Comparison of the Haemodynamic Effects of Three Different Methods at the Induction of Anaesthesia

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Objective: Haemodynamic variations are inevitable during induction of anaesthetic drugs. The present study investigates the haemodynamic variations of three different drugs (thiopental, propofol, and etomidate) used for induction of general anaesthesia together with fentanyl.

Methods: In a randomized, double-blind study, 45 patients were assigned to one of three groups (n=15 each). Fentanyl 1 µg kg⁻¹ was injected over 60 sec followed by propofol 2 mg kg⁻¹ (Group P), thiopentone 6 mg kg⁻¹ (Group T), or etomidate 0.3 mg kg⁻¹ (Group E). Noninvasive measurements of systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), and heart rate (HR) was performed on admittance, immediately before the induction of anaesthesia, and 1, 3, and 5 min thereafter. Cardiac output (CO) values were recorded before induction, immediately after the injection of the drug, and at 1 min after the intubation.

Results: In all groups, during the study period, SAP, DAP, MAP, and CO values decreased with respect to time before induction. Following the administration of the induction dose of propofol (Group P), a significantly greater decrease of systolic and diastolic blood pressure was observed with etomidate (Group E) or thiopentone (Group T). Decrease in CO was also more marked with propofol (Group P) than with etomidate (Group E) or thiopentone (Group T).

Conclusion: It's concluded that, in this study, the combination of fentanyl- etomidate is safer than both the groups of fentanyl-propofol and fentanyl-thiopental in terms of providing haemodynamic stability.

Key Words: Propofol, thiopental, etomidate, induction, haemodynamic changes

Introduction

Stress response resulting from intubation, extubation and surgical stimulus can lead to some haemodynamic changes. Cardiovascular depression emerging during the induction of anaesthesia and the stress response caused by endotracheal intubation are important, especially for patients who are under cardiac risk. This haemodynamic response affects myocardial perfusion in a negative way by increasing myocardial oxygen consumption and cardiac workload, and it can lead to ischaemia (1).

Stimulation of laryngeal and tracheal tissues during intubation causes catecholamine discharge, with an increase in sympathetic-adrenergic activity and also an increase in systemic arterial pressure and heart rate (2, 3). These increases begin with the laryngoscope, reach to the maximum level within 1-2 minutes and decrease to the values before the laryngoscope (4-6). Extrasystoles and ventricular premature beats can also be seen in this period (7, 8).

Use of general anaesthetic agents with intravenous induction can often cause hypotension. Many mechanisms have been described on this issue, but the most important of these are the suppressive effects of these agents on myocardial contractility, sympathetic activity, baroreflex activity and central nervous system activity (9-12).

This study aims to compare the stress response-induced haemodynamic effects of etomidate, propofol and thiopental by measuring cardiac output and arterial tension values in the anaesthetic induction of patients under cardiac risk who undergo elective surgery.

Methods

After getting approval from the ethics committee of Okmeydanı Training and Research Hospital (dated May 07, 2009, numbered 250), the study involved 45 patients aged between 18-65 years who were undergoing elective surgery and who were classified in group II-III according to the risk classification of American Society of Anesthesiology (ASA) and in Class II-III according to the functional classification of New York Heart Association (NYHA) (Table 1).

Written informed consent was obtained from the patients during their preoperative examinations, and they were informed about the method. Patients who had hepatic and renal failure, who were allergic to the medications and who might have difficulty in intubation were excluded from the study.

All patients who were operated were monitored using a Datex Ohmeda S/5 Anaesthesia Monitor (AKG, pulse oximeter and non-invasive blood pressure). Vascular access was established on the hands of the patients with a 20 G cannula, and 0.9% NaCl infusion was initiated at a rate of 10 mL hour⁻¹.

The patients were randomly divided into three groups: the propofol group who received 2 mg kg⁻¹ propofol (Pofol® i.v. ampoule, Sandoz) (Group P, n=15), the etomidate group who received 0.3 mg kg⁻¹ etomidate (Hypnomidate® i.v. ampoule, Johnson & Johnson) (Group E, n=15) and the thiopental group who received 5 mg kg⁻¹ (Pental® sodium vial, İbrahim Etem İlaç) (Group T, n=15). All three groups were exposed to 1 µg kg⁻¹ fentanyl (Fentanyl Citrate® ampoule, Abbott) with an induction agent. While tracheal intubation was performed with 0.15 mg kg⁻¹ cisatracurium (Nimbex® ampoule, Glaxo Smith Kline), 50%-50% oxygen and nitrous oxide and 0.8-1.2 MAC sevoflurane were used for maintenance.

