COMPARISON OF MIDAZOLAM AND THIOPENTONE AS INDUCTION AGENTS IN GENERAL ANAESTHESIA

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Abstract

A single blind parallel group study was performed in 137 patients undergoing elective surgery under general anaesthesia to compare the efficacy and tolerability of midazolam 0.15 to 0.25 mg/kg or thiopentone 6 mg/kg. Induction time was 45.0 ± 17.1 secs in midazolam group in comparison to 32.0 ± 9.5 secs in thiopentone group and the frequency of apnoea was 11.5% and 17.1% respectively. There was no difference in the duration of apnoea in the two groups. No venous intolerance was experienced during the study. It appears that midazolam is a suitable alternative to thiopentone and would be of value where the latter is contraindicated.

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KEY WORDS :Drugs; General Anaesthesia; Induction; Midazolam.

Introduction

Midazolam is 1,4 - benzodiazepine derivative. Earlier studies with midazolam have demonstrated its efficiency in the induction of anaesthesia. Midazolam is considered superior to diazepam for induction of anaesthesia as it causes less burning on injection, is quicker in onset and there is less individual variation in response to a given dosage of midazolam. Midazolam is also short acting with a relatively brief half life. Most of the advantages of midazolam over diazepam are a result of its greater water solubility. The present study compares midazolam with thiopentone as induction agents in patients undergoing surgery under general anaesthesia.

Material and Methods

This was a single blind, randomized, comparative, parallel group study of 137 patients. Anaesthesiologist responsible to induce the patients for anaesthesia was blind to the identity of the drugs.

57 male and 80 female patients participated in this study. They were in ASA class I or II and were scheduled for operation expected to last for less than 120 minutes. Informed consent was obtained from all. Pregnant and breast feeding women and women of child bearing potential were excluded from this study. Patients with decompensated hepatic or renal disease and those with a history of hypersensitivity to barbiturates were also excluded.

All patients were premedicated with injection atropine 0.6 mg 30 min prior to surgery. An intravenous line was established and an infusion of dextrose saline set up before the patient was wheeled in the operation theatre. Midazolam was used as a 1 mg per ml formulation, whereas thiopentone was freshly prepared as a 2.5% solution in water for injection. Patients received midazolam (0.15mg to 0.25 mg) or thiopentone solution (4-6 ml) as initial bolus over a period of 30 seconds. Doses were repeated at 2 minute intervals in increments of 25% of the initial dose if induction

was not achieved but the total dose did not exceed 15 mg in case of midazolam and 6 mg/kg in case of thiopentone. Failure to take deep breaths on being asked to do so and loss of eyelid reflex were the criteria for achievement of induction. Morphine 0.01 mg/kg was administered intravenously 3 min prior to intubation to prevent stress response of tracheal intubation. Suxamethonium 1.5 to 2.0 mg/kg bolus was administered for tracheal intubation. Maintenance of anaesthesia was achieved with a mixture of nitrous oxide and oxygen (2:1); 0.5% halothane was added, if required.

Continuous monitoring of blood pressure, heart rate, SaO_2 , and ECG was done from the moment patient entered the operation theatre till recovery. The efficacy and variables studied were induction time, blood pressure, heart rate, apnoea, duration of apnoea, arterial oxygen saturation and any rhythm disturbances. Patients were reviewed on the next day of surgery and any adverse experience recorded.

Results & Discussion

137 patients were enrolled in this study; 61 patients received midazolam and 76 patients received thiopentone. The mean age of patients in the midazolam group was 40.52 ± 12.51 (SD) years (range 16 to 68 years) and mean age in thiopentone group was 32.25 ± 12.98 (SD) years (Table 1).

Induction with both the agents was smooth. No excitatory effects were observed with either agent. The mean dose for induction with midazolam was 13.00 ± 3.65 mg (0.20 ± 0.03 mg/Kg) and the mean induction with midazolam 45.00 ± 17.07 sec, in the midazolam group and 32.00 ± 9.47 sec. in the thiopentone group. 13 patients in the thiopentone group and 7 patients in the midazolam group had apnoea with administration of the study medication.

The duration of apnoea was 16.71 ± 12.67 sec in the midazolam group and 15.08 ± 6.47 sec in the thiopentone group. The mean oxygen saturation was above 97% after the administration of either study medications (Table-3).

Before drug administration the mean heart rate, systolic and diastolic blood pressure in the midazolam group were 89.4 ± 9.5 beats per minute, 128.5 ± 12.7 mm Hg and 80.7 ± 7.8 mm Hg respectively. The mean heart rate was 90.8 ± 9.5 beats per minute

TABLE 1

Patient demographics

	Midazolam (n=61)	Thiopentone (n=76)
Age (yrs)		
Mean $\pm$ SD	40.52 $\pm$ 12.51	32.25 $\pm$ 12.98
Range	16-68	15-70
Sex (No and percent)		
Male	30 (49.2%)	27 (35.5%)
Female	31 (50.8%)	49 (64.5%)
Weight (Kg)		
Mean $\pm$ SD	56.10 $\pm$ 10.41	56.53 $\pm$ 12.00
Range	36-81	35-96
Duration of anaesthesia (min)		
Mean $\pm$ SD	82.84 $\pm$ 38.31	78.78 $\pm$ 47.53
Range	30-190	20-192
Duration of surgery (min)		
Mean $\pm$ SD	76.90 $\pm$ 36.90	73.95 $\pm$ 46.55
Range	25-182	17-188

