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Klinik çalışma

Effects of Thiopental, Propofol, Etomidate, Midazolam on Hemodynamic State in Anesthesia Induction and Intubation of Hypertensive Patients in the Coronary Artery Bypass Grafting Surgery

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SUMMARY

Objective: *The purpose of this study is to compare the hemodynamic effects of thiopental, propofol, etomidate, midazolam on induction of anesthesia, laryngoscopy, and endotracheal intubation of hypertensive patients who will undergo coronary artery bypass grafting (CABG) surgery.*

Material and Methods: *A total of 80 patients with chronic hypertension, aged between 40 and 75 who are to undergo CABG surgery were included in a prospective, single-blind, and randomized study. Group T received thiopental sodium (5-7 mg kg^{-1}), Group E etomidate (0.2 - 0.5 mg kg^{-1}), Group P propofol (1 - 2.5 mg kg^{-1}), and Group M midazolam (0.1 - 0.4 mg kg^{-1}) anesthetic agents. The induction was achieved by using fentanyl and rocuronium in all groups. Heart rate (HR), systolic arterial pressure (SAP),diastolic arterial pressure (DAP), mean arterial pressure (MAP) were recorded for the first 15 minutes. Also arterial blood gases (ABG) were sampled, and partial arterial carbon dioxide (aCO_2) values were recorded.*

Results: *SAP values decreased prior to laryngoscopy in Group T, E, and P. Only in Group E, increase in SAP during laryngoscopy and tracheal intubation was statistically significant. The decrease in MAP was significant in only Group T. At 15 minutes of intubation increases in MAP and HR in Group P was also statistically significant.*

Conclusion: *We think that the safest induction of anesthesia during laryngoscopy, and endotracheal intubation in hypertensive patients who will undergo CABG surgery will be acvhieved with midazolam (Group M)*

Key words: *anesthesia, bypass, hypertensive, intubation*

ÖZET

Koroner Arter Baypas Greft Cerrahisinde Hipertansif Hastaların Anestezi İndüksiyonu ve Entübasyonunda Tiyopental, Propofol, Etomidat, Midazolam'ın Hemodinamiye Etkileri

Amaç: *Bu çalışmada, koroner arter baypas greft (KABG) cerrahisi geçirecek hipertansif hastalara tiyopental, propofol, etomidat, midazolam anestezi indüksiyonu, laringoskopi ve endotrakeal entübasyonun hemodinamiye etkilerini karşılaştırmayı amaçladık.*

Gereç ve Yöntem: *Elektif koroner arter baypas cerrahisi geçirecek kronik hipertansif, ASA II-III, her iki cinsten yaşları 40-75 arasında, prospektif, tek-kör, randomize olarak toplam 80 hasta çalışmaya dahil edildi. Grup T tiyopental sodyum, Grup E etomidat, Grup P propofol, Grup M midazolam anestezik ajanları verildi. Tüm gruplara fentanil ve rokuronyum kullanılarak indüksiyon tamamlandı. Hastaların kalp hızı (KH), sistolik arter basıncı (SAB), diyastolik arter basıncı (DAB), ortalama arter basıncı (OAB) ilk 15 dk. kaydedildi. Ayrıca arteriyel kan gazı alınıp parsiyel arteriyel karbondioksit basıncı ($PaCO_2$) değerleri kaydedildi.*

Bulgular: *SAB'da Grup T, E ve P'de laringoskopi öncesinde SAB'da azalma saptandı. Sadece Grup E'de laringoskopi ile entübasyon sırasındaki SAB artışı istatistiksel olarak anlamlıydı. OAB'da ise yalnızca Grup T'de laringoskopi döneminde azalma anlamlıydı. OAB ve KH' da entübasyonun 15. dk'da Grup P'de artış istatistiksel olarak anlamlıydı.*

Sonuç: *KABG ameliyatına girecek hipertansif hastaların anestezi indüksiyonunda, laringoskopi ve endotrakeal entübasyonunda en güvenilir anestezi yönteminin midazolam (Grup M) ile olabileceği düşüncesindeyiz.*

