Comparison of the Effects of Combinations of Propofol with Alfentanil, Remifentanil and Sevoflurane-Nitrogen Protoxide on Laryngeal Mask Airway-Classical Insertion

Propofol ile Alfentanil, Remifentanil ve Sevofluran-Azot Protoksit Kombinasyonlarının Klasik Laringeal Maske Yerleştirilmesi Üzerine Etkilerinin Karşılaştırılması

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ABSTRACT Objective: Many studies have been conducted about the anesthesia methods providing optimal conditions for laryngeal mask airway (LMA) insertion. The purpose of the present study was to compare the effects of alfentanil, remifentanil and sevoflurane, co-administered with propofol, on LMA-Classic insertion. **Material and Methods:** After obtaining Faculty Ethics Committee approval and patients' written consents, 60 patients aged 18-70 years, ASA physical status I-III, undergone minor surgical procedures, have been included in the study. Patients were randomized into three groups (n=20). Propofol + alfentanil (Group PA), propofol + remifentanil (Group PR) and propofol + sevoflurane + nitrogen protoxide (Group PS) combinations were administered to groups 1, 2 and 3 respectively. In the first two groups LMA-Classic was inserted 2 minutes after anesthesia induction, and in PS group after end-tidal sevoflurane MAC value reached to 2%. Ease of insertion was graded according to a three-point scale. Grade 1-excellent, Grade 2-acceptable; Grade 3-poor. Additionally for each patient, LMA-Classic insertion attempt number was also recorded. Heart rate, arterial blood pressure, oxygen saturation and end-tidal carbondioxide value were recorded preoperatively, after induction and following LMA-Classic insertion. **Results:** In PR group, Grade 1 ease of insertion was found significantly greater than the other groups. The number of patients that single attempt is adequate for LMA-Classic insertion was significantly greater in PR and PS groups. Minimal hemodynamic changes have been observed in PS group. **Conclusion:** In propofol-remifentanil group, classical laryngeal mask insertion was easier and the success rate of first attempt was higher. Besides we concluded that propofol-sevoflurane combination provides optimal hemodynamic conditions for LMA-Classic insertion.

Key Words: Propofol; laryngeal masks; alfentanil; remifentanil

ÖZET Amaç: Laringeal maske (LM) yerleştirilmesi için optimal koşulları sağlayan ajanı bulmak üzere bugüne kadar birçok çalışma yapılmıştır. Bu çalışmada; elektif minör cerrahi operasyonlarında propofole ilave edilen alfentanil, remifentanil ve sevofluranın klasik LM yerleştirilmesi sırasındaki etkilerinin karşılaştırılması amaçlanmıştır. **Gereç ve Yöntemler:** Yerel Etik Komite onayı alınarak, ASA I-III grubunda, 18-70 yaş arasında, klasik LM yerleştirilmesine uygun minör cerrahi işlem uygulanacak 60 hasta çalışmaya dahil edildi. Hastalar randomize olarak 3 gruba (n=20) ayrıldı. Birinci gruba propofol + alfentanil anestezisi (Grup PA), 2. gruba propofol + remifentanil anestezisi (Grup PR) ve 3. gruba ise propofol + sevofluran + azot protoksit anestezisi (Grup PS) uygulandı. İlk iki gruba anestezi indüksiyonundan 2 dakika sonra hastaya uygun bir klasik LM yerleştirildi. PS grubunda ise inspiratuar ve ekspiratuar azot protoksit ve sevofluran yüzdeleri takip edildi ve sevofluranın end-tidal MAK değeri %2'ye ulaştığında klasik LM yerleştirildi. Klasik laringeal maske yerleştirilmesi Seviye-1 (mükemmel, LM), Seviye-2 (kabul edilebilir) ve Seviye-3 (kötü) şeklinde derecelendirildi ve kaydedildi. Ayrıca her hasta için klasik LM girişim sayısı kaydedildi. Hastaların preoperatif dönem, indüksiyon sonrası ve klasik LM yerleştirilmesi sonrası dönemlere ait kalp atım hızı, kan basıncı, soluk sonu karbondioksit basıncı değerleri kaydedildi. **Bulgular:** Grup PR'de Seviye 1 klasik laringeal maske yerleştirme kolaylığı diğer gruplardan anlamlı olarak daha yüksek bulunmuştur. İlk girişimde başarılı klasik laringeal maske yerleştirilen hasta sayısı PR grubunda PS grubundan anlamlı olarak daha yüksekti. PS grubunda minimal hemodinamik değişiklikler gözlendi. **Sonuç:** Klasik laringeal maske yerleşimi propofol-remifentanil verilen grupta daha kolay ve ilk girişimde başarı oranı daha yüksek bulunmuştur. Ayrıca propofol-sevofluran kombinasyonunun hemodinamik parametreler bakımından optimal koşulları sağladığı kanısına varılmıştır.

