TITLE: PULMONARY VASCULAR RESPONSE TO CYCLOOXYGENASE INHIBITION IS ABOLISHED DURING HALOTHANE ANESTHESIA.

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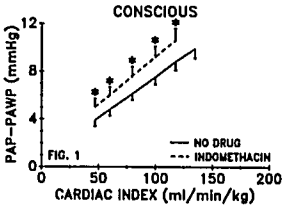
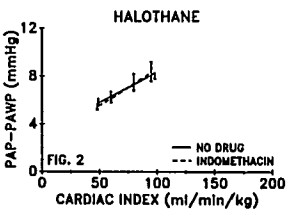
Cyclooxygenase inhibition (COI) results in marked pulmonary vasoconstriction in the conscious state (1). This effect indicates that metabolites of the cyclooxygenase pathway normally exert a tonic vasodilator influence on the pulmonary circulation. We recently reported that the magnitude of the pulmonary vasoconstrictor response to COI is markedly enhanced during pentobarbital anesthesia (2). In the present study, we investigated the effects of halothane anesthesia on the pulmonary vascular response to COI compared to that measured in the conscious state. Multipoint pulmonary vascular pressure-cardiac index ($P/\dot{Q}$) plots were generated in 8 dogs by stepwise inflation of a hydraulic occluder chronically-implanted around the inferior vena cave to decrease $\dot{Q}$. $P/\dot{Q}$ plots were obtained on separate days in conscious and halothane-anesthetized (~ 1.2% end-tidal) dogs before and during COI with indomethacin (5 mg/kg, iv). Controlled ventilation during halothane allowed matching of blood gases to conscious values. Two-way ANOVA and Duncan's multiple range test were used to assess the effects of COI on the $P/\dot{Q}$ plots. COI increased (*$p<0.01$) the pulmonary vascular pressure gradient over a broad range of $\dot{Q}$ in the conscious state (Fig. 1); i.e. COI resulted in active, flow-independent pulmonary vasoconstriction. In contrast, the pulmonary vasoconstrictor response to COI was completely abolished during halothane anesthesia (Fig. 2). These results indicate that regulation of the baseline pulmonary vascular $P/\dot{Q}$ relationship by cyclooxygenase metabolites is entirely obtunded during halothane anesthesia.

1. Am. J. Physiol. 255:H1084-H1090, 1988
2. Am. J. Physiol. 257:H1140-H1146, 1989





A628

TITLE: SUCCESSFUL TRANSPLANTATION OF DOG HEARTS AFTER 24 HOURS COLD STORAGE

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Dog hearts were arrested either with hyperkalemic NIH cardioplegia (group I, n=6) or with the same cardioplegia after addition of R 75231, a nucleoside transport inhibitor (group II, n=6). The hearts were stored cold for 24 hours and then transplanted orthotopically. Myocardial content of high energy phosphates (HEP) was determined in serial biopsies before explantation, after 24 hours of cold storage, and 5, 30, 60, and 120 minutes after reperfusion. Hemodynamics (HR, SAP, DAP, CO, dP/dt, and LVP) were measured 5, 30, and 60 minutes after weaning from cardiopulmonary bypass (CPB). Statistical analyses were performed using unpaired (intergroup differences) and paired (innergroup differences) Students t- test. Statistical significance was accepted at the 0.05 level.

In group I ATP was 50% and CrP 18% of control after 24 hours storage. During 60 minutes reperfusion on CPB, HEP content decreased ($p<0.05$) and all animals developed a stone heart after transplantation. No heart could be weaned successfully from CPB despite maximum inotropic support (dopamine, adrenaline and isoprenaline). After 24 hours storage in group II ATP was 82% and CrP 28% of control ($p<0.05$ vs. group I). After transplantation HEP content remained stable and all hearts could be weaned from CPB without inotropic support except for isoprenaline.

Thus, optimal myocardial preservation is obtained with the combination of cardioplegia and nucleoside transport inhibition.