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RESEARCH ARTICLE

Comparison of the efficacy of esmolol and lidocaine in the control of hemodynamic response associated with intubation: A randomized controlled trial

Entübasyona bağlı hemodinamik yanıtın kontrolünde esmolol ve lidokainin etkinliğinin karşılaştırılması: Randomize kontrollü çalışma

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ABSTRACT

Objectives: The purpose of this randomized study is to compare the effects of esmolol and lidocaine in the control of hemodynamic response caused by endotracheal intubation.

Methods: In this study, 40 patients with ASA I-II physical status and between the ages of 19 and 76 were included and randomly divided into two groups. In the Group E (n = 20), iv bolus injection of 1.5 mg/kg esmolol, in the Group L (n = 20), iv bolus injection of 1.5 mg/kg 2% lidocaine were given with iv bolus injection in 30 seconds. All patients received the same anesthetic technique. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) and heart rate measurements were done at specified times and recorded. Records were assessed by an anesthesiologist blinded to which drug is applied.

Results: There was no difference between the groups in demographic data (p>0.05). In both groups, with the implementation of the study drug, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure decreased compared to controls, this reduction was lower in Group E than Group L. In Group L, SBP values of 1.5 and 7 minutes were higher than Group E (p <0.05). In Group L, DBP and MBP values of 1.5 and 3.5 minutes were higher than Group E (p <0.05).

Conclusion: In conclusion, 1.5 mg/kg esmolol or 1.5 mg/kg lidocaine administered prior to induction were not superior to each other regarding suppression of hemodynamic responses to intubation. *J Clin Exp Invest 2013; 4 (1): 20-27*

Key words: Esmolol, lidocaine, intubation, hemodynamic response

ÖZET

Amaç: Bu randomize çalışmanın amacı endotrakeal entübasyonun neden olduğu hemodinamik yanıtın kontolünde esmolol ve lidokainin etkilerini karşılaştırmayı amaçlamaktır.

Yöntemler: Bu çalışmaya ASA I-II olan 19 ve 76 yaşları arasında 40 hasta dâhil edildi. Rastgele olarak iki grubuna ayrıldı. Grup E' ye (n=20) 1,5 mg/kg esmolol, Grup L'ye (n=20) 1.5 mg/kg %2 lidokain i.v bolus olarak 30 saniyede anestezist tarafından uygulandı. Tüm hastalara aynı anestezi tekniği uygulandı. Sistolik kan basıncı (SKB), diastolik kan basıncı (DKB) ve ortalama kan basınçları (OKB) ile kalp atım hızı için belirlenen zamanlarda ölçümler yapılarak kaydedildi. Bu ölçümler ve daha sonra yapılan değerlendirmeler, hangi ilacın uygulandığını bilmeyen bir anestezist tarafından gerçekleştirildi.

Bulgular: Gruplar arasında demografik veriler açısından fark bulunmadı (p>0.05). Her iki grupta da çalışma ilacının uygulanmasıyla kalp atım hızı, sistolik kan basıncı, diyastolik kan basıncı ve ortalama kan basıncı düzeylerininin kontrol değerlerine göre azaldığını, bu azalmanın Grup E' de daha belirgin olduğunu ve Grup L' ye göre düşük bulundu. Grup L' nin 1,5 ve 7. dakika SKB değerleri Grup E' ye göre daha yüksek bulundu (p<0.05). Grup L' nin 1,5 ve 3,5 dakika DKB ve OKB değerleri, Grup E' ye göre yüksek bulundu (p<0.05).

Sonuç: Çalışmamızda indüksiyon öncesinde uygulanan 1.5 mg/kg esmolol veya 1.5 mg/kg lidokainin entübasyona hemodinamik yanıtı baskılamada birbirlerine göre üstünlükleri olmadığını kanısına varıldı.