Anahtar Kelimeler: Propofol; laringeal maskeler; alfentanil; remifentanil

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The airway management is one of the principal subjects of the anesthesiology practice. Although the use of tracheal intubation and oxygen masks has been the standard method with widespread acceptance for long years, the search for a better alternative in terms of efficiency, safety and side-effect profile still continues. One of the important corner stones of this developmental process is the introduction of the laryngeal mask to the daily clinical practice. Having a distal cuff that functions as a plug around the laryngeal entrance, the laryngeal mask airway is basically a fenestrated tube lodged in the supraglottic airway. It is a ventilation device constituting an alternative option to the oxygen mask and the endotracheal tube. Some of its features, including the ease of its placement in the presence of a difficult intubation and in patients with unsuccesful ventilation attempts with masks; the absence for any muscle relaxant requirement and the relatively lower risk of bronchospasm associated with the laryngeal mask makes it an appropriate option.[1]

The placement of the laryngeal mask necessitates the provision of a sufficient oral aperture length and the supression of the upper airway reflexes including cough, laryngeal gag and laryngospasm.[2] Thus until today many studies have been conducted in search of the best agent providing the optimal conditions for LMA placement.[3] In these studies it has been shown that the amount of time necessary for LMA placement was shorter with intravenous anesthetics than inhalational ones. For this reason usually intravenous anesthetics are preferred for LMA insertion. Among these agents propofol is applied more frequently than others, owing to its supressing effect on airway reflexes.[4] Opioids and muscle relaxants are added to this application in order to reduce the propofol dosage and its dose-related side effects.[5,6] Among the opioid agents alfentanil and remifentanil were reported to have faster onset of action and to improve the tolerance of LMA.[7] Sevoflurane is an anesthetic agent with a low blood/gas distribution coefficient, which is better tolerated than other inhalational anesthetics due to the fact that it causes no irritation on the respiratory tract.

The aim of this study is to compare the effects of alfentanil, remifentanil and sevoflurane during the insertion of the LMA, which are added to propofol in elective minor surgical interventions.

MATERIAL AND METHODS

Following the approval of the Ethics Committee, 60 patients, aged between 18-70 years, ASA I-III, undergoing minor surgical intervention suitable for LMA-Classic were included to the study. This study was conducted according to the basic principles of the 2008 Helsinki Declaration. Patients were randomly assigned into three groups (n=20). Patients with known cardiac, pulmonary, renal and hepatic disorders, history of neurological disease, dementia, depression, chronic alcohol or drug abuse, fluid-electrolyte imbalance and gastroesophageal reflux disease were excluded from the study protocol.

All patients were informed about the method and technique before the surgery and written consents were obtained. The first group received anesthesia with propofol + alfentanil (Group PA), the second group with propofol + remifentanil (Group PR) and the third group with propofol + sevoflurane + nitrogen protoxide (Group PS). The induction of anesthesia was achieved with propofol 2.5 mg kg^{-1} iv in all patients. The injection of propofol and other medications was completed in 90 seconds. The group PA patients received 10 μg kg^{-1} alfentanil iv. bolus dose. Patients in group PR received remifentanil 0.5 μg kg^{-1} iv bolus dose followed by 0.2 μg kg^{-1} min^{-1} remifentanil infusion. While the patients of groups PA and PR were ventilated with 67% air and 33% oxygen during and following the induction of anesthesia, Group PS received 2% sevoflurane with 67% N_2O and 33% oxygen during the induction of anesthesia. The tidal volume was adjusted as 8-10 mL kg^{-1}. In groups PA and PR two minutes following the induction of anesthesia an appropriate size of LMA-Classic was placed to each patient according to the user's manual. Whereas in Group PS the inspiratory and expiratory ratios of nitrogen protoxide and sevoflurane were monitorized and a LMA-Classic was placed, once the end-tidal MAC

