COMPARATIVE STUDY OF CO-INDUCTION WITH THIOPENTONE AND MIDAZOLAM VERSUS THIOPENTONE ALONE IN HYPERTENSIVE PATIENTS

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ABSTRACT

Objective: *To compare the variations of heart rate and diastolic blood pressure in hypertensive patients in co-induction of anesthesia with thiopentone & midazolam versus thiopentone alone.*

Material and Methods: *This comparative study was conducted in Anesthesia Department Khyber Teaching Hospital, Peshawar from April, 2006 to September, 2006. Hundred indoor hypertensive cases of surgical units were included in the study. They were equally divided into two groups of 50 patients each. Group A: 50 cases who were anesthetized with thiopentone sodium alone. Group B: 50 cases who were anesthetized with midazolam/thiopentone sodium combination.*

Results: *A total of 100 cases were studied. In 50 cases of group A (induction with thiopentone alone), the heart rate remained stable in 36% (n=18) cases and the diastolic blood pressure remained stable in 34% (n=17) cases.While in group B (co-induction with thiopentone / midazolam), heart rate remained stable in 72% (n=36) cases and diastolic blood pressure in 70% (n=35) cases. Patients with unstable heart rate and diastolic blood pressure were more in group A (thiopentone induction group) while patients with stable heart rate and diastolic blood pressure were more in group B (co-induction group).*

Conclusion: *Co-induction with thiopentone and midazolam provides better hemodynamic stability as compared to induction with thiopentone alone in hypertensive patients. However large scale randomised controled trials are needed to study the haemodynamic stability of thiopentone and midazolam.*

Key words: *Hypertension, Hemodynamic Stability, Thiopentone, Midazolam.*

INTRODUCTION

Hypertension affects one billion individuals world-Wide,[1] and is endemic in the western world, particularly in the elderly.[2] It is one of the most common diagnosis in the US adult population, has prevalence in excess of 50% in individuals older than 65 years of age. Hypertension represents a major risk factor for coronary artery disease, congestive heart failure,[3] dementia,[4] renal and cerebrovascular disease, and is associated with dyslipidaemia, diabetes, and obesity.[5] The higher the arterial pressure, the higher the risk of myocardial infarction, heart failure, stroke, or kidney disease. Between the age of 40 and 70 years, for each increment of 20 mm Hg in systolic or 10 mm Hg in diastolic arterial pressure, the chance of developing cardiovascular disease doubles across the arterial pressure range from 115/75 to 185/115 mm Hg. Therefore,[6] the need for good arterial pressure control and life-long treatment is undisputed.

Hypertensive patients need special attentionwhile being under general anesthesiafor variety of surgical procedure. Hypertensive patients tend to be haemodynamically unstable and prone to myocardial ischaemia in the perioperative period.[7] Several studies have demonstrated a significant association between perioperative myocardial ischaemia and postoperative ischaemic cardiac events, such as unstable angina, non-fatal myocardial infarction, and cardiac death.[8,9]

Thiopentone is the most commonly used anesthesia induction agent in Pakistan. It has been the gold standard for induction of anesthesia. Its common side effects are hypotension, apnea

AGEWISE GROUP DISTRIBUTION

Age Group	No of cases (n=100)	%Age
30-40	27	27
40-50	36	36
50-60	37	37

Table 1

Minimum = 34
Maximum = 60
Mean age/S.D = 47+7.74

and adverse sequelae associated with accidental extra-vascular injection. The hypotensive effect can be reduced by reducing the dose of the drug by 25 to 50%, but reduction of the dose may lead to awareness. Peri-operative awareness may cause anxiety, pain and haemodynamic instability e.g. rise in heart rate and blood pressure. One of the fundamental features of good quality anesthesia is amnesia i.e. patient should be completely unaware of the events during surgery. Pre-medication with amnesic drugs e.g. midazolam is recommended as one of the technique to prevent awareness. This lead to the concept of co-induction of anesthesia. Co-induction is the concurrent administration of two or more drugs that facilitate induction.

Present study was designed as to compare the variation of heart rate and diastolic blood prressure in hypertensive patients co-inducted of anesthesia with thiopentone & midazolam versus thiopentone alone.

MATERIAL AND METHODS

This comparative study was conducted in Anesthesia Department, Khyber Teaching Hospital, Peshawar for a duration of six months (April 2006 to September 2006, both months inclusive). Hundred indoor cases of surgical units were included in the study. These were equally divided into two groups of 50 patients each.

Group A: 50 cases who were anesthetized with thiopentone alone.

Group B: 50 cases who were anesthetized with midazolam and thiopentone sodium *as* co-induction.

Inclusion criteria:

- ASA Class I, II and III patients.
- Hypertensive males and females of 30-60 years of age.
- Hypertensive with diastolic blood pressure from 90-110 mmHg.
- Pre-operative Hb more than 11 gm%.

Exclusion criteria:

- Emergency cases
- Patients with Ischemic heart diseases, valvular heart diseases or congenital heart diseases.
- Patients with chronic obstructed pulmonary diseases or restrictive lung diseases.

