TITLE: PULMONARY VASCULAR RESPONSE TO CYCLOOXYGENASE PATHWAY INHIBITION MEASURED IN CONSCIOUS DOGS IS MODIFIED DURING PENTOBARBITAL ANESTHESIA

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INTRODUCTION: Metabolites of the cyclooxygenase pathway (prostaglandins) are recognized as important modulators of the pulmonary circulation. Surprisingly, it is entirely unknown whether anesthesia modifies pulmonary vascular regulation by endogenously produced cyclooxygenase metabolites. In the present study, we have investigated the effects of cyclooxygenase inhibition on the pulmonary vascular pressure-flow relationship in conscious dogs, and again during sodium pentobarbital (PB) anesthesia. We have tested the hypothesis that if PB anesthesia alters the influence of endogenous cyclooxygenase metabolites on the pulmonary circulation, then a differential response to cyclooxygenase inhibition should be observed in conscious and PB anesthetized dogs.

METHODS: Eight dogs were chronically-instrumented with catheters in the thoracic aorta, left and right atria, and main pulmonary artery. On the day of each experiment, a Swan-Ganz catheter was positioned in the main pulmonary artery via percutaneous jugular puncture to measure pulmonary blood flow (Q) and pulmonary capillary wedge pressure. Specific effects on the pulmonary circulation were assessed by measuring the pulmonary vascular pressure gradient (pulmonary arterial pressure-pulmonary capillary wedge pressure: PAP-PCWP) at multiple levels of Q, which was varied by stepwise inflation of a hydraulic occluder implanted around the thoracic inferior vena cava. PAP-PCWP/Q plots were generated on separate days before and during cyclooxygenase inhibition (indomethacin 5 mg/kg, iv): 1) with the dogs fully conscious; and 2) following induction of anesthesia with sodium pentobarbital (30 mg/kg, iv). For each individual experiment, linear regression analysis was used to calculate PAP-PCWP at 20 ml/min/kg intervals of Q. Values from individual experiments were averaged over the empirically measured range of Q, and are presented as means ± SEM. The effects of cyclooxygenase inhibition, both in conscious and PB anesthetized dogs, were assessed by two-way ANOVA with repeated measures and Duncan's Multiple Range Test.

RESULTS: In conscious dogs, cyclooxygenase inhibition significantly increased ($p<0.05$) PAP-PCWP at every level of Q, i.e. cyclooxygenase inhibition resulted in active, non-flow dependent pulmonary vasoconstriction (Figure 1). During PB anesthesia, cyclooxygenase inhibition again significantly increased ($p<0.05$) PAP-PCWP at every level of Q (Figure 2). Moreover, as summarized in Figure 3, the magnitude of pulmonary vasoconstriction during cyclooxygenase inhibition was significantly greater ($p<0.05$) during PB anesthesia compared to the conscious state at all but the highest level of Q studied.

CONCLUSION: Thus, in both conscious and PB anesthetized dogs, cyclooxygenase inhibition results in pulmonary vasoconstriction, indicating that metabolites of the cyclooxygenase pathway exert a net vasodilator influence on the pulmonary circulation. The increased magnitude of pulmonary vasoconstriction in response to cyclooxygenase inhibition in PB anesthetized dogs supports the concept that PB anesthesia modifies endogenous regulation of the pulmonary circulation by cyclooxygenase metabolites, particularly at reduced levels of Q.

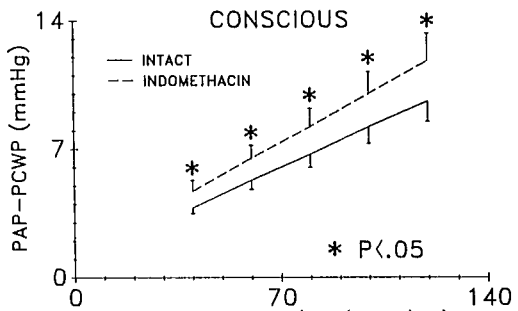

Fig. 1

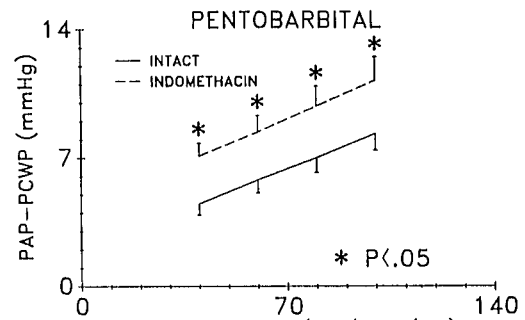

Fig. 2

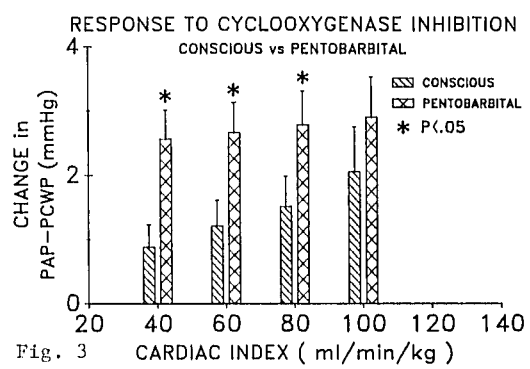

Fig. 3