Title: EFFECT OF PENTOBARBITAL ON THE PULMONARY VASCULAR RESPONSE TO HYPOXIA IN ISOLATED SHEEP LUNGS

Authors: L. D. Martin, M.D. and R. C. Wetzel, M.D.

Affiliation: Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205

Introduction. It has been previously reported that intravenous anesthetic agents do not alter the pulmonary vascular response to hypoxia.[1] However, because of its widespread use in experimental models and the neurointensive care setting, we studied the effect of intravenous pentobarbital (PB) on pulmonary vascular pressure-flow characteristics during normoxia and hypoxia in the isolated, in situ, blood-perfused sheep lung model.[2]

Methods. Six male sheep were initially anesthetized with 50 mg/kg body weight ketamine intramuscularly. A tracheostomy was performed and ventilation provided with warmed, humidified gas at tidal volume of approximately 10 ml/kg, respiratory rate of 10 breaths/minute and positive end-expiratory pressure of 4 mmHg. After heparinization, the animal was exsanguinated, the thorax was opened and the ductus arteriosus was ligated. The left atrium and pulmonary artery were cannulated. The lung perfusate consisted of autologous blood and 3% Dextran-70 in Ringer's lactate solution. Tracheal, pulmonary artery and left atrial pressures were referenced to the level of the pulmonary artery and continuously recorded. Blood temperature was maintained between 39° and 40°C and blood glucose between 90 and 180 mg/dl. Left atrial perfusate pH, partial pressure of oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) were determined at each level of inspired oxygen. Perfusate pH was maintained between 7.30 and 7.45 by the addition of 1 N $NaHCO_3$. The gas mixtures used were PiO_2 = 200 torr (normoxia) and PiO_2 = 30 torr (hypoxia) with $PiCO_2$ 27 to 29 torr and the balance of gas as nitrogen. Instantaneous pressure-flow (P-Q) curves were generated at end-expiration (PEEP = 4) by increasing flow to ≈ 150 ml/kg/min and then turning off the pump, thereby discharging the blood from a standpipe into the pulmonary artery while simultaneously recording pulmonary artery flow and pressure on an X-Y recorder. P-Q curves were generated every five minutes until a steady-state was established. PB (19 ± 3 mg/kg body wt) was added to the reservoir during either normoxia (N = 4) or hypoxia (N = 2) after a steady-state was achieved. Solvent (30% propylene glycol and 2% benzyl alcohol, 10 ml) vehicle was added before PB in two animals.

Results. During normoxia, the control and PB mean P-Q curves did not differ. The mean control P-Q curve during hypoxia was significantly shifted to the right ($P < .001$, Figure) compared to the normoxic curve, indicating an increase in pulmonary vascular tone. During normoxia with PB, the response of the P-Q relationship was significantly attenuated compared to control hypoxia ($P < .001$); however, there was still a significant response compared to normoxia. The P-Q relationship was not changed following addition of the vehicle.

Discussion. Bjertnaes et al. reported that intravenous anesthetics have no dampening effect on the pulmonary pressor response to hypoxia.[1] Our data demonstrated that in the isolated sheep lung PB is a potent pulmonary vasodilator during hypoxia but not during normoxia. In the systemic circulation PB is known to blunt various pressor responses probably by a direct effect on vascular smooth muscle.[3] Possibly by a similar mechanism, PB may blunt the pulmonary vascular pressor response to hypoxia.

References.

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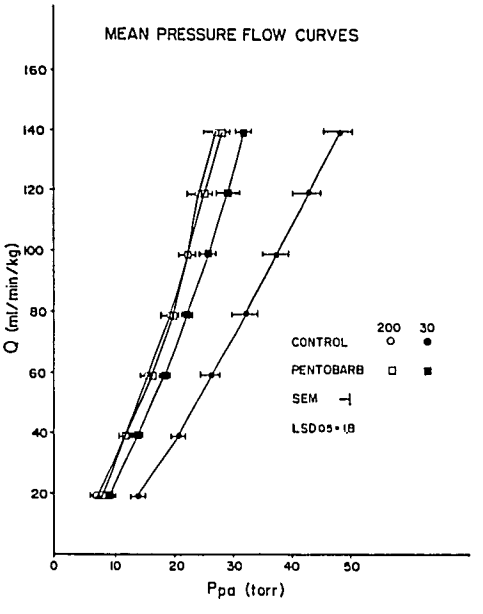

Mean P-Q curves during normoxia (PiO_2 = 200 torr) and hypoxia (PiO_2 = 30 torr) with and without PB.