value of sevoflurane reached 2%. No muscle relaxant agent was used in this study. In all patients heart rate, arterial blood pressure (diastolic, systolic and mean arterial pressure), peripheral oxygen saturation and end-tidal carbondioxide levels were recorded just before the intervention, during the induction, 2 minutes following the induction, during the LMA-Classic placement and 1, 2 and 5 minutes afterwards. Patients having a heart rate of less than 45 beat min^{-1} received 0.5 mg atropine iv while patients detected with mean arterial blood pressure level below 55 mmHg received 10 mg ephedrine iv.

The insertion of the laryngeal mask was rated as Grade 1 (excellent; without any response while inserting the LMA-Classic), Grade 2 (acceptable; gagging, coughing or swallowing during LMA-Classic insertion) and Grade 3 (poor; inability to open the mouth or biting the LMA-Classic) and recorded. Also the number of insertion attempts were recorded for each patient. Heart rate, diastolic, systolic and mean arterial blood pressure, peripheral oxygen saturation and end-tidal carbondioxide value were recorded preoperatively, at anesthesia induction, second minutes after induction, at LMA-Classic insertion, and at first, second and fifth minutes after insertion.

STATISTICAL ANALYSIS:

The sample size was calculated based on the grading for the insertion of the laryngeal mask airway. Power analysis identified 19 patients per group as the total sample size required to detect a 30% difference between groups with a power of 80% (alpha: 0.05 and beta: 0.2). The difference of 30% was identified from both clinical experience and pilot study.

SPSS (Statistical Package for the Social Sciences) Windows version 15.0 software was used for the statistical analysis. Repeated measurements for comparisons between groups were performed with Anova test and Student-Newman-Keuls multiple comparison test. One way analysis of variance was utilized for comparisons between groups. The rating of LMA was compared with Fisher's exact test and one way analysis of variance; the demographical data was analysed with unpaired T test. $P<0.05$ was considered statistically significant.

RESULTS

The comparisons of the patients according to age, body weight and ASA group classification revealed no significant difference between the three groups ($p>0.05$) (Table 1). In all three groups the systolic blood pressure values measured after the induction phase were found to be significantly lower than the preoperative levels ($p<0.001$, Table 2).

The comparison of the groups revealed that the greatest decline in systolic blood pressure level occured on the 2nd minute; in the sevoflurane group the systolic blood pressure values measured on the 2nd minute and during the LMA-Classic insertion were found to exhibit a lesser degree of decline compared to the other groups and the biggest decrease was observed in the remifentanil group ($p=0.021$). The post-induction diastolic blood pressure levels measured in all groups were found to be significantly lower than the preoperative values ($p<0.001$, Table 3).

The comparison of the groups revealed that the greatest decline in diastolic blood pressure level occured on the 2nd min; in the sevoflurane group the diastolic blood pressure values measured on the

TABLE 1: Patients demographics (mean ± SD).

	Group PA	Group PR	Group PS
Gender (female/male)	6 (30%) /14 (70%)	8 (40%) /12 (60%)	11 (55%) /9 (45%)
Age (years)	51.94 ± 14.20	53.75 ± 14.10	52.95 ± 14.03
Weight (kg)	76.73 ± 13.79	76.60 ± 13.58	71.30 ± 12.42
ASA I-II-III patients (number)	20	20	20

ASA: American Society of Anesthesiology; Group PA: Propofol + alfentanil; Group PR: Propofol + remifentanil, Group PS:Propofol + sevoflurane.

TABLE 2: Systolic blood pressure (mmHg) (mean±SD).

