Title: INTRACRANIAL PRESSURE, MEAN ARTERIAL PRESSURE AND HEART RATE FOLLOWING MIDAZOLAM OR THIOPENTAL IN HUMANS WITH INTRACRANIAL MASSES

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Introduction. Midazolam maleate is a water-soluble benzodiazipine that has recently been recommended as an effective intravenous anesthetic induction agent.[1] Minimal cardiovascular effects have been reported with its use in patients with ischemic heart disease.[2] The cerebral metabolic rate for oxygen ($CMRO_2$) is decreased in dogs with doses of midazolam greater than 2.0 mg/kg.[3] In addition, midazolam decreased cerebral blood flow (CBF) by 53% in dogs[3] and 35% in humans.[4] Drugs which decrease CBF and $CMRO_2$ favorably affect intracranial dynamics. Therefore, the effects of midazolam or thiopental on intracranial pressure (ICP) and cerebral perfusion pressure (CPP) were studied in ASA 2-3 patients with poor intracranial compliance who were undergoing craniotomy for excision of tumors.

Methods. In a double-blind study, 13 patients, undergoing elective craniotomy for excision of tumors, were assigned randomly to receive either midazolam or thiopental for intravenous anesthesia induction. Each had previously given informed consent after the approval of the hospital's Human Research Committee. Only steroid drugs were continued on the day of surgery before induction. A radial artery and two peripheral vein catheters were inserted and the electrocardiogram was monitored. A subarachnoid screw was inserted after local anesthesia and intracranial compliance was tested. Saline (1 ml) was injected through the subarachnoid screw, and ICP was recorded. Only patients demonstrating an increase in ICP of greater than 4 mmHg were included. After ICP returned to baseline, either midazolam maleate (0.25 mg/kg) or thiopental (4 mg/kg) was administered. Twenty five percent incremental doses were given every two minutes, if required, until the patient became unresponsive to commands and had lost his/her eyelid reflex. Heart rate (HR), mean arterial blood pressure (MAP), and ICP were continuously recorded. Measurements were noted before and immediately after induction. Arterial carbon dioxide tension ($PaCO_2$) was determined before and after induction. Cerebral perfusion pressure was calculated using the formula, MAP - ICP = CPP. Results were analyzed using the Student's matched pair "t" test.

Results. There were no differences in demographic variables between the two groups. Mean age of the seven patients in the midazolam group was 57 years and the weight 77 kg; for the six thiopental patients, the mean age was 50 years and the weight 64 kg. The mean dose of midazolam was 0.27 mg/kg (ED99); for thiopental, 4.8 mg/kg. There was no significant change in $PaCO_2$. Mean arterial pressure, HR, ICP, and CPP during induction are shown in the table. In the thiopental group, there was no evidence of change in HR, MAP, ICP, or CPP. In the midazolam group, there was no change detected in ICP or CPP but statistically significant decreases in MAP and HR were observed.

Discussion. No change in ICP was apparent during induction with midazolam or thiopental. Athough a decrease in MAP (14%) was demonstrated in the midazolam group, CPP was not significantly decreased and remained in the physiologic range. While the decrease in HR was statistically significant, it was not clinically significant.

While a larger sample is required to substantiate a lack of effect, these preliminary data indicate that midazolam represents an alternative to thiopental for induction of anesthesia in patients with decreased intracranial compliance.

References.

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Table: ICP, CPP, MAP, HR after midazolam (M) or thiopental (T) in patients with intracranial masses.

		Pre-Induction	Post-Induction	Δ ±	Confidence Interval (95%)
MAP (mmHg)	M	96	82	-13	± 12*
	T	96	88	-8	± 15
HR (beats/min)	M	80	71	-9	± 6*
	T	79	81	+2	± 10
ICP (mmHg)	M	13	10	-3	± 5
	T	10.7	9.5	-1.2	± 4.6
CPP	M	83	72	-11	± 13
	T	87	79	-8	± 19

* $p < .05$ matched pair "t" test