Anahtar kelimeler: *anestezi, baypas, hipertansif, entübasyon*

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INTRODUCTION

Stress response of tachycardia and hypertension in laryngoscopy and endotracheal intubation does not present a problem in many patients, but it may imply an increased risk of morbidity and mortality in patients with cardiovascular or cerebral disease [1,2]. For hypertensive patients, induction and endotracheal intubation is generally a hemodynamically unstable period. Most of the hypertensive patients exhibit a hypotensive response after induction [3]. Besides, during tracheal intubation performed under superficial general anestesia, tachycardia and increased blood pressure are observed. Beside the decrease of cardiac performance and myocardial depression are occurred [2]. Therefore, hypertensive and tachycardiac response to laryngoscopy and intubation, should avoid. Deep anesthesia is only one of the several methods [1,3]. Of the most common methods used for the evaluation of the depth of is monitoring of the Bispectral Index-based Scale (BIS) which is the first electroencephalography based monitorization of clinical anesthetic activity [4].

The purpose of this study is comparing the hemodynamic effects of fentanyl, rocuronium with thiopental, propofol, etomidate and midazolam on induction and endotracheal intubation of hypertensive patients in coronary artery bypass grafting surgery.

MATERIAL AND METHODS

The study was approved by the Local Ethics Committee of our hospital, and informed consents were provided from all participants. A total of 80 patients with hypertension, of both sexes, aged between 40-75 that scheduled for coronary artery bypass grafting surgery (CABG) were included in the study. The physical status of patients were ASA (American Society of Anaesthesiologists) II-III. Patients were included in the study as double-blind, prospective and randomized. Intubations were performed by the same patient who had medical specialty education for 3.5-year.

Patients scheduled for elective coronary artery surgery in the department of cardiac surgery and patients with hypertension who used ACE inhibitors, angiotensin II receptor antagonist and / or diuretic therapy were included in this study.

The patients who had ejection fraction lower than 40 %, arrhythmia or no sinus rhythm, uncontrollable hypertension, preoperative inotropic agent and intra-aortic balloon pump, severe organ damage (creatinine >2 mg/dl, aspartate aminotransferase (AST - SGOT) >40 U/L, alanine aminotransferase (ALT - SGPT) >40 U/L, HTC <30 %), valve replacement or other surgical procedure, allergy to opioids, barbiturates, benzodiazepines and egg, neuromuscular disease, active or previous cerebrovascular case, carotid artery blocking disease, neurological or psychiatric drug use history, obese patients who had body mass index of or above 30 kg/m^2, patients with whom difficulties in intubation were experienced and patients who did not give consent to the study were excluded.

A total of 80 patients were grouped randomly in single-blind manner, into 20 patients in 4 groups. In the operation room every patient was treated with preoxygenization for 1-2 minutes (min) after the monitorization.

Groups were treated with following hypnotic agents; Group T thiopental sodium (Pental Sodyum, Ulagay) 3-7 mg kg^{-1}; Group E etomidate (Etomidate-lipuro, B.Braun-İrengün) 0.2-0.5 mg kg^{-1} Group P propofol (Propofol, Fresenius) 1-2.5 mg kg^{-1}, Group M, midazolam (Dormicum, Roche) 0.1-0.4 mg kg^{-1}. The induction was completed by using 10 micrograms (μg) kg^{-1} of fentanyl (Fentanyl, Jassen) and 0.6 mg kg^{-1} rocuronium (Esmeron, Schering Plough) in all groups.

The patient's before induction (BI), 1, 2, and 3 minutes after induction (AI1, AI2, AI3), before laryngoscopy (BL), laryngoscopy (L), endotracheal intubation (ET), and first 15 min with one minute intervals after intubation values were recorded (ET 1,2,3,4,5,6,7,8,9,10,15). Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), ECG changes in DII and V5 derivations, side effects of medications, duration, intubation quality scoring and score were recorded by an investigator who did not know in advance which drug was to be used. As arterial blood gases (ABG) were sampled, end tidal carbon dioxide ($ETCO_2$) values were recorded simultaneously. Blood gas levels were aimed to be kept at normocapnic levels $PaCO_2$ = 35-45 mmHg [5]. Regarding intubation conditions, mouth opening (ease of laryngoscopy),

vocal cords situation and the response to intubation, Cooper et al.'s scoring was used [6].