	Group PA	Group PR	Group PS
Preoperative period	135.00±14.06*,#	150.80±17.68&,$	142.20±19.16£
Immediately after induction	110.63±17.96*,#	127.11±24.21&,$	116.75±16.14
2. min after induction	93.84±11.98*	105.40±18.83&	105.15±25.92£
During LMA-Classic placement	100.00±15.72#	109.05±21.84$	117.35±20.76£
1 min after LMA-Classic placement	102.42±13.03	108.35±18.47	115.80±20.79
2 min after LMA-Classic placement	104.89±13.09	112.25±17.15	111.50±18.90
5 min after LMA-Classic placement	102.74±11.27	108.45±15.44	110.65±16.39

*,#,&,$,£: p<0.001, between groups

LMA: Laryngeal mask airway; Group PA: Propofol + alfentanil; Group PR: Propofol + remifentanil; Group PS: Propofol + sevoflurane

TABLE 3: Diastolic blood pressure (mmHg) (mean ± sd).

	Group PA	Group PR	Group PS
Preoperative period	81.95±8.74*	86.75±12.81&,$	89.20±9.81£
Immediately after induction	69.05±12.43	71.00±13.37&,$	74.85±10.28
2. min after induction	57.31±10.74*	60.70±13.10&	73.00±11.92£
During LMA-Classic placement	64.69±13.09*	62.35±14.70$	77.95±13.94£
1 min after LMA placement	65.69±12.60	61.90±12.89	72.90±14.62
2 min after LMA-Classic placement	63.26±8.82	63.85±14.72	70.10±12.46
5 min after LMA-Classic placement	63.68±10.34	60.55±13.19	68.95±12.10

*,#,&,$,£: p<0.001, between groups

LMA: Laryngeal mask airway; Group PA: Propofol + alfentanil; Group PR: Propofol + remifentanil; Group PS: Propofol + sevoflurane

2nd min and during the LMA-Classic insertion were found to exhibit a lesser degree of decline compared to the other groups and the highest decrease was observed in the remifentanil group (p=0.012). The post-induction mean arterial blood pressure levels measured in all groups were found to be significantly lower than the preoperative values (p<0.001, Table 4).

The greatest decline in mean arterial blood pressure levels was observed on the 2nd min in the propofol-alfentanil and propofol-remifentanil groups and on the 5th min following LMA-Classic insertion in propofol-sevoflurane group. In the sevoflurane group the mean arterial blood pressure values measured on the 2nd min and during the LMA-Classic insertion were found to exhibit a

TABLE 4: Mean arterial blood pressure (mmHg) (mean ± sd).

	Group PA	Group PR	Group PS
Preoperative period	99.63±9.28*,#	108.11±13.59&,$	106.87±11.60£
Immediately after induction	82.91±12.99*	89.70±15.54&,$	88.82±9.91
2. min after induction	69.48±10.19*	75.58±14.56&	83.72±12.95£
During LMA-Classic placement	76.47±13,28#	77.91±16.53$	91.09±15.27£
1 min after LMA-Classic placement	77.92±11.97	77.38±13.97	87.20±16.02
2 min after LMA-Classic placement	77.14±9.37	79.99±14.89	83.89±13.19
5 min after LMA-Classic placement	76.70±9.86	76.51±13.34	82.85±12.39

*,#,&,$,£: p<0.001, between groups

LMA: Laryngeal mask airway; Group PA: Propofol + alfentanil; Group PR: Propofol + remifentanil; Group PS: Propofol + sevoflurane

lesser degree of decline compared to the other groups and the biggest decrease was observed in the remifentanil group (p=0.011). In group PR the heart rate showed a statistically significant decline whereas in group PS it demonstrated a statistically significant increase (Table 5). The greatest decline in SpO_2 levels was observed in the alfentanil group, nevertheless this difference was statistically nonsignificant. Comparison of the $ETCO_2$ levels measured during the induction as well as other time points revealed no significant difference (p>0.05). In propofol-alfentanil group the convenience of LMA-Classic insertion was rated as Grade 2 in 6 patients and Grade 1 in 14 patients. Five of the patients rated as Grade 2 exhibited hiccups while one patient experienced cough. In the propofol-remifentanil group 19 patients were rated as Grade 1 while only one patient was rated as Grade 2, who demonstrated hiccups. In the propofol-sevoflurane group 16 patients were categorized as Grade 1 and 4 patients as Grade 2. Those patients classified as Grade 2 experienced hiccups as well.

