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ORIGINAL ARTICLE

Comparing the effect of two different induction regimens with thiopental on hemodynamics during laryngoscopy and tracheal intubation in hypertensive patients

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ABSTRACT

Objective: Inj thiopental is known to result in hypotension during induction, and the effect is more pronounced in hypertensive patients. This study aimed to compare the effect of two different anesthesia induction regimens with pentothal in managing the hemodynamic response to laryngoscopy and endotracheal intubation in known hypertensive patients.

Methodology: The study was conducted in Van Educational Research Hospital in 2014 after approval from the ethics committee and informed consent from patients were obtained. The prospective, double-blind, randomized study included the American Society of Anesthesiologists (ASA) grade II–III 90 patients, aged 40–65 y, scheduled for elective abdominal surgery with general anesthesia. Thiopental (3–7 mg/kg) was given to the patients in Group 1 (n = 45) with single dose injection in 20 s. In Group 2 (n = 45), first 75% of the thiopental dose was given, and after the bispectral index–based scale (BIS) value was < 60 and after injecting neuromuscular blocking agent, the rest of the thiopental dose was added and injection duration was recorded. In both groups, midazolam 0.05–0.1 mg/kg was administered for premedication. Fentanyl and rocuronium were used in both groups to complete induction. During the first 25 min, systolic arterial pressure, diastolic arterial pressure, mean arterial pressure, and heart rate of the patients were recorded. Also, BIS values after induction and total additional fentanyl requirement were recorded.

Results: Heart rate, mean arterial pressure, and additional fentanyl requirement was significantly lower in Group 2. BIS values were also lower in Group 2. Induction duration was higher in Group 2, but hemodynamic control was more satisfying.

Conclusion: The study indicated that injection of thiopental in divided doses is more comfortable and safe when considering hemodynamic instability during anesthesia induction in hypertensive patients.

Key words: Anesthesia; Hemodynamic control; Hypertension; Thiopental

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INTRODUCTION

Hypertension is one of the most important risk factors for cardiovascular morbidity and mortality in patients undergoing elective surgery under general anesthesia.[1] Hypertensive patients are generally hemodynamically unstable during induction and endotracheal intubation. Most of them exhibit a hypotensive response after induction. All hypertensive patients, whether their arterial blood pressure is under control or not, exhibit a similar increase in blood pressure in response to intubation.[2] Prevention of hypertensive and tachycardia response to laryngoscopy and intubation is important because hypertension associated with tachycardia may cause myocardial depression.[3] Deep anesthesia is one of the several methods shown to be effective in this regard,[3,4] and bispectral index–based scale (BIS), which is the first electroencephalography-based monitoring of clinical anesthetic activity, is one of the most common methods used for evaluating the depth of anesthesia.[5]

It is advocated that thiopental is a perfect agent for anesthesia induction.[6] It is superior to other agents with rapid onset of effect (15–30 s) and smooth induction of anesthesia.[6]

This study aimed to compare the efficacy of thiopental given in divided doses on the prevention of hemodynamic response to laryngoscopy and endotracheal intubation.

METHODOLOGY

The study was conducted in Van Educational Research Hospital in 2014 after approval from the ethics committee. The study involved 90 patients aged 40–65 years, undergoing elective abdominal surgery with general anesthesia, and classified as American Society of Anesthesiologists (ASA) physical status 2 or 3. The exclusion criteria were as follows: unwillingness of the patient, grade 3 hypertension [systolic arterial pressure (SAP) ≥ 180 mmHg and diastolic arterial pressure (DAP) ≥ 110 mmHg)], use of drugs with hemodynamic and autonomic effects, electrocardiographic abnormalities [cardiac dysrhythmia, premature ventricular contractions, and heart rate (HR) less than 55 bpm], a difficult airway, obese status [body mass index (BMI) ≥ 30 kg/m^2], decompensated heart failure or significant heart block. History of acute myocardial infarction, severe valvular disease, severe hepatic, renal, or pulmonary impairment, other disorders known to affect autonomic function, allergy to the drugs used in the study, and refusal to participate in the study were the other exclusion criteria.