TABLE 2

Induction parameters (mean $\pm$ SD)

	Midazolam (n=61)	Thiopentone (n=76)
Dose (mean $\pm$ SD)		
Total (mg)	13.00 $\pm$ 3.65	313.46 $\pm$ 40.33
per/kg	0.20 $\pm$ 0.03	5.3 $\pm$ 0.40
Induction time (sec)	45.00 $\pm$ 17.07	32.00 $\pm$ 9.47
Number of patients with apnoea	7	13
Duration of apnoea (sec)	16.71 $\pm$ 12.67	15.08 $\pm$ 6.47

TABLE 3

Respiratory rate and oxygen saturation (mean $\pm$ SD)

	Midazolam (n=61)	Thiopentone (n=76)
Respiratory rate		
Preinduction	17.2 $\pm$ 1.6	16.2 $\pm$ 1.2
After induction	17.6 $\pm$ 1.5	16.4 $\pm$ 1.0
Oxygen saturation (%)		
Preinduction	96.1 $\pm$ 2.6	96.1 $\pm$ 9.5
1 min after induction	98.4 $\pm$ 1.4	98.4 $\pm$ 0.9
3 min after induction	99.5 $\pm$ 0.7	99.3 $\pm$ 1.0

TABLE 4

Heart rate and arterial blood pressure (mean $\pm$ SD)

	Midazolam (n=61)			Thiopentone (n=76)		
	Heart rate (bpm)	Systolic (mm Hg)	Diastolic (mm Hg)	Heart rate (bpm)	Systolic (mm Hg)	Diastolic (mm Hg)
Preinduction	89.4 $\pm$ 9.5	128.5 $\pm$ 12.7	80.7 $\pm$ 7.8	94.1 $\pm$ 11.9	127.3 $\pm$ 11.0	81.37 $\pm$ 7.5
Induction	90.8 $\pm$ 9.5	125.7 $\pm$ 14.4	79.8 $\pm$ 8	94.6 $\pm$ 12.1	118.0 $\pm$ 12.2	75.7 $\pm$ 9.1
Post induction	93.6 $\pm$ 10.2	132 $\pm$ 14.2	82.2 $\pm$ 7.6	98.9 $\pm$ 10.1	134.2 $\pm$ 19.5	84.9 $\pm$ 9.7
Post intubation						
At 10 min	86.9 $\pm$ 9.2	129 $\pm$ 10.4	79.2 $\pm$ 5.7	86.9 $\pm$ 11.9	120 $\pm$ 10.7	77.6 $\pm$ 6.1
At 20 min	84.7 $\pm$ 9.4	123.3 $\pm$ 11.3	78.0 $\pm$ 6.0	84.2 $\pm$ 12.4	119.4 $\pm$ 10.4	76.4 $\pm$ 6.7
At 30 min	82.9 $\pm$ 9.1	122.2 $\pm$ 10.4	78.3 $\pm$ 6.1	93.2 $\pm$ 11.3	119.3 $\pm$ 9.6	76.3 $\pm$ 5.5
Recovery	89.9 $\pm$ 9.3	126.3 $\pm$ 8.6	80.2 $\pm$ 6.0	87.9 $\pm$ 10.2	119.3 $\pm$ 6.1	77.3 $\pm$ 4.8

after induction and the pressures, systolic and diastolic, were 125.7 $\pm$ 14.4 and 79.8 $\pm$ 8.0 mm Hg respectively. During intubation the heart rate increased to 93.6 $\pm$ 10.2 beats per minute and systolic and diastolic blood pressures to 130.2 $\pm$ 14.2 and 82.2 $\pm$ 7.6 mm Hg respectively. All these parameters remained stable in post intubation and recovery phases.

In the thiopentone group, the heart rate, systolic and diastolic blood pressures before the drug administration were 94.1 $\pm$ 11.9 beats per minute, 127.3 $\pm$ 11.0 and 81.7 $\pm$ 7.5 mm Hg respectively. Soon after induction the mean heart rate remained almost unaltered (94.6 $\pm$ 12.1) beats per minute but systolic and diastolic blood pressures showed a slight fall to 118.0 $\pm$ 12.2 and 75.7 $\pm$ 7.1 mm Hg respectively. During intubation, the heart rate increased to 98.9 $\pm$ 10.1 and systolic and diastolic blood pressures to 134.2 $\pm$ 19.5 and 84.9 $\pm$ 9.7 mm Hg, respectively. Heart rate and blood pressure were stable both in post intubation and recovery phases.

Both the study medications were well tolerated. No patient in either group, experienced any venous intolerance. 1 patient each in either group developed multiple ventricular ectopics and was treated and controlled with lignocaine 100 mg iv bolus, followed by infusion upto recovery.

Midazolam is a safe and effective induction agent and could be used as an alternative to thiopentone where the latter is contraindicated.

References

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