In propofol-alfentanil group the insertion of LMA-Classic was significantly more difficult than the propofol-remifentanil group (p<0.05). Comparison of the propofol-alfentanil and propofol-remifentanil groups with propofol-sevoflurane group revealed no significant difference (p>0.05). The three groups were also compared regarding the quantity of LMA-Classic intervention attempts.

Following the analysis of the peroperative complications as a whole, one noticeable event was a patient in propofol-remifentanil group who had a mean arterial blood pressure measurement below 55 mm Hg and received 10 mg iv ephedrine as a consequence. Apart from this incidence no other complication or unwanted side-effect was observed. LMA-Classic was placed succesfully in all of the patients. No any complication was encountered during the wake-up or the postoperative recovery period. In order to prevent the emergence of application-related differences, in all of the subjects the application of anesthesia and the insertion of LMA-Classic was performed by the same researcher.

DISCUSSION

In this study designed to compare the effect of alfentanil, remifentanil and sevoflurane combined to propofol on LMA-Classic insertion we have detected that, compared with the propofol-alfentanil and the propofol-remifentanil groups, the propofol-sevoflurane-N_2O combination facilitates the LMA placement better and provides anesthesia under appropriate conditions. There are many studies in the literature dealing with the LMA insertion and the determination of the required doses of the medications given. For example Goyagi et al.[8] demonstrated that fentanyl 2 μg kg^{-1} combined to propofol provided a 60% decrease in the propofol dosage yet they also encountered significantly prolonged respiratory supression. They have attributed this respiratory supression to the synergistic effect of propofol and fentanyl combination. In our study the respiratory supression or the duration of the apnea interval was not

TABLE 5: Heart rate (beat min^{-1}) (mean ± sd)

	Group PA	Group PR	Group PS
Preoperative period	78.68 ±15.13*	85.90 ± 18.68&,$	83.75 ± 9.73£
Immediately after induction	83.16 ± 12.710	83.20 ± 18.42&,$	94.30 ± 12.70
2. min after induction	79.21 ± 16.68	75.10 ± 17.1&	96.05 ± 13.39£
During LMA-Classic placement	79.00 ± 15.90	73.45 ± 14.76$	96,30 ± 16.86£
1 min after LMA-Classic placement	77.16 ± 17.65	73.55 ± 16.57	93.35 ± 16.55
2 min after LMA-Classic placement	72.26 ± 11.53*	71.80 ± 15.91	92.55 ± 16.83
5 min after LMA-Classic placement	73.32 ± 11.71	69.65 ± 15.97	91.65 ± 17.54

*,#,&,$,£: p<0.001, between groups

LMA: Laryngeal mask airway; Group PA: Propofol + alfentanil; Group PR: Propofol + remifentanil; Group PS: Propofol + sevoflurane

evaluated in the group of patients receiving 2.5 mg kg^{-1} propofol and 10 μg kg^{-1} alfentanil. Tan and Wang[9] also studied fentanyl and concluded that 1.0 mcg kg^{-1} as the optimal dose of fentanyl when used in addition to propofol 2.5 mg/kg for the insertion of the classic LMA. Besides, Yöndem et al.[10] declared that magnesium sulphate facilitates the insertion of LMA and reduces the pain on injection of propofol. In another study, it was revealed that the ideal conditions for LMA placement was achived with alfentanil, which is a short acting opioid.[11] The investigators indicated that the analgesic effect of the opioid agent combined to the antitussive effect of propofol was the primary reason of this finding. In our study it was obvious that this effect, which is an expected result in the opioid groups, can not be achieved in the propofol-sevoflurane group. On the other hand, Yazicioglu et al.[12] have investigated various doses of remifentanil combined to propofol and reported serious respiratory depression in additon to reduced levels of blood pressure and heart rate, although the latter two measurements were found to be clinically non-significant. The reason for the respiratory depression was indicated as the muscular rigidity. In parallel with this findings similar significant reductions were also observed in hemodynamical variables including blood pressure and heart rate in the propofol-remifentanil group of our study. Nevertheless the relaxation of the jaw muscles was not included in the parameters being evaluated in the study. For that reason it would be a useful idea to analyze these parameters in future with similar studies.

