuff inflation, and postoperative sore throat were assessed using VRS (verbal rating score) (0: none, 1: mild, 2: moderate, 3: severe).

Following the intubation, in both groups the rate of remifentanyl infusion remained unchanged while sevoflurane concentration was reduced to 2% in group II and the rate of propofol infusion was adjusted to 6 mg/kg/h for first 30 minutes.

### Statistical analysis

The gender of the patients, the intubating conditions quality, chest rigidity during mask ventilation, coughing at the intubation and after the cuff inflation, and sore throat were compared between the two groups using chi-square test. The age, weight, height, heart rate, mean arterial pressure values, and time required for BIS to be smaller than 60 were compared between the groups using Mann Whitney-U test. Heart rate and mean arterial pressure values were compared within the groups using Wilcoxon Signed Ranks test.  $P < 0.05$  was considered statistically significant. A 30% difference in the successful (optimal to good) intubating conditions between two groups was used in computing the power analysis (Minitab for Windows). Also, a type I error of 5% as well as a type II error of 20% were used in the power analysis. The results of the power analysis indicated that a minimum of 33 patients were needed in each group. A P value of less than 0.05 was accepted significant.

**Table 2.** Patients demographics.

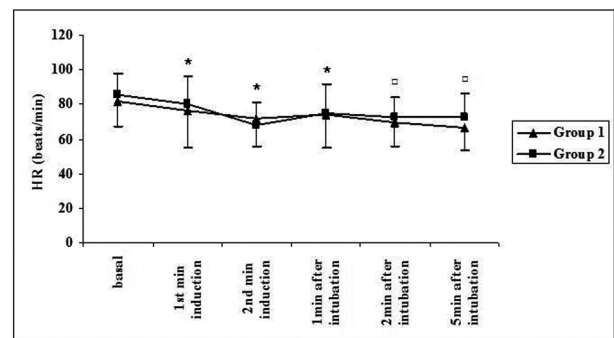
	Sevoflurane+remifentanyl (n=40)	Propofol+remifentanyl (n=40)
Age (year)	38.5±18.0	46.9±16.6
Weight (kg)	68.1±15.2	69.7±9.5
Height (cm)	165.3±7.9	167.3±5.9

Data are expressed as mean±standard deviation

## RESULTS

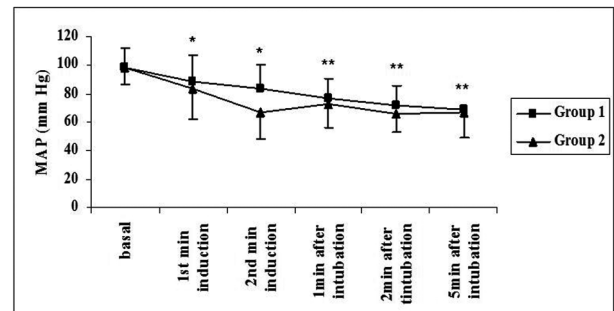
There were no differences in the demographic characteristics between the groups (Table 2).

In both of the groups, there was a decrease in heart rate and mean arterial pressure compared to baseline (Figures 1, 2). However, no patient developed a heart rate less than 45 beats/min. No patient needed atropine or efedrine. The heart rate, mean arterial pressure and SpO<sub>2</sub> values showed no differences between two groups.



**Figure 1.** Heart rate (HR) with standard deviation.

\* $p < 0.05$  compared with basal level in groups 1 and 2;  
□ $p < 0.01$  compared with basal level in groups 1 and 2



**Figure 2.** Mean arterial pressure (MAP) with standard deviation.

\* $p < 0.05$  compared with basal level in groups 1 and 2;  
\*\* $p = 0.000$  compared with basal level in groups 1 and 2

**Table 3.** Induction and tracheal intubation.

	Sevoflurane+remifentanil (n=40)	Propofol+remifentanil (n=40)
Optimal intubating conditions	18 (45%) <sup>□</sup>	36 (90%)
Good intubating conditions	14 (35%)	4 (10%)
Marginal intubating conditions	8 (20%)	0
Poor intubating conditions	0	0
Hypoxemia during induction (SpO <sub>2</sub> < 90%)	0	0
<i>Muscle rigidity</i>		
-none	32 (80%)	34 (85%)
-mild	8 (20%)	6 (15%)
-moderate	0	0
-severe	0	0
<i>Coughing after intubation</i>		
-none	24 (60%) <sup>□</sup>	38 (95%)
-mild	6 (15%)	2 (5%)
-moderate	10 (25%)	0
-severe	0	0
<i>Coughing after cuff inflation</i>		
-none	24 (60%) <sup>*</sup>	36 (90%)
-mild	8 (20%)	2 (5%)
-moderate	8 (20%)	2 (5%)
-severe	0	0
<i>Sore throat</i>		
-none	28 (70%)	23 (57.5%)
-mild	10 (25%)	15 (37.5%)
-moderate	2 (5%)	2 (5%)
-severe	0	0
Time for BIS < 60 (sec)	111.9±60.6 <sup>**</sup>	47.1±27.2

Data are expressed as mean±standard deviation where appropriate. \*p<0.05, <sup>□</sup>p<0.01, <sup>\*\*</sup>p<0.001

**Table 4.** End-tidal CO<sub>2</sub> concentration at the induction.

	Sevoflurane+remifentanil (n=40)	Propofol+remifentanil (n=40)
End-tidal CO <sub>2</sub> at 1 <sup>st</sup> min of induction	21.5±9.2	25.8±17.9
End-tidal CO <sub>2</sub> at 2 <sup>nd</sup> min of induction	24.2±8.1	33.2±20.3

Data are expressed as mean±standard deviation

Optimal intubation conditions were achieved more often in group II than in group I (90% versus 45%, p=0.002). The ratio of patients showing successful (optimal or good) intubating conditions was 80% in group I and 100% in group II (p=0.035) (Table 3).