Anahtar kelimeler: Esmolol; lidokain; entübasyon; hemodinamik yanıt

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INTRODUCTION

In general anesthesia applications, the control of airway with laryngoscopy and intubation often causes a reflex response in the respiratory and cardiovascular system.[1,2] The release of catecholamines with the increase in sympathetic activity causes increase in blood pressure and heart rate and arrhythmias.[3] This response may cause aggravate the existing pathology and even life-threatening complications in the patients with coronary heart disease and cerebrovascular disease and hypertension.[1,3] During intubation, an increase in heart rate and systemic blood pressure, as well as an increase in pulmonary blood pressure and pulmonary wedge pressure occur. This situation raises the risk of pulmonary edema and cardiac failure. In addition, the increase of the intracranial pressure increases the risk of cerebral hemorrhage.[4]

There are some factors influencing the severity of the reflex response to laryngoscopy and intubation . These are; the depth and duration of anesthesia, the patient's age, the history of diabetes and heart disease. Different drugs may use for the control of haemodynamic response caused by laryngoscopy and intubation. Among these drugs, narcotic analgesics, anesthesia performed via inhalation, local anesthetics, beta-blockers, calcium channel blockers, vasodilators, and magnesium are available.[5-7]

Esmolol is a rapid onset with a short-term effect beta-1 selective (cardioselective) adrenoceptor blocker. Distribution half-life of after intravenous infusion is 2 minutes, the elimination half-life is approximately 9 minutes. Esmolol can be titrated at the level of a complete beta-blocking effects quickly and if it is necessary, turned down quickly. The beta-1 effects of esmolol continues during the infusion. After termination of the infusion, in 10 to 20 minutes, the beta-blocking dissapears. All hemodynamic parameters return to normal in 30 minutes after discontinuation of infusion. Due to these features, esmolol may be a useful agent preferred in the immediate control of heart rate and blood pressure.[8] Esmolol is indicated for induction, tracheal intubation and in cases of tachycardia and hypertension during surgery, tachycardia, and hypertension in recovery of anesthesia and post-operative period. In this study, we aimed to compare the effects of esmolol and lidocaine in the control of hemodynamic response caused by endotracheal intubation.

METHODS

For this study which was planned as a prospective, randomized, double-blind study, the consent of the local ethics committee and informed patient consents were taken. In this study who were admitted to Haseki Educational And Research Hospital of Anesthesiology outpatient clinic, 40 patients with ASA I-II physical scores, between the ages of 19 and 76, requiring endotracheal intubation whose elective surgery was planned in the supine position were included. The patients with cardiovascular, pulmonary, hepatic, renal, neurologic, allergic, endocrine, and intracranial vascular pathology (aneurysm, AV malformation, etc.), pregnant women, nursing mothers, patients with addiction of alcohol and drugs, the patients using beta-adrenergic blockers, antihypertensive, sympathomimetic, calcium channel blockers, MAO inhibitor and the patients with contraindications for the use of beta-blocker were excluded from the study. In addition, the patients whose orotracheal intubation could not be performed less than 30 seconds and in one-time, or the patients that the complications related to intubation were observed in, the patients with heart rate less than 50 beats / min or more than 100 beats / minute, blood pressure less than 90/60 mmHg or more than 180/100 mmHg were excluded from the study.

All patients were fasted for eight hours and no premedication was given. For the patients taken to the operating table, 10 mL / kg / h infusion of 0.9% NaCl was started by opening vascular access with 20 G intravenous cannula on the right hand. Standart monitoring was performed with PETAS KMA 260R (İstanbul,Turkey) monitor. The values before induction of the patients such as systolic (SBP) and diastolic (DBP), mean (MBP) blood pressure, and heart rate (HR) were recorded as baseline value.

Patients were separated into two study groups by performing randomization with sealed envolope method. For Group E (n = 20) 1.5 mg / kg esmolol, for Group L (n = 20) 1.5 mg / kg of 2% lidocaine were given with iv bolus injection in 30 seconds. Measurements and records were assessed by an anesthesiologist blinded to which drug is applied. Following the administration of the drug i.v. thiopental sodium 6 mg / kg i.v. in 45 seconds and vecuronium bromide 0.1 mg / kg in 15 seconds was injected. Ventilation of patients during induction was achieved with 100% O_2. After waiting for the appropriate time, laryngoscopy and endotracheal intubation was performed by the same person. Anesthesia was maintained in all groups with 50% (2 l / min) O_2 and 50% (2 l / min) N_2O and 6% desflurane. When muscle relaxation was needed, 0.01 mg / kg iv vecuronium bromide was administered. During the operation, the position of the patients was not changed. Measurements in all groups were noted as baseline values, after the working agent and vecuronium bromide with sodium thiopental, after induction before intubation and after intubation at 1.5, 3.5, 5, 6, 7, 8, 9, 10, 13 and 15 minutes. After incision, the recording process continued after 5 minutes break. Side effects were recorded.