Procedure:

All the in-door hypertensive patients of surgical department were included in the study as per criteria. Informed consent from patient or their relatives. Odd numbers were included in group A and even number were put in group B. Pre-operative reading of heart rate and blood pressure were taken five minutes before giving pre-medication. Pre-medication with injection Tramadol intravenous 1mg/kg body weight was given to all patients of both groups. Injection vecuronium (0.1mg/kg) was given as muscle relaxant in both groups. In *group A* induction of anesthesia was done with thiopentone alone (dose 4mg/kg body weight). In *group B* for co-induction thiopentone and midazolam (dose 2mg/kg, and 0.02mg/kg) were given. Midazolam was given 1 minute before thiopentone sodium with premedication. Isoflorane inhalation agent for maintenance was given in both groups. Intravenous fluids Ringer Lactate was given to both groups (for deficits and maintenance). Reversal was done with pyrolate-N in both groups. Peri- operative reading of heart rate and blood pressure were taken with 5 minutes interval. Postoperative reading of heart rate and blood pressure were taken 5 minutes after extubation. All these changes were recorded. *All* the relevant information regarding patient's name, sex, age, address, pulse, blood pressure, smoking history, chest, ASA class, premedication, preoxygenation, antibiotics were entered into a proforma especially designed for this purpose.

RESULTS

Among the 100 patients selected, 27 were from age group 30-40 years, 36 from age group 40-50 years and 37 from age group 50-60 years. Mean age of the patients was 47 years with a standard deviation $\pm$ 7.74 years. Minimum age recorded was 34 years and maximum age 60 years. (table no 1). Thirty cases were currently smokers and 70 were non smoker. Fifty one were female and 49 were males. It is important to note that after randomizatin both the groups were statistically equal in terms of genders and smoking habits.

The results of logistic regression are summarized in table 2 and 3. The patients with unstable heart rate and unstable diastolic blood pressure were more in group A. The Patients with stable heart rate and stable diastolic blood pressure were more in group B.

HEART RATE VARIATION IN GROUP A AND B

Heart Rate	Group		*p* Value	Odd Ratio	C.I
	Group A	Group B			
Un-Stable	32 (64%)	14 (28%)	0.005	4.57	1.96 -- 10.65
Stable	18 (36%)	36 (72%)			
Total	50	50			

Table 2

p value, odd ratio and confidence intervals are shown in (table No.2 and 3). In terms of stability of heart rate and diastolic blood pressure there was statistically significant difference between the two groups.

DISCUSSION

We studied 100 hypertensive cases, who were equally divided into two groups of 50 patients each. Fifty patients of group "A" were anesthetized with thiopentone alone while 50 patients of group "B" were anesthetized with midazolam and thiopentone co-induction. The results showed that patients with unstable heart rate and diastolic blood pressure were more likely in group A and patients with stable heart rate and diastolic blood pressure were more likely in group B. In terms of stability of heart rate and diastolic blood pressure there were statistically significant differences among the two groups (Table No.2 and 3). Our finding regarding the stability of heart rate and diastolic blood pressure are in concurrence with Reves JG et al [10] who studied the pharmocology and uses of midazolam.In search of the world english literature no refrence could be found where thiopentone was used in combination with midazolam in hypertensive patients regarding the effect on heart rate and diastolic blood pressure.

A study was conducted in the department of anesthesiology Agha Khan Universty Hospital in 2003. [11] Theyincluded 90 normotensive ASA class I and II patients in their study and divided them into three groups. Our study was conducted on 100 hypertensive patients divided into two groups. In their study group A were given thiopentone 4mg/kg and 3ml normal saline. To group B patients, thiopentone 3mg/kg and midazolam 0.02mg/kg was given. Group C received thiopentone 2mg/kg and midazolam 0.02 mg/kg. The dosage received in groups A and C were similar to our study groups A and B. According to their study systolic and diastolic blood pressure in group B and C (co- induction groups) showed least variation from the base line and the results were statistically significant when group B and C were compared with group A (Induction group). Also the heart rate was clinically more stable in group B and C but the data for heart rate was statistically not signifiacant.

Approximately the same results are endorsed by our study, but there are some differences as well. Our results are statistically significant both for diastolic blood pressure and heart rate. The other major difference is that, our study was conducted on hypertensive patients and that study was on normotensive patients. According to that study in group B the dose of thiopentone was reduced to 25% and in group C the dose of thiopentone was reduced to 50%. The best haemodynamic stability was recorded in group B (thiopentone dose reduced to 25%). In our study the dose of thiopentone given was 2mg/kg (reduced by 50% of induction dose). But still we recorded statistically significant stability of heart rate and diastolic blood pressure in hypertensive patients. The reason may be that hypertensive patients are haemodynamically more unstable and are more sensitive to the hypotensive effect of thiopentone when given in full induction dose but by reducing the dose of thiopentone sodium to 50% by combination with midazolam better haemodynamic stability is acheived. Baykara N et al [12] studied the effects of midazolamthiopentone coinduction compared with thiopent induction on recovery and showed that the induction dose of thiopent one was significantly lower in the coinduction group. There were no significant

DIASTOLIC BLOOD PRESSURE VARIATION IN GROUP A AND B

Diastolic Blood Pressure	Group		*p* Value	Odd Ratio	C.I
	Group A	Group B			
Un-Stable	33 (66%)	15 (30%)	0.005	4.53	1.956 10.51
Stable	17 (34%)	35 (70%)			
Total	50	50			

Table 3

differences in awakening times and the frequency of nausea and vomiting in the recovery period was lower in the coinduction group. However the haemodynamic response could not be assessed as Isoflurane concentration was adjusted to keep blood pressure within ± 20% of the preoperative value. Studies have been conducted on midazolam-propofol coinduction and have been found to have synergistic effect in induction but the haemo-dynamic effect of this coinduction has been inconsistant. [13,14] In our study we were not able to arrange assesment of the cardiac status within 72 hours post operatively. However we would recommend that all patients who are hypertensive may be preferably induced with combination of thiopentone and midazolam.

CONCLUSION

Co-induction of anesthesia with thiopentone and midazolam provide better effect profile and haemodynamic stability as compared to induction with thiopentone alone in hypertensive patients. However large scale randomised controlled trials are needed to study the haemodynamic effects of thiopentone and midazolam.

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