DATA AND STATISTICAL ANALYSIS

Data were analyzed with the package program SPSS (Statistical Package for Social Science) for Windows 11.5. Distribution of continuous variables was analyzed by using the Shapiro-Wilk test to investigate if it was close to normal or not. Descriptive statistics for continuous variables were shown in the form of mean ± standard deviation or median (minimum-maximum), nominal variables were shown as the number of cases and percentage (%) and $p < 0.05$ was considered significant. The difference between-groups were studied by one-way Analysis of Variance (One-Way ANOVA) to investigate whether it was significant in terms of average values and by Kruskal-Wallis test in terms of median values. In case the result of one-way ANOVA analysis was significant, post hoc Turkey test was performed to detect the groups causing significant difference. Nominal variables were analyzed by employing Pearson's chi-square test. To evaluate whether there was a statistically significant difference within-group, repeated hemodynamic measurements were evaluated by using Repeated Measure Analysis of Variance. In cases when repeated measure ANOVA resulted in a significant difference, multiple comparison test with Bonferroni correction was performed to detect the measurement times causing significant difference and the new $\alpha = \alpha / 4 = 0.0125$ taking the form of the level of $p < 0.0125$ was considered statistically significant.

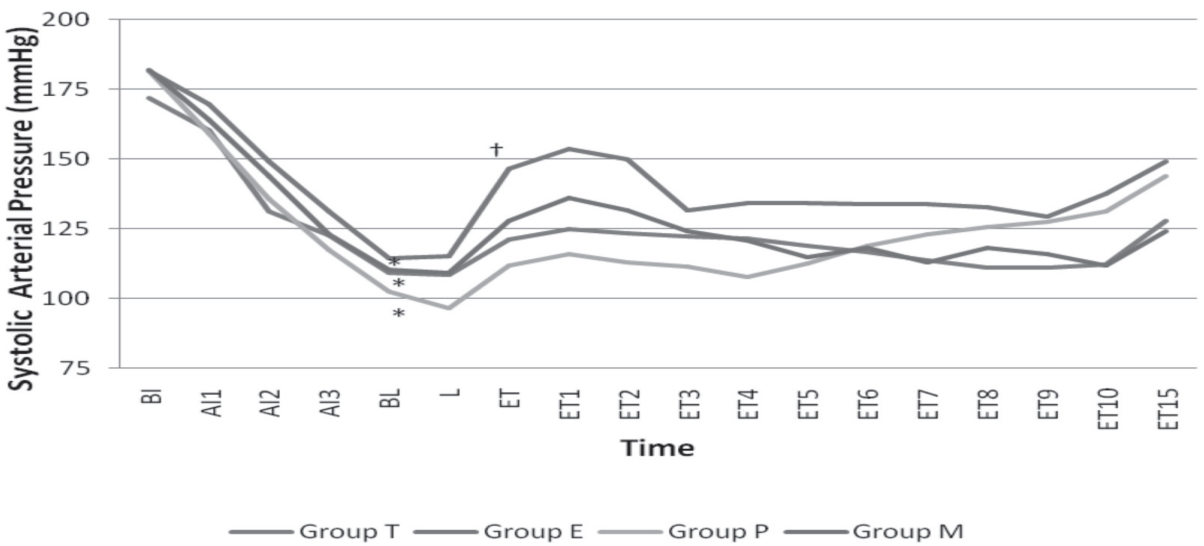
RESULTS

Patient's age, sex, body weight, height, drugs and duration of hypertension, EF % were found to be statistically similar ($p > 0.05$) (Table 1). Distribution of additional diseases was similar between-groups ($p > 0.05$).