Statistical analysis

SPSS for Windows 10.0 statistical package program was used to analyze the datas. Student's t test for comparisons between groups and one-way analysis of variance and bonferonni tests for repeated measures within groups were performed. All datas were given as mean ± standard deviation (mean ± SD). $p < 0.05$ was considered statistically significant.

RESULTS

There was no statistical difference in terms of the distribution of mean age (respectively 44.4 ± 12.2, 45.2 ± 14.1) and gender (F / M, 11/9) between the two groups ($p > 0.05$).

SBP values of Groups L in 1.5 and 7 minutes were significantly higher than the values of Group E ($p < 0.05$). For the other times monitored, there was no difference between the groups in terms of systolic blood pressure values ($p > 0.05$, Table 1). SBP values of Groups L in 3.5, 13 and 15 minutes decreased significantly compared to the baseline values ($p < 0.05$). For the other times monitored, there was no difference compared to baseline values ($p > 0.05$). SBP values of Groups E in 1.5 and 3.5 minutes were significantly decreased compared to the baseline values ($p < 0.01$). For the other times monitored, there was no significant difference compared to baseline values ($p > 0.05$, Figure 1).

Table 1. Comparison of the groups in terms of systolic blood pressures

SBP	Lidocaine	Esmolol	p
Start	137.05 ± 15.25	134.8 ± 14.99	NS
1,5. min.	129.8 ± 16.44	118.3 ± 12.72	0.018*
3,5. min.	123.05 ± 17.26	116.15 ± 16.94	NS
5. min.	130.35 ± 15.18	127.6 ± 15.2	NS
6. min.	131.7 ± 17.48	131.8 ± 15.2	NS
7. min.	128.15 ± 13.23	138.2 ± 16.1	0.037*
8. min.	132.3 ± 10.31	134.5 ± 15.52	NS
9. min.	138.2 ± 16.64	131.9 ± 13.67	NS
10. min.	127.45 ± 11.75	128.95 ± 15.06	NS
13. min.	124.35 ± 9.41	124.15 ± 11.94	NS
15. min.	119.5 ± 10.84	126.4 ± 10.8	NS

Data are given as mean ± standard deviation.
SBP:Systolic Blood Pressure (mmHg), NS:Not significant, *: Significant difference
SBP values of Groups L in 1.5 and 7 minutes were significantly higher than the values of Group E ($p < 0.05$). For the other times monitored, there was no difference between the groups in terms of systolic blood pressure values ($p > 0.05$).

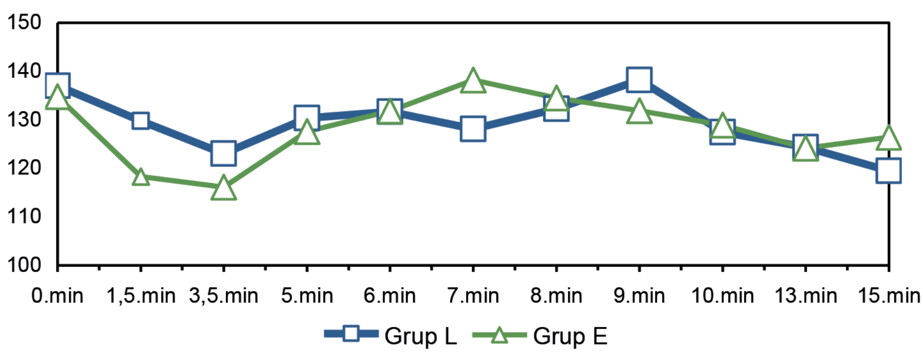

Figure 1. Temporal distribution of the average value of systolic blood pressure (mmHg)

DBP values of Group L in 1.5 and 3.5 minutes were significantly higher than the values of Group E ($p < 0.05$). For the other times monitored, there was no difference between the groups in terms of DBP values ($p > 0.05$, Table 2). DBP values of Group L in 10, 13 and 15 minutes decreased compared to baseline values ($p < 0.01$, $p < 0.001$). For the other times monitored, there was no significant difference compared to the baseline values ($p > 0.05$). DBP values of Group E in 1.5, 3.5, 13 and 15. minutes decreased compared to baseline values ($p < 0.05$, $p < 0.01$). For the other times monitored, there was no significant difference compared to the baseline values ($p > 0.05$, Figure 2).

