Title: AN EVALUATION OF THE HEMODYNAMIC EFFECTS OF DOXACURIUM DURING AORTIC VALVE REPLACEMENT SURGERY FOR AORTIC STENOSIS IN PATIENTS RECEIVING OXYGEN FENTANYL ANESTHESIA

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Introduction. Isolated aortic stenosis (AS) is the most common lesion in patients with valvular heart disease[1]. AS is characterized by left ventricular (LV) outflow obstruction with pressure overload, LV hypertrophy with relative subendocardial ischemia, decreased LV compliance, and a high myocardial oxygen demand. These pathophysiologic principles dictate that anesthetic management be based upon the avoidance of systemic hypotension and tachycardia, the latter being particularly deleterious due to its potential for exacerbating myocardial ischemia and the transvalvular pressure gradient. Consequently, a muscle relaxant devoid of cardiovascular effects would benefit these patients. doxacurium is an investigational non-depolarizing neuromuscular blocking agent, which is long acting and does not cumulate during repeated dosing. Doxacurium has been shown to have no cardiovascular side effects in healthy patients[2], and initial reports, in patients with cardiac disease, indicate small, but often statistically significant, cardiovascular changes in doses ranging up to 50 µg/kg (2 X ED_{95}) during O_2-sufentanil-midazolam[3] or O_2-fentanyl-diazepam anesthesia[4]. The purpose of this study was to determine the hemodynamic response to doxacurium, in patients with AS prior to aortic valve replacement surgery (AVR) during O_2-fentanyl anesthesia.

Methods. With institutional approval, and written informed consent from each patient, 8 patients undergoing elective AVR, for treatment of AS, were studied. Patients' ages ranged from 44 to 77 years, all were ASA PS 3 or 4, and all were New York Heart Association functional class 2 or 3. The patients were premedicated with a combination of morphine (0.08 to 0.10 mg/kg, IM), scopolamine (0.003 to 0.005 mg/kg, IM), diazepam (0.07 to 0.15 mg/kg, PO), or lorazepam (0.05 to 4.0 mg, IM, IV) as determined individually for each patient. Cardiac medications were continued up to the time of surgery. Each patient was monitored by electrocardiographic leads II and V5, pulse oximetry, and radial and pulmonary artery catheters connected to aneroid calibrated transducers zeroed at the level of the right atrium. Anesthetic induction was accomplished intravenously with fentanyl (25 to 50 µg/kg) while the patient breathed 100% oxygen via face mask. Tracheal intubation was facilitated by succinylcholine (1.0 to 1.5 mg/kg). End-tidal CO_2 was maintained near 30 mmHg. During a stable state of fentanyl anesthesia, after complete recovery from the succinylcholine, baseline hemodynamic measurements were obtained in triplicate. Immediately thereafter, an intravenous bolus of doxacurium, 50 µg/kg, was administered. Hemodynamic measurements were repeated at 2 minutes, 5 minutes, and 10 minutes.

Data were analyzed by repeated measures ANOVA, with significance defined as $p < 0.05$. All values are expressed as mean ± standard error of the mean.

Results. The hemodynamic measurements, and derived parameters, are presented in the table. After administration of doxacurium, there were statistically significant decreases in HR (2,5,10 min), MAP (2,10 min), MPAP (2,5,10 min), PCWP (2,5,10 min), and CO (2,5,10 min), and there was a statistically significant increase in SVR (5,10 min). There was a notable absence of hemodynamic changes requiring intervention, as well as, an absence of myocardial ischemia as determined by ST-segment analysis.

Table (Mean ± SE)

	B	2'	5'	10'
HR (BPM)	84±8	73±7*	74±8*	70±6*
MAP (mmHG)	96±3	90±4*	93±4	91±4*
MPAP(mmHG)	36±4	32±3*	32±3*	31±3*
PCWP(mmHG)	27±3	24±2*	24±2*	23±2*
CVP(mmHg)	15±1	14±1	15±1	14±1
CO (LPM)	5.4±0.5	4.8±0.4*	4.5±0.4*	4.4±0.5*
SVR (dynes.sec.cm^{-5})	1277±117	1346±128	1453±124*	1489±142*
PVR (dynes.sec.cm^{-5})	136±16	141±23	153±18	143±16
SV (mL)	69±10	68±8	65±8	67±9

*$p < 0.05$

Discussion. The hemodynamic response associated with BW A938U administration in patients with critical AS has not been reported. Although further investigation is warranted to elucidate the mechanism of the observed statistically significant hemodynamic changes, our preliminary data suggest that BW A938U, 50 µg/kg, was associated with no clinically significant hemodynamic effects in patients with critical AS scheduled for AVR, indicating that BW A938U may be well suited in this patient population.

References.

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