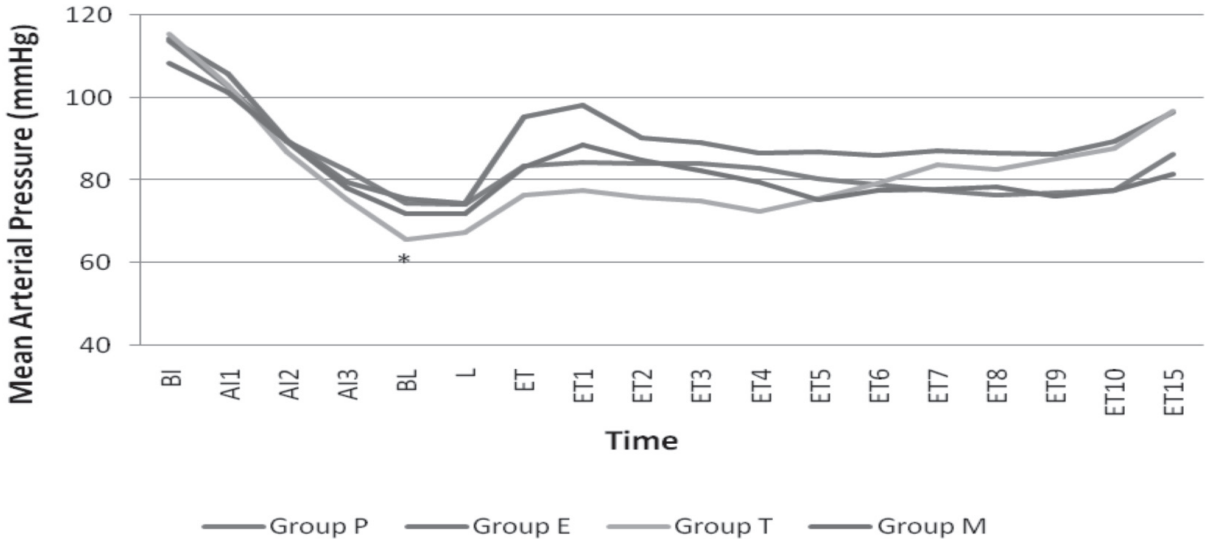
Table 1. Age, gender, body weight and height levels according to the groups.

Variables	Group T (n = 20)	Group E (n = 20)	Group P (n = 20)	Group M (n = 20)	P
Age (years)	60±9	59±10	60±9	61±8	0.927
Gender F / M	4/16	2/18	4/16	5/15	0.641
Body Weight (kg)	76±10	71±9	72±10	74±10	0.691
Height (m)	1.69±0.07	1.67±0.06	1.68±0.07	1.69±0.06	0.701

According to the comparisons between-groups, $p < 0.05$ was considered statistically significant.(F: Female, M: Male)



Graphic 1. Systolic arterial pressure levels of groups according to the follow-up times.
** There was statistically significant decrease in SAP between BI and BL within-group, in Group T, Group E and Group P ($p < 0.0125$).*
† Increase in SAP between L and ET was statistically significant in group E ($p < 0.0125$).
(BI: Before Induction, AI: After İnduction, BL: Before Laryngoscopy, L: Laryngoscopy, ET: EndoTracheal intubation)



Graphic 2. Mean arterial pressure levels of groups according to the follow-up times.
** In Group T, decrease between the period BI and BL was statistically significant within-groups (p <0.0125).*
(BI: Before Induction, AI: After İnduction, BL: Before Laryngoscopy, L: Laryngoscopy, ET: EndoTracheal intubation)

Change in HR was not statistically significant over time within groups. 15 minutes after intubation (ET15) and ET period were compared between-groups. Change in heart rate were found to be significant in ET15 period compared to ET, in Group P and M (p <0.0125). While there was an increase in heart rate in Group P, there was a decrease in Group M. When all the other periods in all groups were analyzed, no statistically significant results were found (p> 0.0125).

Before induction and before laryngoscopy period, there was a statistically significant decrease in SAP within-group values for Group T, Group E, Group P (p <0.0125). In addition, in Group E, increase in SAP between the laryngoscopy and ET period was statistically significant (p <0.0125). Changes in SAP were statistically similar between-groups in all periods (p >0.0125) (Graphic 1).