Cardiac output (CO) of the patients was measured through impedance cardiograph method (Bo Med Medical Manufacturing Irvine CA) before induction (basal value, T0), before intubation (T1) and in the 1st minute after intubation (T2). Moreover, heart rate (HR) and systolic (SAP), diastolic (DAP) and mean arterial pressure (MAP) were recorded before induction (basal value, T0), before intubation (T1) and in the 1st (T2), 3rd (T3), and 5th (T4) minutes after intubation (T2).

Statistical analysis

Statistic Package for Social Sciences for Windows 15.0 (SPSS, Chicago, IL, USA) was used for the statistical analysis. In addition to descriptive statistics, such as mean and standard deviation, Kruskal-Wallis test was employed for comparing multiple groups, Bonferroni-corrected Mann-Whitney U test was used as a post hoc test and chi-square test was used for comparing qualitative data. The results were evaluated with 95% confidence interval and a significance value of $p < 0.05$.

Table 1. New York Heart Association functional classification

Class 1	Patient with normal physical activity and without any symptom
Class 2	Symptomatic patient with normal physical activity, mild limitation in activity
Class 3	Symptomatic patient with less physical activity, apparent limitation in activity
Class 4	Symptomatic patient with any activity

Table 2. Demographic data (n=45)

	Group P	Group T	Group E	<i>p</i>
Gender (M/F) (n)	9/6	8/7	8/7	0.914*
Age (year) (Mean±SD)	48.4±11.0	41.4±15.7	47.7±11.2	0.273*
Height (cm) (Mean±SD)	167.4±5.9	168.9±6.9	168.7±6.2	0.775*
Weight (kg) (Mean±SD)	78.0±6.3	75.3±7.6	73.9±7.7	0.307*
NYHA (II/III) (n)	9/6	8/7	8/7	0.914*

NYHA: New York Heart Association functional classification; M: Male; F: Female; Mean±SD: mean±standard deviation. *chi-square test, #Kruskal-Wallis test

Figure 1. Systolic arterial pressure measurements of the groups

Results

The demographic data of the groups are presented in Table 2.

In the comparison of the groups for SAP values, the decreases seen in Group P after induction (T1) and in the 5th minute after intubation (T4) were statistically significantly different than the SAP values of Group T and Group E that were recorded at the same time ($p < 0.01$) (Figure 1).

In the comparison of the groups for DAP values, the decrease in Group P after induction (T1) was found to be statistically significantly different from the simultaneously recorded DAP values of Group T and Group E ($p < 0.01$) (Figure 2).

In the comparison of the groups for MAP values, the decreases seen in Group P after induction (T1) and in the 1st minute after intubation (T2) were statistically significantly different than the MAP values of Group T and Group E that were recorded at the same time ($p < 0.01$) (Figure 3).

In terms of HR values, the groups were compared, and no statistically significant difference was found (Figure 4).

Figure 2. Diastolic arterial pressure measurements of the groups

Figure 3. Mean arterial pressure measurements of the groups

Figure 4. Heart rate measurements of the groups

Comparison of the groups for CO values revealed that the decreases in Group P after induction (T1) and in the 1st minute after intubation (T2) were statistically significantly different than the CO values of Group T and Group E that were recorded at the same time ($p < 0.01$). Paired comparisons of the groups are also shown in Table 3.

Discussion

During anaesthesia induction or tracheal intubation, some distinct changes can be observed in haemodynamic parameters, depending on the effects of the anaesthetic drugs and adrenergic status of the patients. With supraglottic stimulation by laryngoscopy, an increase occurs in the arterial pressures of patients. Moreover, the levels of catecholamine increase with stimulation of infraglottic receptors during insertion of the endotracheal tube (13).

The mechanism of the cardiac-depressive effect caused by intravenous anaesthetic agents has not been explained clearly. It is thought that this effect results from decreased preload and afterload and direct myocardial depression (14-17). Although the mechanism of negative inotropic effects caused by intravenous anaesthetics is not exactly known, informa-

tion on this issue is increasing day by day with *in vivo* and *in vitro* studies (18-22). The use of etomidate, having less of a cardiac-depressive effect, is safer in cardiac patients, but the sympathoadrenal-suppressive effects limit its usage (17, 23). The multilateral cardiovascular effects of anaesthesia can be influenced by anaesthetic drug combination, antihypertensive drugs received by the patients, beta-blockers and calcium channel blockers, the way of respiration, acid-base equilibrium and fluid-electrolyte balance, and they can become more complex.

