Title: METABOLIC AND HEMODYNAMIC EFFECTS OF MIDAZOLAM IN CRITICALLY ILL INFANTS

Authors: O.E. Mohan, M.D., M.B. Hershenson, M.D., J.A. Schena, R.R.T. and R.K. Crone, M.D.

Affiliation: Department of Anaesthesia, Harvard Medical School, The Children's Hospital, Boston, Massachusetts 02115.

Introduction. Midazolam has been used as an anxiolytic and sedative in critically ill children[1] and adults.[2] In unpremedicated adult male patients undergoing cardiac catheterization, intravenous administration of midazolam, 0.2 mg/kg, significantly reduced both blood pressure and total-body oxygen consumption,[3] suggesting that midazolam blunts stress-induced changes in sympathetic tone and metabolic rate. Such changes have been shown to be deleterious in newborn infants.[4] We therefore examined the effect of midazolam on hemodynamics and oxygen consumption in critically ill infants.

Methods. After informed parental consent, 11 infants, age 1-36 months (9.8±11.1, mean±S.D.) were studied. All infants required pharmacologic sedation during intermittant mandatory ventilatory support; 5 of 11 were admitted to the intensive care unit for post-operative management. Seven patients were previously treated with either fentanyl or morphine (premedicated group). Four awake patients received no previous medication (unpremedicated group).

Heart rate (HR, beats/min), respiratory rate (RR, breaths/min), systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg) and oxygen consumption (VO_2, cc/kg/min) were determined before (control) and 5 minutes after intravenous administration of midazolam, 0.2 mg/kg. Oxygen consumption was measured using a closed circuit apparatus, which consisted of a 500 cc anesthesia bag in a plexiglass box, respiratory tubing, a CO_2 adsorber and spirometer. (The relationship between known volume and measured volume during volumetric calibration of the apparatus was not significantly different from the line of identity; measured volume = 1.03•actual volume - 5.83, r = 0.98.) Only patients without endotracheal tube leaks at the relevant ventilator pressures were included for study. Recorded oxygen consumption values were taken as the average over 15 minutes.

Results. The effect of midazolam on mean heart rate, respiratory rate, blood pressure and oxygen consumption are shown in the Table. In the premedicated group, midazolam had no significant effect on any of the measured parameters. In the unpremedicated group, however, midazolam significantly reduced both systolic blood pressure ($p<0.001$, paired t test) and oxygen consumption ($p<0.05$). When both groups were combined, midazolam-induced changes in systolic blood pressure were proportional to changes in oxygen consumption ($r=0.94$, $p<0.01$, ANOVA, Figure).

Discussion. We have shown that midazolam decreases systolic blood pressure and oxygen consumption in unpremedicated critically ill patients. Further, changes in O_2 consumption varied with those of systolic blood pressure. Midazolam appeared to have little effect in patients who were already receiving narcotics.

These data demonstrate that midazolam reduces metabolic rate, and may reduce the stress-induced sympathetic response in infants. This response has been shown to be deleterious in newborn infants.[4] In addition, reductions in total-body oxygen consumption, which are indicative of reduced energy expenditure, may be beneficial in acutely ill infants in whom oxygen delivery to the tissues may be limited. Midazolam may therefore be a useful adjunct in the care of critically ill infants.

References. 1. Lloyd-Thomas AR and PD Booker. Infusion of midazolam in paediatric patients after cardiac surgery. Br J Anaesth 58: 1109-1115, 1986.

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Table. Effect of midazolam on heart rate, respiratory rate, blood pressure and oxygen consumption (mean±S.D., *$p<0.05$, **$p<0.001$, paired t test).

	PREMEDICATED (n=7)		UNPREMEDICATED (n=4)	
	CONTROL	MIDAZOLAM	CONTROL	MIDAZOLAM
HR	150±12	148±19	132±19	140±17
RR	44±16	41±13	51±16	53±13
SBP	97±18	94±18	84±15	68±13**
DBP	52±13	49±8	50±13	43±9
VO_2	9.1±2.5	8.8±2.4	12.0±2.4	9.9±1.6*

Figure. Relationship between midazolam-induced changes in oxygen consumption and systolic blood pressure ($\Delta SBP = 1.01 \bullet \Delta VO_2 - 0.27$, $r=0.94$, $p<0.01$, ANOVA).