Table 2. Comparison of the groups in terms of diastolic blood pressures

DBP	Lidocaine	Esmolol	p
Start	84.75 ± 5.72	84.05 ± 8.10	NS
1.5. min.	82.07 ± 10.60	75.45 ± 7.95	031*
3.5. min.	80.05 ± 9.57	73.25 ± 11.44	048*
5. min.	84.00 ± 10.11	83.25 ± 10.14	NS
6. min.	85.60 ± 10.78	81.85 ± 11.39	NS
7. min.	79.55 ± 9.01	84.65 ± 9.63	NS
8. min.	80.75 ± 7.22	81.45 ± 8.91	NS
9. min.	83.10 ± 10.11	79.40 ± 8.25	NS
10. min.	73.05 ± 12.01	78.65 ± 8.80	NS
13. min.	76.85 ± 6.83	75.50 ± 7.32	NS
15. min.	75.40 ± 6.75	75.15 ± 6.07	NS

Data are given as mean ± standard deviation.
DBP:Diastolic Blood Pressure (mmHg), NS:Not significant, *: Significant difference
DBP values of Group L in 1.5 and 3.5 minutes were significantly higher than the values of Group E (p <0.05). For the other times monitored, there was no difference between the groups in terms of DBP values (p> 0.05).

MBP values of Group L in 1.5 and 3.5. minutes were significantly higher than the values of Group E (p <0.05). MBP values of Group E in 7th minutes significantly higher than the values of Group L (p <0.05). For the other times monitored, there was no significant difference between the groups in terms of MBP values (p> 0.05, Table 3). MBP values of Group L in 3.5, 10, 13 and 15 minutes decreased compared to baseline values (p <0.01, p <0.00). For the other times monitored, there was no significant difference between the groups in terms of baseline values (p> 0.05). In Group E, mean blood pressure values in 1.5, 3.5, 13 and 15 minutes decreased compared to baseline values (p <0.05, p <0.01). For the other times monitored, there was no significant difference in terms of baseline values (p> 0.05, Figure 3).

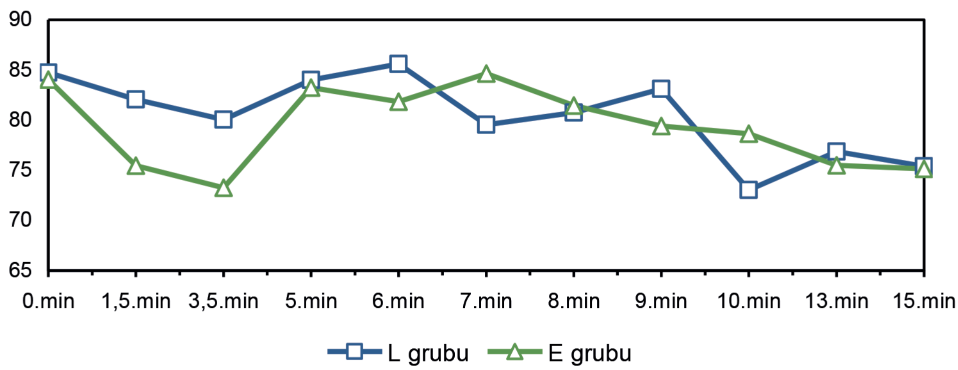

Figure 2. Temporal distribution of the average value of diastolic blood pressure (mmHg).

