EFFECTS OF 5-HYDROXYTRYPTAMINE INHIBITION ON GAS EXCHANGE AND PULMONARY HEMODYNAMICS IN ACUTE CANINE PULMONARY EMBOLISM

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INTRODUCTION

5-Hydroxytryptamine (Serotonin; 5-HT), a potent vasoconstrictor of pulmonary arteries, has been reported to play an important role in cardiopulmonary dysfunction that accompanies pulmonary embolization (Huval et al., 1983). The quantitative effects of 5-HT on gas exchange efficiency, however, have not been systematically investigated in pulmonary embolism. Using a new type of selective serotonin receptor antagonist, we examined the distribution of ventilation-perfusion (VA/Q) ratios and pulmonary hemodynamics to clarify the effects of serotonin on gas exchange in acute canine pulmonary embolism.

MATERIALS AND METHODS

Fourteen healthy mongrel dogs weighing between 10 and 15 kg were studied. Each was anesthetized with pentobarbital sodium (25 mg/kg iv) and paralyzed with pancuronium bromide (0.2 mg/kg iv). Their lungs were mechanically ventilated with room air in supine position. The tidal volume was 10 ml/kg and the respiratory rate was adjusted between 20 and 30 /min. Polyethylene catheters were placed in the internal jugular vein and the femoral vein and artery. A thermal dilution Swan-Ganz catheter was positioned in the pulmonary artery and cardiac output as well as pulmonary arterial pressure were measured (Model RMP-6008, Nihon Kohden, Tokyo). A specially made 5 F thermodilution-impedance catheter (Model HE-2900, Elecath Inc., NJ) was positioned in the abdominal aorta through the femoral artery. Using the thermal-saline double indicator dilution method (Ishibe et al., 1987), we measured extra-vascular lung water volume with a lung water computer.
Normal saline containing six inert gases, including SF₆, ethane, cyclopropane, halothane, diethyl ether and acetone, was infused at a rate of 2.0 ml/min for 40 minutes through the femoral vein. Under a steady state, we collected expired gas and arterial and mixed venous blood samples to measure the concentrations of the indicator gases with a gas chromatograph (Model GC-163 Hitachi Ltd.).

After these control measurements were obtained, glass-beads (diameter 0.1mm), 0.4-0.6 g/kg, were given intravenously via the internal jugular vein until mean pulmonary arterial pressure (PAP) reached between double and triple the baseline. Thirty minutes later we again collected the expired gas and the arterial and mixed venous blood samples under a steady state.

One half of the animals were randomly assigned to a treatment group (DV(+) group) and the others were assigned to a control group (DV(-) group). The DV(+) group received a bolus injection of 0.1 mg/kg of DV-7028 (a new type of selective 5-HT₂ receptor antagonist) when PAP reached maximum and was followed by the continuous infusion at a rate of 1 mg/kg/hr.

Gas exchange was assessed by alveolar-arterial Po₂ gradient (AaDo₂), the continuous V̇A/Q distributions, retention of SF₆ (RSF₆) and 1-excretion of acetone (1-Eacetone). We used the multiple inert gas elimination technique reported by Wagner et al. (1974) to determine the continuous V̇A/Q distributions. We calculated RSF₆ and 1-Eacetone by the following equations.

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\text{RSF}_6 = \frac{\text{Pa}_{SF6}}{\text{Pv}_{SF6}}
\]

\[
1-\text{Eacetone} = 1-\frac{\text{P}_{Acetone}}{\text{P}_{Vacetone}}
\]

PaSF₆ is the arterial partial pressure of SF₆; PvSF₆ is the mixed venous partial pressure of SF₆; Peacetone is the mixed expired gas partial pressure of acetone; PVacetone is the mixed venous partial pressure of acetone.

All data in the table and text are presented as the mean ± standard deviation. Statistical analysis was performed using Wilcoxon's rank sum test for the paired data and Student's t-test for the non-paired data. We accepted p<0.05 as statistically significant.

RESULTS

Changes of gas exchange, hemodynamic variables, airway pressure, hematological parameters and arterial blood serotonin 30 minutes after glass-bead embolization are shown in Table 1. After embolization PaO₂ decreased in both groups and AaDo₂ increased only in the DV(-) group. Shunt and dead space also increased in some cases of both groups but showed no statistical significance. Mean pulmonary arterial pressure (PAP), pulmonary vascular resistance (PVR) and airway pressure (P_{AIRWAY}) increased significantly in both groups.