The demographic information of the patients (sex, age, and body weight), presence of comorbid diseases, and ASA physical status were recorded. All these data were statistically insignificant in two groups.

The patients were examined and briefed prior to surgery. The simple random assignment method was used to divide patients into two groups.

Group 1: The thiopental dose calculated for the weight (4 mg/kg) was given to the patients (n = 45) with single dose injection in 20 s.

Group 2: (n = 45), first 75% of the thiopental dose was given, and at < 60 BIS following injection with a neuromuscular blocking agent, the rest of the thiopental dose was administered.

Midazolam 0.05–0.1 mg/kg was administered as premedication 30 min before the surgery. Then the patients were taken to the operating room and HR, non-invasive SAP, DAP, and MAP values were recorded (T1) after standard monitoring. In addition to standard monitoring, BIS was used to monitor the depth of anesthesia. All study parameters including BIS value were recorded before induction (T2). Fentanyl 50 μg, lidocaine (1 mg/kg), thiopental (4 mg/kg), and rocuronium (0.6 mg/kg) were used in Group 1 after monitorization and 2–3 min of preoxygenation. In Group 2, fentanyl 50 μg, lidocaine 1 mg/kg, and 75% of thiopental dose (4 mg/kg) were used. On achieving ≤ 60 BIS value, rocuronium 0.6 mg/kg and the rest of the thiopental were administered. All the patients were intubated with simple Macintosh blade, 90 s after administration of rocuronium by the same anesthesiologist. HR, SAP, DAP, MAP, and BIS values of the patients were recorded before induction (T2), after induction (T3), after intubation(T4) and 5 min after intubation(T5). Fentanyl 50 μg was administered to the patients who exhibited 20% or more increase in SAP during laryngoscopy and endotracheal intubation with reference to the value before induction. 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.[7] The scoring proposed by Cooper et al. was used for intubation conditions, mouth opening (ease of laryngoscopy), condition of vocal cords, and response to intubation.[8]

Personal characteristics of the patients and HR, SAP, DAP, MAP and BIS values recorded at T1, T2, T3, and T4 and T5, total dose of fentanyl required, and effect of different doses of thiopental on hemodynamic response to laryngoscopy and endotracheal intubation were compared between the two groups.

The chi-square test was used to examine the association between categorical variable. Normality

tests were used to determine the distribution. Student's t-test and Mann–Whitney U test were used for continuous variables.

RESULTS

No statistically significant difference was found in gender distribution between Group 1 (n = 45) and Group 2 (n = 45). In Group 1, 33.3% of the patients were females, and 66.7% were males. In Group 2, the proportion was 35.6% and 64.4%, respectively (p = 0.824).

A total of 45 patients required additional fentanyl. In Group 1, 64.4% of the patients and, in Group 2, 13.3% of the patients received additional fentanyl; the difference between the two groups was statistically significant (p = 0.000) (Table 1).

Comparing the MAPs between the two groups, the differences found at time T2 (p < 0.0005), T3 (p = 0.004) and T5 (p = 0.002) were statistically significant (Table 2).

Comparing HRs between the two groups, the differences found at time T2 (p = 0.004), T3 (p = 0.002), T4 (p = 0.033), and T5 (p = 0.046) were statistically significant (Table 3).

Comparing the BIS values, at time T3, 51.1% of the patients in Group 1 and 26.7% of the patients in Group 2 had the BIS value lower than 40, and the difference between the two groups was statistically significant (p = 0.017). At time T6, the percentage of patients having the BIS value lower than 40 was 42.2% and 17.8% in Group 1 and Group 2, respectively; the difference between the two groups was also found to be statistically significant (p = 0,011) (Table 4).

Comparing the BIS values at time T3, 20.0% of the patients in Group 1 and 4.4% of the patients in Group 2 had the BIS value higher than 60, and the difference between the two groups was statistically significant (p = 0.024) (Table 5).