Table 3. Comparison of the groups in terms of mean blood pressures

MBP	Lidocaine	Esmolol	p
Start	102.18 ± 7.31	100.97 ± 9.54	NS
1.5. min.	97.98 ± 12.12	89.73 ± 9.13	020*
3.5. min.	94.38 ± 10.69	86.23 ± 12.73	035*
5. min.	99.45 ± 9.92	98.03 ± 10.91	NS
6. min.	100.97 ± 12.45	98.50 ± 10.92	NS
7. min.	95.75 ± 9.49	102.50 ± 11.19	047*
8. min.	97.93 ± 6.66	99.13 ± 10.39	NS
9. min.	101.47 ± 11.43	96.90 ± 9.29	NS
10. min.	91.18 ± 9.58	95.42 ± 10.02	NS
13. min.	92.68 ± 6.71	91.72 ± 7.66	NS
15. min.	90.10 ± 6.85	92.23 ± 5.75	NS

Data are given as mean ± standard deviation.
MBP:Mean blood pressure , NS:Not significant, *: Significant difference
MBP values of Group L in 1.5 and 3.5. minutes were significantly higher than the values of Group E (p <0.05). MBP values of Group E in 7th minutes significantly higher than the values of Group L (p <0.05). For the other times monitored, there was no significant difference between the groups in terms of MBP values (p> 0.05).

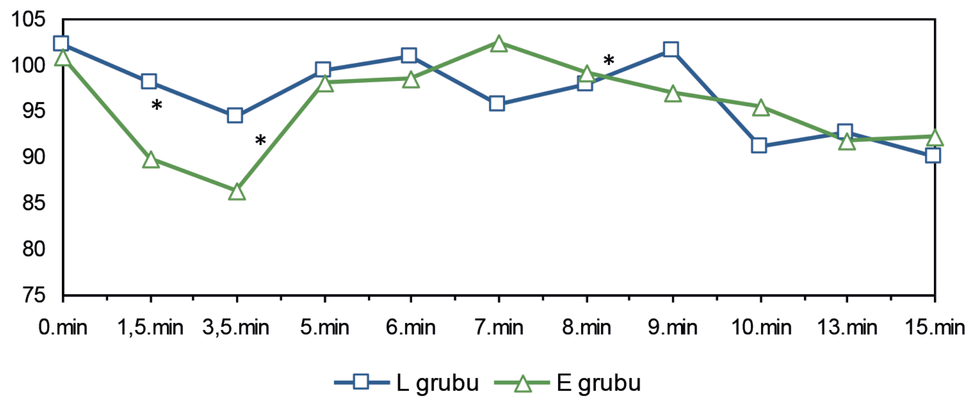

Figure 3. Temporal distribution of the average value of mean blood pressure (mmHg).

Heart rate values of Group E in 7 and 15 minutes were significantly higher than the values of Group L, p <0.05). For the other times monitored, there was no difference between the groups in terms of heart rate values (p> 0.05, Table 4). The heart rate values of Group L in 15 minutes decreased compared to baseline values (p <0.01, p <0.001). For the other times monitored, there was no significant difference between the groups in terms of baseline values (p> 0.05). The heart rate values of Group L in 1.5 and 3.5 minutes decreased compared to baseline values (p <0.05, p <0.01). For the other times monitored, there was no significant difference in terms of baseline values (p> 0.05, Figure 4).

Table 4. Comparison of the groups in terms of heart rate

HR	Lidocaine	Esmolol	p
Start	85.80 ± 12.67	85.54 ± 9.94	NS
1.5. min.	81.85 ± 12.72	75.30 ± 9.67	NS
3.5. min.	81.35 ± 12.23	74.65 ± 9.17	NS
5. min.	90.50 ± 10.14	86.85 ± 10.39	NS
6. min.	89.80 ± 14.61	92.85 ± 10.10	NS
7. min.	86.45 ± 11.12	94.05 ± 9.48	0.025*
8. min.	86.75 ± 11.12	91.03 ± 13.96	NS
9. min.	85.80 ± 10.56	88.05 ± 12.56	NS
10. min.	82.95 ± 6.33	86.25 ± 16.23	NS
13. min.	79.70 ± 6.04	82.40 ± 10.52	NS
15. min.	73.30 ± 5.98	82.50 ± 7.36	<0.001*

Data are given as mean ± standard deviation.
HR:Heart rate, NS:Not significant, *: Significant difference
Heart rate values of Group E in 7 and 15 minutes were significantly higher than the values of Group L, p <0.05). For the other times monitored, there was no difference between the groups in terms of heart rate values (p> 0.05).

