Anesthesiology
V 75, No 3A, Sep 1991

A1117

TITLE: Changes in systemic and pulmonary hemodynamics and acid-base balance during prolonged apneic oxygenation

AUTHORS: S. Ikeda, M.D., J.F. Schweiss,M.D.
AFFILIATION: Anes. Dept. St. Louis University, St. Louis, Mo. 63110

Apneic oxygenation has been reported to provide adequate oxygenation and support life for several hours.[1] However, hemodynamic changes during prolonged apnea have not been well studied. In this study, systemic and pulmonary hemodynamics and metabolic changes were studied in dogs during apnea and throughout recovery from a prolonged apneic oxygenation.

Studies were performed in nine mongrel dogs with an average body weight of 22.1 kg, utilizing a protocol approved by the Institutional Animal Care Committee. Instrumentation was performed under pentobarbital anesthesia. Systemic (BP), pulmonary artery (PA) and right atrial (RA) pressures and EKG were continuously monitored. Cardiac output and right heart function (ejection fraction, end-diastolic volume, stroke volume and end-systolic volume) were measured with an Edwards REF-1 computer. When apnea was induced, a cannula was inserted through the endotracheal tube to the carina and a continuous flow of 350 ml/kg/min of oxygen was delivered for 2 hours. During the 60 minute recovery period the lungs were mechanically ventilated with a tidal volume 150% of that used during the control period. Blood samples were obtained from the femoral, the pulmonary artery, and the superior sagittal sinus every 15 minutes and cerebrospinal fluid (CSF) was obtained every 30 minutes. Lactate and pyruvate concentrations in blood and CSF were measured. Repeated analysis of variance was employed to compare control values with values at each sample time. A P value $< .05$ was considered statistically significant.

BP increased initially, peaking at 130% at 60 to 75 min., then gradually decreased to 81% of the control. On resumption of ventilation after 2 hours of apnea, the BP returned to the control level within 15 min. PA and RA pressures increased in the first 45 min and remained elevated during apnea, returning to the control level during recovery. No heart rate trend was apparent during the apnea and recovery periods. Cardiac output showed changes similar to systemic BP, however it was less than control values during recovery. Right heart function did not change significantly throughout the experiments. Systemic vascular resistance (SVR) increased during the first 60 minutes of apnea, and remained elevated during apnea. SVR was elevated 16% during the recovery period. Pulmonary vascular resistance increased to 259% of control during apnea. It decreased to 189% of the control during recovery. Both lactate and pyruvate concentrations significantly decreased during apnea. Arterial blood gases and pH showed severe respiratory and metabolic acidosis. The changes in arterial blood gases and pH were similar to those previously reported.[1] Blood gases and pH of mixed venous blood paralleled those of arterial blood. No dog died during the 2 hour apneic period and the lowest paO_2 was always above 100 mmHg. However, both arterial and mixed venous oxygen saturation dropped to 82% and 75% respectively. This finding suggests that saturation, not partial pressure is the more reliable monitoring variable during hypercapnia. Hemodynamic variables deteriorated rapidly after one hour and a half. When mechanical ventilation was resumed after two hours of apnea, most of the variables returned to the control values within 60 min.

Reference:
1. Slutsky AS, et al: Anesthesiology 63:278-286, 1985.

A1118

TITLE: PHOSPHODIESTERASE INHIBITORS DILATE HUMAN INTERNAL MAMMARY ARTERY IN VITRO

AUTHORS: J.H. Levy,M.D.,M. Salmenpera, M.D.,Ph.D., K. Meyer,B.S., D.G. Harrison, M.D.
AFFILIATION: Depts. of Anesth. and Cardiology, Emory Univ. School of Medicine, Atlanta, GA

INTRODUCTION: Papaverine, amrinone, and milrinone are phosphodiesterase (PDE) inhibitors. By inhibiting PDE to increase cyclic nucleotides in vascular smooth muscle, these drugs produce vasodilation[1] by a mechanism of action different than endothelial relaxing factor, nitroglycerine, or calcium entry blockers. They offer a unique therapeutic approach for internal mammary artery (IMA) or coronary spasm. One of the mediators of perioperative spasm in both IMA and coronary arteries may be thromboxane A_2 since its levels are increased during cardiopulmonary bypass and potentially following protamine administration.[2] Therefore, we examined the ability of different PDE inhibitors to produce dilation of human IMA after thromboxane-induced vasoconstriction.
METHODS: Following approval, the discarded, distal end of human IMA segments were collected in oxygenated cold (4°C) Krebs solution. Three mm rings were trimmed and stretched to their optimal resting tension in organ-baths in Krebs maintained at 37°C and aerated with 95% O_2 and 5% CO_2 mixture. After at least 30 minutes of equilibration they were constricted submaximally (50 to 80%) with a thromboxane analog, U46619 (Upjohn). Drugs were added in a cumulative fashion to relax the preparations. Using logistic curve-fitting, a mean concentration-relaxation curve was constructed using six rings from six different patients. The concentration causing 50% relaxation (EC_{50}) was determined.
RESULTS: All PDE inhibitors produced dose-dependent dilation of the IMA as shown in Figure 1. The EC_{50} for each drug are shown in Table 1.
DISCUSSION: Papaverine, which is used to prepare the IMA during cardiac surgery, produces vasodilation by nonspecific inhibition of PDE. However, papaverine cannot be administered systemically. Amrinone or milrinone offer a potential therapeutic option for the treatment of acute spasm of the IMA during cardiac surgery.

References: 1. Biochem Pharmacol 35:787-800, 1986
2. Anesthesiology 66:597-604, 1987

Figure 1. Concentration of PDE inhibitors for relaxation of human IMA. Standard deviation bars represent EC_{50}, the drug concentrations for 50% relaxation (mean ± S.D.).

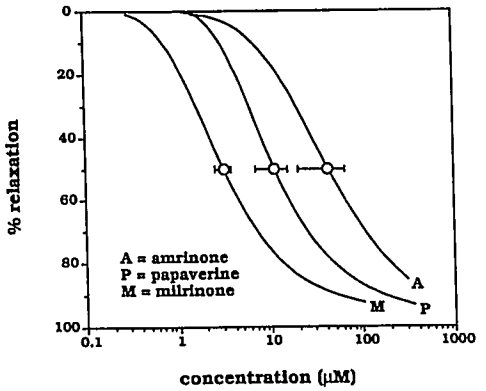

Table 1. EC_{50} For IMA Relaxation (X ± S.D)	
DRUG	EC_{50}
Amrinone	42.5 ± 21.9 μM
Papavarine	11.1 ± 4.2 μM
Milrinone	2.9 ± 0.4 μM