There was no statistically significant change in DAP according to evaluation, when Group T, Group E, Group P and M were analyzed separately within-groups (p> 0.0125). In periods before induction and before laryngoscopy and in periods up to ET1, DAP was statistically similar between-groups. In Group P and M, change in DAP was significant in ET15 compared to ET (p <0.0125).

In Group T, decrease in MAP was statistically significant before laryngoscopy period compared to MAP before induction (p <0.0125). There was no statistically significant change in MAP by the time, when Group E, Group P and M were analyzed separately within-groups. MAP was statistically similar between-groups (p> 0.0125) (Graphic 2).

ECG changes occurred in 7 of 80 patients. Changes in Group T consisted of 1 patient having atrial fibrillation, 3 patients having ventricular extra systole. Tachycardia was observed in 1 patient in Group E, Ventricular ectopic beats (VEBs) were observed 1 patient in Group P and bradycardia was observed in 1 patient. There was no statistically significant ECG change between-groups (p> 0.05).

After induction and intubation 4 patients of Group Tand 9 patients of Group P needed to use ephedrine, 11 patients of Group E needed to use nitroglycerin, 1 patient was needed to use nitroglycerin, 1 patient was needed to use atropine,1 patient was needed to use efedrin in Group M. Between Group E - Group M and between Group P - Group M, the needs of additional medication were statistically significant (p <0.0125).

In the evaluation of the quality of intubation with intubation score, mouth opening (MO), vocal cords status (VCS), intubation response (IR) were analyzed and there was no statistically significant difference between-groups (p>0.05).

There was a slight increase in $PaCO_2$ in arterial blood gases before laryngoscopy and 2 minutes after intubation in all four groups, this increase was similar within-groups ($p> 0.05$). Before laryngoscopy and 2 minutes after intubation, there were no statistically significant changes in $ETCO_2$ and CO_2 in ABG ($PaCO_2$) between-group ($p> 0.05$).

DISCUSSION

There are no certain rules in anesthesical methods or drugs to be used in hypertensive and cardiac surgery patients, there are some distinctive priorities about drugs and methods frequently chosen. Especially with choosing agents which shall not make sudden and important changes in hemodynamic data, shall not cause any extraordinary response to tracheal intubation and surgical stimulation and which shall not change the nutrition of tissues negatively; ischemic complications were reduced [7,8]. From this point of view, when looking at statistical difference between groups in patients who are having antihypertensive treatment due to the diagnosis of hypertension; hemodynamics is not stable in endotracheal intubation and induction applied with Group P and Group E. The group, in which the most hypotension and ephedrine need occured was Group P after induction. In Group E, hypertensive response to intubation occured and it became the group which had the most need to nitro-glycerine. Group T differed from other groups with the most ECG changes. The anesthetic induction made with Group M anesthetic agent became the group in which the response to laryngoscopy and endotracheal intubation was more stable and which showed the least side effects and additional drug need and had no ECG changes.

Anestheticians usually face with patients with hypertension who were already cured or not among those who have coroner artery diseases. It reduces cardiac ischemic complication incidence by preventing serious hypertension and tachycardia [7]. Besides, cardiovascular depression, which is seen during the induction, gives its place to hypertension and tachycardia after larygoscopy and endotracheal intubation [2,8,9]. While da Silva Neto et al [10] were evaluating the hemodynamic results of induction and intubation in two groups consist of normotensive and hypertensive patients under the treatment; DAB after induction reduces in normotensive and hypertensive patients; and this decrease in DAB was found more apparent in hypertensive patients. In periods of laryngoscopy and intubations; DAB and SAB increased in both two normotensive and hypertansive groups. But increase in hypertensive patients was more. In the 5th minutes after intubation; there is no difference determined between DAB, SAB and HR. Yoo KY et al [8] examined cardiovascular system responses in endotracheal intubations separately in normotensive and hypertensive patients. While there are no difference in HR values in groups, a sufficient increase was determined in MAP and blood norepinephrine levels of hypertensive patients in the endotracheal intubation as per normotensive patients [9]. It was observed that hypertensive patients show more increase than normotensive group in cardiovascular response. In our study, there is an increase occurred in DAP and HR in Group P in ET15, but also decreased in Group M. In periods of after laryngoscopy and intubations; SAP increased in only Group E. It was the Group Tin which decrease in SAP and MAP was seen. Group T and P were not stable hemodynamically after induction and intubation.