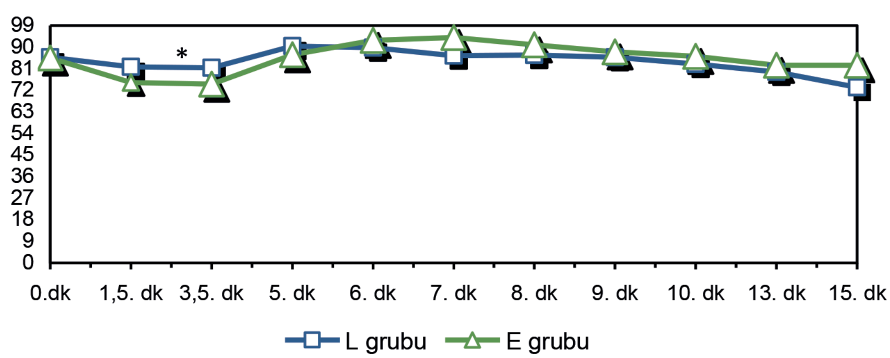

Figure 4. Temporal distribution of the average value of heart rate

DISCUSSION

In the study performed with the patients with ASA I-II physical score and operated under general anesthesia, we compared bolus doses of esmolol and lidocaine in the control of hemodynamic changes caused by intubation. We determined that, with the implementation of the study drug in both groups heart rate, SBP, DBP and MBP levels decreased compared to control values, this decrease was found to be more significant in the esmolol group and significantly lower than lidocaine group. We believe that, the induction agents used have a role in this downward trend. In esmolol group, the reduction of blood pressure started earlier than the lidocaine group and reached to control values earlier. After intubation, in both groups, heart rate, SBP, DBP and MBP values increased significantly higher than the values of before intubation, but these increases were not found to be statistically significant. For both drugs, there was no significantly difference in terms of the activities on blood pressure and heart rate after intubation. In our study, we did not determine advantages of 1.5 mg / kg esmolol or 1.5 mg / kg of lidocaine administered prior to induction, to each other in terms of the suppression of hemodynamic responses to intubation.

Korpinen et al.[9] in their studies, concluded that 2 mg / kg iv esmolol given by bolus given 2 minutes before laryngoscopy and endotracheal intubation was enough to prevent tachycardia compared to control group and insufficient for suppressing of consisting hypertension. In our study, 1.5 mg / kg i.v. bolus esmolol was found to be enough to prevent blood pressure and tachycardia.

Steven et al.[10] have reported that in their study comparing the effectiveness of esmolol, fentanyl, lidocaine and placebo in preventing tachycardia and hypertension related to tracheal intubation, esmolol 150 mg, 200 mg of lidocaine, fentanyl, esmolol 150 mcg were used, but only esmolol provided a continuous and reliable protection against increase in heart rate and SBP which accompanied laryngoscopy and intubation, fentanyl and lidocaine groups were is inadequate to protect against increases in heart rate. Each of the three drugs were found to be effective to protect against the increase in systolic blood pressure, however, it has been reported that there was no significant difference between them. In our study that we compared esmolol and lidocaine, 1.5 mg / kg iv bolus dose of esmolol was enough for suppressing systolic blood pressure and heart rate, but this situation was observed that not to be constant. We beleive that, the maintenance of continuity in the control of hemodynamic response may be provided with infusion following of a bolus doses of the application.

Keskin and Bilgin[11] studied the effects of esmolol and lidocaine on hemodynamic changes due to laryngoscopy and tracheal intubation in their studies. In this study, similar to the results of our study, it has been observed that, esmolol and lidocaine was effective in the control of SBP responses occuring due to intubation but there was no superiority to each other. Helfman et al.,[12] in their study investigating which drug can control better the tachycardia and hypertension consisting due to tracheal intubation, compared three groups given 200 mg lidocaine, 200 mcg fentanyl and 150 mg esmolol and concluded that esmolol group was more effective, consistent and reliable in terms of systolic blood pressure and heart rate values prevention associated with laryngoscopy and tracheal intubation than fentanyl and lidocain groups. In our study, bolus doses of drugs were applied to 1.5 mg per kilogram by calculating the weights of the patients. The difference from our study is that they used fixed-dose applications for each patients which were higher than our doses that we applied. With this increased doses, only in esmolol group, desired effect was obtained.