Table 1: Comparison of additional fentanyl requirements in two groups

	Group 1 (Thiopental 100%)	Group 2 (Thiopental 75%)	p
Fentanyl use			
No	16 (35.6)	39 (86.7)	0.000
Yes	29 (64.4)	6 (13.3)	
Fentanyl dosage			
50 mcg	18 (62.2)	4 (66.7)	0.608
100 mcg	11 (37.9)	2 (33.3)	
Total	29	6	

Table 2: Comparison of mean arterial blood pressure levels of the study subjects [mean ± SD mmHg]

Time	Group 1 (Thiopental 100%)	Group 2 (Thiopental 75%)	p
Before pre-medication	110.4 ± 9.2	109.2 ± 8.9	0.500
T1	103.4 ± 9.0	103.2 ± 8.5	0.904
T2	96.3 ±27.8	75.8 ± 19.2	**0.000**
T3	85.5 ± 22.8	73.9 ± 13.8	**0.004**
T4	76.4 ±19.2	73.2 ± 11.7	0.352
T5	85.4 ± 20.0	74.3 ± 13.1	**0.002**

Table 3: Comparison of means of mean heart rates (beats/min) of the study subjects

Time	Group 1 (Thiopental 100%)	Group 2 (Thiopental 75%)	p
Before premedication HR	85.8 ± 17.3	90.5 ± 17.0	0.19
T1 HR	82.7 ± 14.3	81.9 ± 10.2	0.77
T2 HR	85.5 ± 15.6	76.2 ± 14.1	**0.004**
T3 HR	84.4 ± 15.6	74.7 ± 12.3	**0.002**
T4 HR	78.8 ± 13.2	72.9 ± 12.5	0.033
T5 HR	78.1 ± 13.8	72.8 ± 10.8	**0.046**

DISCUSSION

Anesthesia induction and endotracheal intubation are a risk factor for hemodynamic instability.[9] Regardless of preoperative blood pressure levels, some hypertensive patients may present a significant hypotensive response to anesthesia induction followed by an exaggerated hypertensive response to intubation.[9,10] Sympathomimetic amines are secreted as a result of stimulation of receptors in the larynx and trachea by endotracheal intubation. Sympathetic stimulation causes tachycardia and an increase in blood pressure. In normotensive patients, this increase is 20–25 mmHg, but it is higher in hypertensive patients,[10,11,12] The difference between SAP and DAP seen immediately after the induction of anesthesia is much higher in hypertensive patients.[10] Therefore, it is important to be sure about the adequate level of anesthesia.

De Silva Neto et al. evaluated the hemodynamic results of induction and intubation in two groups: normotensive patients and hypertensive patients under treatment.[13] In this study, diastolic blood pressure was reduced during drug administration, with a smaller percentage reduction in hypertensive patients under treatment. During laryngoscopy

and intubation, DAP and SAP increased for both normotensive and hypertensive groups, but a smaller increase was recorded in hypertensive patients.13 In the fifth minute after intubation, no difference was found between DAP, SAP, and HR.

Yoo et al. examined cardiovascular system responses in endotracheal intubation separately in normotensive and hypertensive patients.[14] No differences in HR values were found in both the groups, but a sufficient increase was recorded in MAP and blood norepinephrine levels of hypertensive patients during endotracheal intubation compared with normotensive patients.[15] The cardiovascular response was more apparent in hypertensive patients. The present study found that administering thiopental in divided doses caused less hemodynamic changes than administering in one dose.

Kovac et al. showed that the arterial blood pressure response could be resolved by increasing the anesthetic depth.[4] The benefits of BIS monitorization could be summarized as standardizing the hypnotic component, allowing quick compilation by decreasing drug consumption and unwanted side effects of such as hemodynamic instability.[16,17] All patients were intubated when the BIS value was 60 or lower. Thus, hemodynamic response during intubation was not caused by insufficient depth. The present study showed that the administration of thiopental in divided doses was more appropriate for keeping BIS values in the hypnotic state.

