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Title : MIDAZOLAM VERSUS DIAZEPAM: HEMODYNAMIC COMPARISON

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Introduction. Midazolam maleate (M), the investigational water soluble 1-4 benzodiazepine, and diazepam (D) have minimal cardiovascular effects in patients with ischemic heart disease (1,2,3). This present study compares midazolam and diazepam effects on hemodynamic variables during induction of anesthesia.

Methods: Twenty patients electively scheduled for myocardial revascularization surgery were randomly assigned to receive midazolam or diazepam (10 patients in each group) (after informed consent and approval by the IRB). Premedication consisted of morphine sulfate 0.1 mg/kg IM and scopolamine 6-8 µg/kg IM 60-90 min prior to induction. Catheters were placed in two peripheral veins, a radial artery and the pulmonary artery via the right internal jugular vein (Edwards Swan-Ganz triple lumen thermodilution catheter). ECG (V_5 and II), heart rate (HR), rhythm, systemic systolic/diastolic (SBP/DBP), and mean blood pressure (MAP), mean right atrial pressure ($\overline{RAP}$), pulmonary artery systolic/diastolic (PASP/PADP) and mean pressure ($\overline{PAP}$), pulmonary artery occluded pressure ($\overline{PAO}$), thermodilution cardiac output in duplicate (CO), and ABGs were measured serially. Derived data consisted of cardiac index (CI), stroke index (SI), heart rate systolic blood pressure product (RPP), systemic (SVRI) and pulmonary vascular resistance index (PVRI), and left (LVSWI) and right ventricular stroke work index (RVSWI). Measurements were made at the following time periods: 1) baseline breathing room air (AIR), 2) baseline breathing 100% oxygen (repeated every 5 min until values stable ± 10%) (O_2), 3) second min after diazepam (0.5 mg/kg IV) or midazolam maleate (0.2 mg/kg IV), 4) fifth min after D or M. Ventilation was monitored continuously by end expired CO_2, documented by ABGs at each measurement and assisted when respiratory depression or apnea occurred. Following the above measurement periods, the patients were placed on 50% N_2O in O_2, given pancuronium 0.1 mg/kg, intubated, and surgical positioning and prep begun. The data was analyzed by using multifactorial analysis of variance and the New Duncan's Multiple Range Test with $p < 0.05$ considered significant.

Results: There was no significant difference in the demographic variables between the two groups. The mean age was 55 years, wt. 83 kg, BSA 2.0 m^2. Sixteen patients had three vessel coronary disease and one had left main stenosis. Nine patients had an LVEDP > 18 at catheterization, 16 were on propranolol and at surgery 3-6 grafts were performed on all patients. All patients were successfully induced with diazepam or midazolam. No adjuvant anesthetic, inotropic, or antiarrhythmic drugs were required throughout the study and intravenous crystalloid was limited to "keep open". The measured and derived hemodynamic responses for patients induced with D and M are shown in the table. $Drug_{1-2}$ and $Drug_{4-5}$ refer to the hemodynamic measurements made during the second and fifth minutes following drug administration. There were no significant differences between the two groups for the baseline values. There was a slight increase in the HR in the midazolam group and a significant decrease in the MAP, $\overline{PAP}$, $\overline{PAO}$, SI, LVSWI, and RVSWI in the midazolam patients. There was a significant difference between M and D patients for HR, MAP, and LVSWI at the fifth minute time period.

Discussion: There are no previous studies comparing in a random fashion these two benzodiazepine anesthetics. A small but definite increase in heart rate and decrease in MAP occurs with midazolam. Cardiac index was well maintained with both drugs. $\overline{PAO}$ decreased moreso with midazolam; an effect perhaps of value in patients with abnormally elevated $\overline{PAO}$. The results indicate that midazolam like diazepam effectively maintains hemodynamic variables during anesthetic induction in patients with ischemic heart disease. It appears that midazolam with its shorter duration of action and absence of pain on IV injection will have a definite role for the induction of anesthesia especially for shorter procedures in patients with cardiac disease.

References:

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VARIABLE		MEASUREMENT PERIOD: AIR	O_2	$DRUG_{1-2}$	$DRUG_{4-5}$
HR	M	68 ± 4.4	64 ± 5.0	71 ± 2.3	71 ± 2.5*
	D	68 ± 2.1†	61 ± 2.0	65 ± 2.4	62 ± 1.6
MAP	M	102 ± 5.6	108 ± 5.3	90 ± 3.5†	75 ± 4.1†*
	D	102 ± 3.1	110 ± 4.9	102 ± 4.9	97 ± 4.5
$\overline{RAP}$	M	8 ± 1.3	10 ± 1.0	9 ± 1.0	9 ± 1.2
	D	9 ± 1.3	9 ± 1.8	9 ± 1.8	9 ± 1.4
$\overline{PAP}$	M	19 ± 2.0	22 ± 2.3	18 ± 1.7	14 ± 1.3†
	D	18 ± 1.5	19 ± 2.0	16 ± 1.6	15 ± 1.5
$\overline{PAO}$	M	12 ± 1.6	16 ± 1.5	12 ± 1.0	9 ± 1.0†
	D	11 ± 2.0	13 ± 2.2	12 ± 1.7	10 ± 1.5
RPPx10^3	M	10.9 ± 1.32	10.4 ± 1.34	9.3 ± 0.70	7.6 ± 0.58
	D	10.3 ± 0.42	9.9 ± 0.49	9.6 ± 0.40	8.3 ± 0.45
CI	M	2.5 ± 0.11	2.4 ± 0.15	2.4 ± 0.13	2.2 ± 0.16
	D	2.7 ± 0.16	2.4 ± 0.19	2.3 ± 0.20	2.2 ± 0.13
SI	M	38 ± 1.8	38 ± 2.1	34 ± 1.6	31 ± 2.1†
	D	40 ± 2.2	39 ± 2.3	36 ± 2.8	36 ± 1.9
SVRI	M	786 ± 60.0	896 ± 97.2	714 ± 66.2	675 ± 87.5
	D	664 ± 36.5	841 ± 72.4	800 ± 70.9	774 ± 48.2
PVRI	M	54 ± 6.6	59 ± 11.4	49 ± 6.1	49 ± 3.9
	D	46 ± 6.5	49 ± 6.8	41 ± 5.2	44 ± 3.9
LVSWI	M	45.8 ± 2.27	47.0 ± 2.64	35.7 ± 2.04†	27.4 ± 2.19†*
	D	49.3 ± 3.17	51.6 ± 3.65	44.0 ± 3.64	42.5 ± 2.64
RVSWI	M	5.4 ± 0.44	6.3 ± 0.80	3.9 ± 0.55†	2.3 ± 0.26†
	D	4.9 ± 0.53	5.3 ± 0.71	3.6 ± 0.70	3.0 ± 0.56

WHERE: *$p < 0.05$ M vs D; †$p < 0.05$ $\bar{x}$ (M or D) vs respective O_2 control; M = midazolam patients; D = diazepam patients; HR (beats/min); MAP; $\overline{RAP}$; $\overline{PAP}$; $\overline{PAO}$ (mmHg); RPP (beats · mmHg/min); CI (L/min/m^2); SI (ml/min/m^2); SVRI; PVRI (dynes·sec·cm^{-5}/m^2); LVSWI; RVSWI (g·m/m^2).