All patients could be ventilated via a face mask after induction of anesthesia. No patient developed hypoxemia during the study period (Table 3). There were no complications during intubation.

The incidence of muscle rigidity was similar between the two groups (Table 3).

The ratio of patients experiencing no cough at intubation was higher in group II than in group I (95% versus 60%, p=0.008), (Table 3).

The ratio of patients experiencing no cough after the cuff inflation was higher in group II than in group I (90% versus 60%, p=0.028), (Table 3).

The incidence of sore throat was similar between the two groups (Table 3).

Time required for BIS to be smaller than 60 was shorter in the group II than in group I (47.1±27.2 sec versus 111.9±60.6 sec, p=0.000) (Table 3).



End-tidal CO<sub>2</sub> concentrations at the first and second minutes of the induction showed no differences between the groups (Table 4).

In group I, end-tidal sevoflurane concentration at the first, second and third minutes of the induction and 1 min after intubation were 4.8±2.0, 4.5±2.1% and 2.7±1.1% respectively.

## DISCUSSION

In this study, Propofol offered successful intubating conditions in 100% of the patients within 47.1 seconds while sevoflurane provided successful intubating conditions in 80% of the patients within 111.9 seconds. No cough experience ratio was higher in propofol receiving patients than sevoflurane receiving patients. Propofol offered better intubating conditions than sevoflurane and shortened the anesthesia induction period.

We used BIS monitorization to detect anesthesia depth during the induction, and we could intubate patients as soon as BIS became smaller than 60. The monitorization of BIS shortened the anesthesia induction period compared to the previous studies using propofol-remifentanyl combination for intubation without muscle relaxants.<sup>1,9-11</sup> In these studies, the intubation was attempted at least 90 seconds after the hypnotic administration. BIS monitorization was also used in the study conducted by Hanna et al., where the authors investigated the effects of rapid sequence propofol and remifentanyl induction on intraocular pressure.<sup>12</sup> They administered remifentanyl after the decrease of BIS below 60 following propofol injection, and they performed the intubation 60 seconds after the administration of remifentanyl. They obtained excellent or good intubating conditions in 87% of the patients. As we used a simultaneous infusion of propofol and remifentanyl, we could successfully intubate 100% of the patients after an apparently shorter induction period.

Propofol is suggested to be the agent of choice for intubation without muscle relaxants because of its significant myorelaxant properties on pharyngeal and laryngeal structures.<sup>13</sup> Although sevoflurane has intrinsic muscle relaxant properties, we had better intubating conditions with propofol than sevoflurane, and that made us think that propofol may have stronger laryngo-pharyngeal myorelaxant effect than sevoflurane.<sup>9</sup>

Although the induction of anesthesia with a volatile agent is common in pediatric patients, sevoflurane's low blood solubility in combination with its nonpungency makes possible mask induction of anesthesia in adults. In the present study, the end-tidal sevoflurane concentration just before intubation was 4.47%, strongly higher than the concentration determined by Cros et al. (2.5%), but it is well comparable with the concentration determined by Joo et al. (4.3%).<sup>9,14</sup> The mask end-tidal concentrations of sevoflurane just before successful tracheal intubations were 5.6% and 5.1% for the sevoflurane/oxygen and sevoflurane/nitrous oxide inhalations respectively.<sup>8</sup> Kimura et al. determined MAC<sub>ei</sub> (endotracheal intubation) for a 50% nonresponse to intubation as 4.5%.<sup>15</sup>

Trabold et al. and Joo et al. suggested that intubating conditions are better when remifentanyl is injected after propofol, due to decreased risk of stiff chest and hypoventilation.<sup>9,16</sup> In the present study, remifentanyl was accompanied by a simultaneous infusion of propofol or an inhalation of sevoflurane. The ratio of patients showing no muscle rigidity was 70% and 85% for group I and II consecutively, while Joo et al. encountered no muscle rigidity in 44% of their patients.<sup>9</sup> The pretreatment with diazepam and slow administration of remifentanyl probably prevented muscle rigidity in the present study.

Higher number of patients with acceptable intubation conditions are obtained by increasing the remifentanyl dose. However, the higher dose of remifentanyl also results in a greater decrease in mean arterial pressure.<sup>9</sup> Although remifentanyl is associated with bradycardia or hypotension, or both in 50% of healthy patients during anesthetic induction and intubation, its bradycardic effect can be avoided with the pretreatment with anticholinergic agents.<sup>10,17,18</sup> We did not observe severe bradycardia in the absence of atropine pretreatment. It is probably related to shorter induction of anesthesia.

While Mencke et al. suggest that intubation without muscle relaxants may result in more laryngeal damage, the results of the study conducted by Baillard et al. revealed no difference between intubation with and without muscle relaxants concerning postoperative sore throat and vocal cord sequelae.<sup>19,20</sup> Bouvet et al. highlighted that tracheal intubation without muscle relaxants may be efficiently and safely performed when both large doses

of opioids and small endotracheal tubes are used.<sup>21</sup> We chose to use small endotracheal tubes (7.0 mm for women and 8.0 mm for men) in order to prevent laryngeal damage. The ratio of patients free of sore throat was 70% and 57.5% respectively for sevoflurane and propofol groups.

A limitation of the study is the impossibility of the blindness of the intubating anesthetist because of the residual smell of sevoflurane and white intravenous agent in the intravenous tubing.

In conclusion, under BIS monitorization, propofol-remifentanyl combination offered better intubation conditions than sevoflurane-remifentanyl and shortened the anesthesia induction period.

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