Kim et al. evaluated the hemodynamic response to tracheal intubation between normocapnia and hypercapnia ventilation before tracheal intubation.18 They found that hypercapnia during mask ventilation before tracheal intubation could cause an exaggerated increase in SAP in intubation response compared with normocapnia. Ventilation was important in minimizing hemodynamic responses during induction regardless of using drugs. $EtCO_2$ was monitored in normocapnic levels during and after preoxygenation in both Group 1 and Group 2 in the present study.

Table 4: Distribution of the patients having BIS values lower than 40 [n (%)]

Time	Group 1 (Thiopental 100%)	Group 2 (Thiopental 75%)	Total	p
T2 BIS	20(44.4%)	17 (37.8%)	37	0.520
T3 BIS	23(51.1%)	12(26.7%)	35	**0.017**
T4 BIS	28(62.2%)	20(44.4%)	48	0.091
T5 BIS	21(46.7%)	16(35.6%)	37	0.284

* Percentages are based on total 45 patients in group 1 and group 2.

Table 5: Distribution of the patients having BIS values higher than 60 [n (%)]

Time	Group 1 (Thiopental 100%)	Group 2 (Thiopental 75%)	Total	p
T2 BIS	10 (22.2%)	4 (8.9%)	14	0.081
T3 BIS	9 (20.0%)	2 (4.4%)	11	**0.024**
T4 BIS	3 (6.7%)	0 (0.0%)	3	0.242
T5 BIS	5 (11.1%)	0 (0.0%)	5	0.056

* Percentages are based on total 45 patients in group 1 and group 2.

Sørensen et al. showed that thiopental had a more rapid onset of effect compared with propofol in elderly patients.[19] The present study compared the hemodynamic safety of different administrations of thiopental. It found that, while using thiopental in divided doses, induction and laryngoscopy interval was shorter and additional fentanyl dosage was less.

Laryngoscopy and tracheal intubation are usually accompanied by increases in arterial blood pressure and HR. Various methods have been suggested to attenuate these responses, including the use of inhaled anesthetics,[20] sympathetic blockers,[21,22,23] vasodilators,[24] local anesthetics,[25] narcotics,[26,27,28] and combinations of these drugs.[29] Many studies have reported a beneficial effect of fentanyl as an adjunct to barbiturate induction. Dahlgren and Messeter showed that 5 μg/kg of fentanyl given before intubation effectively blunted the cardiovascular stress responses to intubation in neurosurgical patients.[26] Using 8 μg/kg fentanyl preloading, Martin et al. demonstrated that fentanyl abolished both the HR and blood pressure increases related to tracheal intubation and prevented an increase in pulmonary capillary wedge pressure during the induction of anesthesia with thiopental.[27] In a double-blind study, two doses of fentanyl (2 and 6 μg/kg) were evaluated as an adjunct to thiopental induction in normotensive patients, and the large dose of fentanyl completely prevented the increase in pulse rate and arterial pressure.[28] In the present study, fentanyl was administered to explore tachycardia and hypertensive response when the BIS value was $\geq$ 60 after induction.

CONCLUSION

Consequently despite there being no rules regarding any particular anesthesia methods or drugs to be used in cardiac surgery and/or hypertensive patients, distinctive priorities exist about drugs and methods frequently chosen. Ischemic complications should be avoided by choosing agents that are less likely to make sudden and important changes in hemodynamics, less capble to obtund sympathetic response to tracheal intubation and surgical stimulation, and have a negative effect on the nutrition of tissues.

Our study proved that response to laryngoscopy and intubation is optimal, anesthesia depth is more stable, and there is less requirement of additional opioids in patients who receive thiopental in divided dosage.

Conflict of Interest: The authors declare that they have no conflict of interest. The authors has no financial relationship with the companies that manufactured the materials used in this study.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Authors' contribution:

SGU - Concept, conduction of the study

DY - Concept, data collection

TS - Manuscript writing & editing, data collection

ME - Statistical analysis, manuscript writing

HS, HBA - Manuscript writing & editing

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