Title: ISOFLURANE BLUNTS THE CORTISOL AND EICOSANOID RESPONSE TO CARDIOPULMONARY BYPASS

Authors: P. Flezzani, M.D., N. Croughwell, C.R.N.A., R.W. McIntyre, M.D., J.S. Rankin, M.D., A.S. Wechsler, M.D., J.G. Reves, M.D.

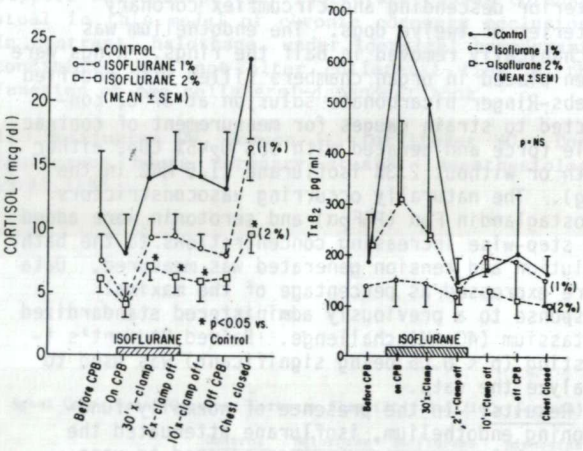
Affiliation: Departments of Anesthesiology and Surgery, Duke University Medical Center, Durham, North Carolina 27710

Introduction: Cardiopulmonary bypass (CPB) elicits a complex neurohumoral response (1). Various anesthetics administered prior to CPB have consistently been associated with increased catecholamines and cortisol during CPB, despite presumed adequate anesthetic depth. Eicosanoids, (thromboxane primarily) have also been shown to increase significantly during CPB, but the specific effects of anesthetics on their metabolism have not been studied (2). We tested the hypothesis that anesthetic depth blocks the cortisol and eicosanoid response to CPB. We employed an inhalation agent since these anesthetics can be given at a constant concentration and have been proven effective in blunting the hormonal response to various stimuli without causing side-effects, such as the prolonged respiratory depression associated with opioids. Isoflurane was selected because of its vasodilating effect.

Methods: Eighteen patients scheduled for elective coronary revascularization gave informed consent. General anesthesia was induced with fentanyl (30mcg/kg) and oxygen and maintained with a continuous infusion of fentanyl (0.2mcg/kg/min), not to exceed a total dose of 75mcg/kg. The fentanyl infusion was terminated just before the beginning of CPB. Six patients were then randomly assigned no further anesthetic, while the other twelve received a continuous inspired concentration, either 1% or 2% isoflurane, from the beginning of CPB until five minutes after the removal of the aortic cross clamp. During CPB, mean perfusion flow was kept constant at 1.6 $l/min/m^2$, mean pressure at 50±10mmHg, and temperature at 24±3°C. Plasma cortisol, thromboxane B_2 and 6-keto - $PGF_{1\alpha}$ the stable metabolites of thromboxane and prostacyclin, were determined by radioimmunoassay. Statistical analysis was performed using analysis of variance and least squares means.

Results: Results are in the figure: There was an isoflurane dose-related decrease in cortisol release while TxB_2 was lower in isoflurane patients. There was no difference between groups with regard to dose of fentanyl, type and degree of coronary disease, aortic cross-clamp time and duration of CPB. Directly measured and derived hemodynamics were not significantly different during and after CPB. However, during CPB, the control group received more ($P \geq 0.08$) vasodilators (SNP) and the 2% isoflurane groups received more ($P \geq 0.05$) vasoconstrictors (phenylephrine).

Discussion: Cortisol release reflects the adrenocortical (stress) response to CPB. Our results support previous reports that opioids administered prior to CPB result in increased levels of stress related substances (catecholamines and cortisol) during CPB (1,3). However we have demonstrated that the administration of an anesthetic agent such as isoflurane, during CPB, blunts the cortisol response to CPB and that there is a dose related effect of isoflurane. Our study suggests that isoflurane blunts the thromboxane rise but not in a dose related fashion. Since prostacyclin metabolism did not change, we conclude that isoflurane, given during CPB, may offer some protection from the effects of thromboxane.



References:

1. Stanley IM, Berman L, Green D, et al. Plasma catecholamine and cortisol responses to fentanyl-oxygen anesthesia for coronary artery operation. Anesthesiology 53:250-253, 1980.
2. Watkins WD, Peterson MB, Kong DL, et al. Thromboxane and prostacyclin changesduring cardiopulmonary bypass with and without pulsatile flow. J Thorac Cardiovasc Surg 84:250-256, 1982.
3. Sebel PS, Bovill JG, Schellekens APM. Hormonal responses to high-dose fentanyl anaesthesia. Br J Anaesth 53:941-947, 1981.