Title: TIME COURSE AND HEMODYNAMIC EFFECTS OF α_1-ADRENERGIC BOLUS ADMINISTRATION IN ANESTHETIZED PATIENTS

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INTRODUCTION: Phenylephrine (Phe), an α_1-adrenergic agonist, is frequently administered as a bolus intravenous dose to increase blood pressure during anesthesia and surgery. While hemodynamic effects of continuous Phe infusion have been well documented in animals and humans[1], the beat-to-beat hemodynamic effects of a bolus dose of Phe have not been reported. From infusion studies, the mechanism of blood pressure elevation by Phe is increased systemic vascular resistance (SVR). SVR is related to mean arterial blood pressure (MAP), central venous pressure (CVP) and cardiac output (CO) by the equation: SVR=(MAP-CVP)/CO. Recent advances in esophageal doppler techniques permit near continuous monitoring of CO, hence permitting hemodynamic evaluation of bolus Phe administration. We assessed the time course and hemodynamic effects of α_1-adrenergic stimulation with bolus Phe in patients with myocardial disease during coronary artery bypass graft (CABG) surgery.

METHODS: 34 bolus doses of Phe ranging from 50-300 micrograms (mcg) were given to 13 patients undergoing elective CABG. Baseline ejection fraction (EF) ranged from 31-63%. Patients were anesthetized with various anesthetic agents including fentanyl, sufentanil, ethrane and forane. Once intubated, a Lawrence L3000 Cardiac Output Monitor^R probe was placed in the esophagus and positioned until maximum signal strength (SS) was elicted from blood flow in the descending aorta. Using research software (version 2.4) from Lawrence Medical Systems, heart rate (HR) and SS were updated every six heart beats. CO was calculated using the equation: CO=(HR)(SS)(constant). Initial CO was calibrated against the thermodilution technique, and the constant for a given trial calculated. A bolus dose of Phe was then given and MAP, HR, and SS were collected every 5 seconds for the ensuing 2 minute period. SVR was calculated and the times to peak change in MAP, SVR, and CO measured. Comparison of time to peak MAP and SVR was made using the two-tailed Wilcoxon Sign-Rank test.

RESULTS: MAP and SVR increased in all patients given Phe. Time to peak MAP and peak SVR were not significantly different, occurring at 40.6 $\pm$ 9.7 seconds and 40.9 $\pm$ 8.6 seconds (mean $\pm$ SD), respectively, and were not affected by EF or by Phe dose. CO decreased transiently in all patients, concurrent with peak MAP. Time to lowest CO was 41.2 $\pm$ 9.4 seconds. Peak hemodynamic effect of a single bolus of Phe varied with the dose as shown in Table 1. Hemodynamic effects of 100 mcg Phe in a single patient are illustrated in Figures 1 and 2. There were no ischemic events associated with Phe in any patient.

DISCUSSION: Phe increases MAP in a safe and predictable manner. The time course and hemodynamic effects of bolus Phe in cardiac surgery patients have been documented in this study. This information is particularly useful for evaluating α_1-adrenergic responsiveness in patients with myocardial disease where continuous Phe infusion may be contraindicated. Also, clinically, in the setting of hypotension during cardiac surgery, Phe will increase SVR and transiently decrease CO, concurrent with a rise in blood pressure.

REFERENCES:
1) Woodman OL, Vatner SF. Cardiovascular responses to the stimulation of alpha-1 and alpha-2 adrenoceptors in the conscious dog. J Pharmacol Exp Ther 1986;237(1):86-91.

TABLE 1

Phe Bolus Dose	n	% Change From Baseline * MAP	CO	SVR
50 mcg	14	+16±10	-21±12	+54±34
100 mcg	12	+25±12	-17±07	+52±26
150 mcg	3	+21±03	-23±12	+66±26
≥200 mcg	5	+28±04	-33±19	+115±80

*mean±SD