Alexander et al.[13] used 100 mg and 200 mg doses of esmolol for the control of haemodynamic response to intubation and 200 mg esmolol was observed to provide a more effective control. It has been reported that, maximum cardiac depression with esmolol occured in the second minutes. In our study, the maximum depression has emerged 3.5 minutes after bolus dose application in esmolol group.

Kindler et al.[14] compared two different doses of esmolol with lidocaine in their randomized, double-blind, placebo-controlled study. They divided 90 patients with physical status ASA I and II and whose elective gynecological surgery planned under general anesthesia into six groups and 1.5 mg / kg lidocaine, 1 mg / kg esmolol, 2 mg / kg esmolol, 1.5 mg / kg lidocaine with 1 mg of esmolol, lidocaine of 1.5 mg / kg with / kg, 2 mg / kg esmolol and saline were administered for the groups respectively. It has been reported that, with the implementation of esmolol and lidocainetogether significantly suppressed the increase in blood pressure and heart rate, but the use of esmolol alone was only effective on heart rate. In our study, we detected that, both drugs controlled blood pressure and heart rate values in post-intubation period, in esmolol group, hemodynamic balance was obtained in the short-term period. The heart rate and mean blood pressure values of esmolol group measured 3 minutes after intubation were significantly higher than those of lidocaine group.

Samaha et al.[15] have reported that both drugs were not sufficient in suppresing hypertension in their study comparing 1.5 mg / kg of esmolol and 1.5 mg / kg of lidocaine administered 2 minutes prior to endotracheal intubation. Figueredo et al.[16] have reported that esmolol was dose-dependent effective on the inhibition of adrenergic response occurring with intubation, it should be applied in the form of a continuous infusion in order to minimize the side effects. We detected that, in tachycardia and hypertension due to endotracheal intubation were suppressed in in both groups that we used 1.5 mg / kg i.v. bolus of esmolol and 1.5 mg / kg bolus of lidocaine.

Hussain and Sultan[17] studied bolus doses of esmolol and fentanyl in suppression of intubation-induced hemodynamic response to laryngoscopy in their study. Sixty patients with physical scores ASA I and II were included in the study and 0.9% NaCl, 2 mcg/kg bolus doses of fentanyl, 2 mg/kg bolus doses of esmolol were administered respectively. As a result of the study, it has been reported that, 2 mg / kg fentanyl administered 2 minutes before intubation was not able to prevent the increase in systolic blood pressure and heart rate, 2 mg / kg esmolol was able to suppress the heart rate response but insufficient to control blood pressure. Despite they used higher doses esmolol than we used in our study, they have not been successful in controlling blood pressure. The reason for this may be the implementation of esmolol 2 minutes ago. Due to distribution half-life of esmolol is 2 minutes, the elimination half-life of is 9 minutes, we considered that, the administration of esmolol 2 minutes before intubation in order to suppress hemodynamic activity occurring due to intubation was not sufficient. In our study, we administered esmolol 3.5 minutes before intubation.

Sharma et al.[18] have used bolus doses of iv100 mg and 200 mg esmolol 2 minutes prior to intubation in their studies. According to the control group, they suggested that, 200 mg esmolol was sufficient for the suppression of tachycardia and hypertension consisting after intubation, 100 mg iv dose of esmolol was insufficient. Ebert et al.[19] in a similar the study used iv bolus doses of 100 mg and 200 mg esmolol and they reported that, both doses of esmolol were sufficient in terms of suppression of tachycardia, hypertension and rate-pressure product compared to the control group. In our study, we used doses which were proportional to the weight of the patients.

As a result, it is possible to find alternative methods in many studies, in the literature, applied for the suppression of hemodynamic response occurring due to intubation. There is no consensus yet on the use of the esmolol in which dose range in order to control of hemodynamic changes occuring due to intubation. Many studies have shown that, esmolol is able to suppress intubation-induced increase in heart rate, prevent arrhythmias but no able to suppress blood pressure changes. In our study, we concluded that, 1.5 mg / kg i.v. bolus of esmolol was not superior to 1.5 mg / kg lidocaine in terms of the suppression of the blood pressure and the heart rate.

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