TITLE: COMPARISON OF MIDAZOLAM AND THIOPENTAL FOR ANESTHESIA INDUCTION

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INTRODUCTION - Midazolam maleate(M)is a water soluble potent benzodiazepine salt with a shorter duration of action than diazepam.[1 2 3] The purpose of this study was to compare midazolam and thiopental(T) as intravenous induction agents, especially with reference to the incidence of phlebitis, the rate of onset, mean arterial pressure(MAP) and heart rate(HR) change,respiratory depression, and the speed and quality of recovery.

METHODS - Participating in this study, which was approved by the Human Investigation Committee, were 49 ASA Class I-II nonpregnant females or males(age range 18-60 years)who had given informed consent. Blood hematology and chemistry, urinalysis, chest x-ray, and EKG were all within normal limits. Subjects were premedicated 45 to 75 minutes prior to induction with glycopyrrolate, 0.005 mg/kg, and meperidine hydrochloride, 1.0 mg/kg. Ethrane-N_2O-O_2 was used for maintenance. Most patients were intubated for their surgical procedure. Neuromuscular blocking agents were given in a separate IV site after all the criteria for the induction of anesthesia were present and post-induction vital signs had been recorded. The IV site was the cephalic vein at either side of the mid-forearm, and identical techniques were used for every patient. This was a double-blind(third party open)parallel study; the anesthesiologist prescribing the premedication and administering the study drug was not blinded. The anesthesiologist monitoring the patient during the operation and the investigator making postoperative visits at 24-hours, 1,2,4 and 8 weeks were blinded. Induction of anesthesia was defined as the moment when all of the following signs were present: loss of response to commands, loss of eyelid reflex and loss of purposeful movement in response to placement of mask. The initial dose of either M or T was given at a constant rate over 20 seconds. The doses of M were: 0.2 mg/kg($M_{0.2}$;N=12) 0.3mg/kg($M_{0.3}$;N=6);0.4mg/kg($M_{0.4}$;N=6) The doses of T were: 3.5mg/kg($T_{3.5}$;N=13); 4.0mg/kg($T_{4.0}$;N=12). If induction of anesthesia did not occur after 2 minutes from the start of the injection an additional 25% of the initial dose was given every two minutes up to two times.

RESULTS - Comparisons between the M and T treatment groups are presented below.

Rate of Onset

Induction time: lost of response to command

DOSES	INDUCTION TIME(SEC)	PROBABILITY
$M_{0.2}$	88.33	P < 0.21
$T_{3.5}$	67.28	
$M_{0.3}$	115.67	P < 0.002
$T_{4.0}$	57.17	
$M_{0.4}$	88.80	P < 0.013
$T_{4.0}$	57.17	

Induction time: Loss of eyelid reflexes

DOSES	INDUCTION TIME(SEC)	PROBABILITY
$M_{0.2}$	94.67	P < 0.19
$T_{3.5}$	73.86	
$M_{0.3}$	116	P < 0.0082
$T_{4.0}$	64.5	
$M_{0.4}$	99	P < 0.010
$T_{4.0}$	64.5	

Induction time: Loss of purposeful movement

DOSES	INDUCTION TIME(SEC)	PROBABILITY
$M_{0.2}$	95.33	P < 0.10
$T_{3.5}$	70.14	
$M_{0.3}$	117.33	P < 0.0023
$T_{4.0}$	57.92	
$M_{0.4}$	89.2	P < 0.02
$T_{4.0}$	57.92	

6/12 patient of $M_{0.2}$ and 6/13 patient of $T_{3.5}$ needed additional doses. 3/6 $M_{0.3}$ require second dose. 1/6 $M_{0.4}$ and 0/12 $T_{4.0}$ needed second dose.

MAP and HR Changes During Induction: HR did not change significantly in any of the groups. Changes in MAP as followings:

	$M_{0.2}$	$T_{3.5}$
Preinduction MAP(mmHg)	88.89±10.06	93.38±10.59
Postinduction MAP(mmHg)	82 64±11.48	89.28±11.66
	(P < 0.001)	
	$M_{0.4}$	$T_{4.0}$
Preinduction MAP(mmHg)	84.38±16	84.36±12.56
Postinduction MAP(mmHg)	79.38±6	79.66±10.81
	(P < 0.06)	

The incidence of respiratory depression during induction was 10/12 in $M_{0.2}$; 9/13 in $T_{3.5}$; 3/6 in $M_{0.3}$; 5/6 in $M_{0.4}$; 12/12 in $T_{4.0}$. There were no significant differences in speed or quality of recovery among any of the groups. All groups were negative for phlebitis in examinations on postoperative days 1,7 and 14, and in subsequent followups 4 and 8 weeks postoperatively.

DISCUSSION - This study has shown that 0.2-0.4mg/kg of M is comparable to 3.5-4.0mg/kg of T for safe induction of anesthesia, but has a slightly slower onset. Neither drug caused phlebitis. Like T, M only decreased MAP 4 to 6 torr during induction with no significant change in HR. Similar to T, M also decreased ventilation during induction, therefore respiratory support is needed.

REFERENCES

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