Title: EFFECT OF ISOFLURANE ANESTHESIA ON ALPHA-1-ADRENERGIC RESPONSIVENESS IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY

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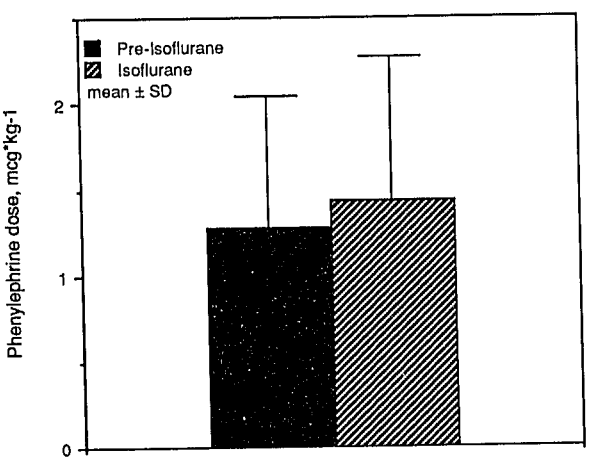
INTRODUCTION: Isoflurane is a potent systemic vasodilator (1), however the mechanism by which isoflurane produces this effect remains to be elucidated. Decreases in systemic vascular resistance may be mediated via the adrenergic nervous system. Therefore we tested the hypothesis that isoflurane produces vasodilation via inhibition of vascular alpha-1-adrenergic responsiveness.

METHODS: After institutitional approval and informed patient consent, 16 patients undergoing coronary artery bypass graft surgery were enrolled in the study. All patients had good ventricular function as evidenced by an ejection fraction ≥40% and were premedicated with intramuscular scopalamine 0.2 - 0.4 mg and morphine 0.1 $mg*kg^{-1}$ within 2 hours of surgery. After placement of routine hemodynamic monitors and with patients resting quietly, a phenylephrine (Phe) dose response curve was generated (denoted "pre-isoflurane") using a bolus Phe technique. In brief, 20 mcg Phe was injected intravenously via the proximal port of the pulmonary artery catheter and the peak mean arterial blood pressure (MAP) occurring in the ensuing 2 minutes was recorded. Five minutes later, after MAP had returned to baseline value, a second bolus dose of Phe (40 mcg) was given. Again the peak MAP achieved in the ensuing 2 minutes was recorded. Five minutes later, once hemodynamic parameters had returned to baseline value, a third Phe dose (80 mcg) was given. This was continued through the Phe dose range: 20, 40, 80, 120, 160, 200 . . . until peak MAP reponse to Phe increased 20% above baseline. At this point the Phe dose response curve was considered complete. Anesthesia induction was then accomplished with isoflurane, nitrous oxide, and oxygen via mask with spontaneous ventilation. After loss of response to verbal command, nitrous oxide was discontinued, isoflurane and oxygen continued, vecuronium given intravenously, and patients were intubated. End-tidal isoflurane concentration was titrated to a 20% decrease in MAP. Ten minutes post-intubation a second Phe dose response curve was generated as previously described and was denoted "isoflurane." The amount of Phe required to increase MAP 15 mmHg (denoted pressor dose 15mmHg, PD15mmHg) was calculated using second order polynomial regression of the Phe log dose response curve. Paired t-tests were used to compare the effect of isoflurane on PD15mmHg in each patient.

RESULTS: 14 patients completed the study (2 patients required vasodilator therapy for hypertension during isoflurane induction and were therefore excluded from the study). No patient had EKG evidence of myocardial ishemia during the study period. End-tidal isoflurane concentrations ranged from 0.6 - 1.5%; PD15mmHg was not correlated with end-tidal isoflurane concentration. There was no significant effect on PD15mmHg by isoflurane (Figure 1). Hence, the same amount of Phe was required to increase MAP 15mmHg prior to isoflurane and during isoflurane anesthesia.

DISCUSSION: These results suggest that isoflurane vasodilation is not mediated via alpha-1-adrenergic receptor blockade, hence disproving our hypothesis. Previous work (2) has shown that isoflurane has no direct action on alpha- or beta-adrenoceptors in isolated rat parotid gland; our results suggest this finding is very important clinically since it demonstrates that alpha-1-adrenergic stimulation with Phe will be effective in correcting hypotension in patients receiving isoflurane anesthesia.

Phenylephrine Pressor Dose 15mmHg



REFERENCES:
1. Eger EI. The pharmacology of isoflurane. Br J Anaesth 1984; 56: 71S-99S
2. Ostman M, Henrickson R, et al. Isoflurane--A study of adrenoceptor interaction in the isolated rate parotid gland. Anesthesiology 1986; 64: 734-738.