For LMA insertion intravenous and inhalational anesthetics were utilized in a great variety of combinations. In our study the propofol-sevoflurane group most facilitated the placement of LMA. This finding is supported by the results of various other studies as well. Siddik-Sayyid et al.[3] compared sevoflurane, propofol and sevoflurane-propofol combination during LMA placement and found out that the success rate of LMA insertion on the first attempt was higher with the sevoflurane-propofol combination. They have suggested that this finding was caused by the fact that sevoflurane induces rigidity of the jaw muscles and propofol leads to jaw laxity; additionally at higher MAC levels sevoflurane supresses laryngeal reflexes. Ti et al.[13] also compared propofol with propofol-sevoflurane combination and concluded in their study that the combination of propofol with sevoflurane facilitated LMA placement more profoundly than the other agents. They suggested a more softer transition to the maintenance phase with sevoflurane as the reason for this finding. Similarly in our study the most succesful group regarding the LMA insertion on the first attempt was the propofol-sevoflurane group. The best group based on the rating of the LMA placement was the propofol-remifentanil group. The rating of LMA and the number of attempts revealed no correlation. Among the patients classified as LMA Grade 2 and the patients in which LMA was placed on the second attempt the body weight of the patients and the difficulty of LMA placement also revealed no correlation, because only two of them were patients having heavier body weight than normal limits.

In our study LMA was placed 120 seconds after the administration of the drugs, which represented the time interval for remifentanil and alfentanil to reach their peak effects. The depth of anesthesia during LMA insertion affects the general conditions related to the insertion procedure.

The comparison of groups for blood pressure and heart rate variations revealed that the greatest reduction in heart rate was observed in the propofol-remifentanil group whereas in the propofol-sevoflurane group there was not a decline but an increase in heart rate. Taking the grade of LMA insertion and the number of attempts into account, these variations in the hemodynamic data suggest that in the propofol-sevoflurane group LMA placement was achieved under better conditions and through an easier way. On the other hand, Al-Qattan et al.[14] showed in their study that in the alfentanil and remifentanil groups the average arterial pressure exhibited significant reductions yet these reductions represented no significant difference between the two groups.

The comparison of groups for end-tidal carbondioxide pressure and oxygen saturation revealed no significant difference. None of the

patients demonstrated a movement in an extremity or any other motion during the insertion of LMA. This fact proved that the dosages of propofol and other agents were sufficient for LMA placement.

STUDY LIMITATIONS

Some of the limitations of this study deserve mentioning. First of all, our study lacks a control group where propofol is used by its own. As it has been reported in several previous studies, single-handed propofol usage proved ineffective for LMA placement and a dose augmentation in order to provide necessary conditions for its actions was regarded to be unsafe owing to its detrimental effect on the hemodynamic functions and the suppression of the ventilation; thus in this study we have decided not to include a control group with propofol alone. The fact that most of the patients belonged to the groups ASA I and II whereas only one patient represented the group ASA III made the evaluation of the hemodynamic responses in the ASA III patients unfeasible. Nevertheless this study mainly dealed with the convenience of LMA insertion thus it is believed that the ASA classification possessed little significance other than the evaluation of the hemodynamic variables. In this study the depth of anestesia was not evaluated yet LMA insertion started after a latent period of 120 seconds. New and similar studies can be designed to evaluate the depth of anesthesia with BIS utilizaton and to compare the effect of the depth of anesthesia on LMA placement. Another weakness of our study was the lack of the cost-effectiveness analysis between the groups. Because in some studies comparing propofol with sevoflurane it was reported that regarding the cost-effectiveness profile sevoflurane demonstrated a superiority over the other groups.[13]

CONCLUSION

In the current study three different agents combined to propofol were compared with each other. The results of this study suggest that based on the convenience of LMA insertion and the effects on the hemodynamic parameters the anesthesia with propofol-sevoflurane-nitrogen protoxide combination confers a superiority over the alternative agents for LMA placement.

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