Kovac et al [11] who attribute the arterial blood pressure response could be resolved by increasing the anesthetic depth. The benefits of BIS monitorization could be summarized as standardizing the hypnotic component of, allowing quick compiling by decreasing drug consumption and decreasing unwanted side-effects of such as hemodynamic instability [12,13]. When the BIS value of 60 or lower was, all patients were intubated. Thus hemodynamic responce could be occurred in the intubation was not caused by insufficient depth.

Cardiac reserve capacities of patients who have also cardiac insufficiency, decreases under much more. With the decrease of cardiac performance and sympathic activity, myocardial depression is occurred. Thus, etomidate, which results the least cardiac depression becomes the most popular drug [2,14] Kubota et al [15] compared propofol-fentanyl and midazolam-fentanyl in CABG surgery in terms of hemodynamics and determined very important decreases in arterial blood pressure especially after induction in patients which take propofol that inotrope support was required. According to another research; responses of

propofol and etomidate in CABG, at the end of the induction, there was a sufficient decrease in MAP and SVR in propofol group. But in etomidate group, a sufficient increase in MAP was observed [16]. While hypotension after induction is seen very often in Group P, also no hypotension is seen after induction in Group E; but the response of hypertension in the period after intubation takes attention in Group E.

Kim et al [17] evaluated the hemodynamic response in tracheal intubation in two groups that were generated hypercapnically and normocapnically, in a study. According to this, before tracheal intubation, increase of carbon dioxide in ventilation with mask could cause an exaggerated increase of SAP in intubation response [17]. Therefore in our study, carbon dioxide changes after expiration are confirmed with $PaCO_2$ in synchronous blood gas; carbon dioxide changes between groups were similar. Moreover, in our study, in laryngoscopy intervals and the assessment of intubation quality with intubation score was assessed no difference was determined statistically between groups. Thus, it was shown that changes in laryngoscopy and intubation were based on the differences only in induction agents.

According to this study, Copenhan Conference consensus was applied for criteria in tracheal intubation in rocuronium for two suggested effective dosage intervals were (ED95) 0.3- 0.6 mg kg^{-1}. In these two dosages; some effects such as laryngoscopy, vocal cords, tube position in tracheal intubation and chest move and coughs in cuff blowing were reviewed [18]. In our study, rocuronium was used in the dosage of 0.6 mg kg^{-1} to all patients as neuromuscular blocking agent. Intubations were assessed with intubation quality scoring. There is no intubation quality scoring differences between groups.

Consequently, despite the fact that there are no certain rules in anesthesical methods or drugs to be used in cardiac surgery and hypertensive patients. There are some distinctive priorities about drugs and methods frequently chosen. Especially with choosing agents which shall not make sudden and important changes in hemodynamic data, shall not cause any extraordinary response to tracheal intubation and surgical stimulation and which shall not change the nutrition of tissues negatively; ischemic complications were reduced. From this point of view, when looking at statistical difference between groups in patients who are having anti-hypertensive treatment due to the diagnosis of hypertension; hemodynamics is not stable in endotracheal intubation and induction applied with Group P and Group E. After induction the group in which the most hypotension response and needed to use ephedrine was Group P. In Group E, hypertensive response to intubation occured and it became the group which had the most need to nitro-glycerine. Group T differed from other groups with the most ECG changes. The anesthetic induction with midazolam (Group M) anesthetic agents became the group in which the response to laryngoscopy and endotracheal intubation was more stable and which showed the least side effects and had no ECG changes. In the anesthetic induction of hypertensive patients who shall have CABG operation; we think that the most trustable anesthesia method could be with midazolam besides fentanyl and rocuronium in laryngoscopy and endotracheal intubation.

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