It was found that the contractility of the heart changed a little, and heart rate, cardiac output and stroke volume stayed stable in patients receiving etomidate (17, 20, 21). These studies suggest that etomidate is a safe drug for anaesthesia induction in cardiac patients (23).

Mulier et al. (16) evaluated the cardiovascular effects of propofol and etomidate in induction in their study, and they found a significant decrease in CO, especially during the first 4 minutes after induction in the group receiving a 2.5-mg kg⁻¹ dose of propofol compared to the group taking thiopental in two different doses, 4 mg kg⁻¹ and 6 mg kg⁻¹ ($p < 0.05$). In our study, a significant decrease in CO was observed in the propofol group (Group P), particularly in the 1st minute after induction (T1), compared to the thiopental group (Group T) ($p < 0.05$).

Another important factor contributing to the cardiovascular instability that occurs after giving intravenous anaesthetic agents is the negative inotropic effect on the heart. Glissen et al. (24) investigated the inotropic effects of propofol, etomidate and thiopental on heart muscle and revealed that propofol and etomidate at clinical concentrations did not influence myocardial contractility in the heart muscle, but thiopental had a significant negative inotropic effect.

Haris et al. (25) evaluated thiopental (4 mg kg⁻¹), etomidate (0.3 mg kg⁻¹) and propofol (2.5 mg kg⁻¹) in tracheal intubation by adding 2 µg kg⁻¹ fentanyl or not. They detected that there was a significant decrease in SAP values in the group receiving only propofol, and there were significant increases in SAP values in the group receiving only thiopental and etomidate after intubation. In our study, remarkable decreases in SAP values were observed, especially in the propofol group in the 1st minute after induction (T1) and in the 5th minute after intubation (T4). No significant differences were seen in HR values. These results are consistent with those of a study conducted by Harrison et al.

Vohra et al. (26) measured patients' cardiac outputs through thoracic impedance in order to evaluate the haemodynamic responses to intubation in two groups of patients who were administered thiopental (5 mg kg⁻¹) and propofol (3 mg kg⁻¹) with 1.5 µg kg⁻¹ fentanyl. They found no significant difference between the two groups in terms of HR after induction, but a statistically significant increase was observed in HR val-

Table 3. Cardiac output measurements

	Group P (Mean±SD)	Group T (Mean±SD)	Group E (Mean±SD)	P ¹	Comparison of the groups	
					P ²	
T0	3.4±0.4	3.6±0.3	3.5±0.4	0.278	P---T P---E T---E	0.246 0.711 0.683
T1	2.5±0.3	2.8±0.2	3.0±0.2	0.001*	P---T P---E T---E	0.249 0.001* 0.044*
T2	2.8±0.2	2.9±0.1	3.1±0.1	0.006*	P---T P---E T---E	0.531 0.005* 0.073

Mean±SD: mean±standard deviation; ¹Kruskal-Wallis test, ²Mann-Whitney U-test

ues of the two groups after intubation ($p < 0.01$). CO values after induction and intubation were decreased significantly in both groups. On the other hand, no significant difference was found for CO and HR values in the comparison of the groups. They did not find significant differences in MAP and systemic vascular resistance (SVR) after induction in the thiopental group, but they detected statistically significant increases in both values during the 1st minute after intubation. Statistically significant decreases were determined in MAP and SVR values after induction in the propofol group. However, they observed no significant difference in these two values in the measurements performed in the 1st minute after intubation. They compared the two groups in terms of MAP and SVR and found a greater increase in the thiopental group than in the propofol group. In our study, the thiopental (Group T) and propofol (Group P) groups were compared, and no statistically significant difference was revealed between the decreases in HR and CO values. The difference between the results of Vohra et al. (26) and our study might have resulted from the lower doses of the drugs and slower drug infusion in our study.

Conclusion

In our study, it was detected that among three different methods, etomidate-fentanyl (Group E) affected haemodynamic responses the least, and propofol-fentanyl (Group P) affected haemodynamic responses the most. However, during the periods after induction or intubation, critical decreases in blood pressure and cardiac output were not observed in any group.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Okmeydanı Training and Research Hospital.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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