

TITLE: PULMONARY MACRO- AND MICROHEMODYNAMICS DURING NORMOXIC AND HYPOXIC VENTILATION

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Introduction: The changes of pulmonary macrohemodynamics provoked by alveolar hypoxia are well described. In contrast a detailed analysis of the alterations in the consecutive segments of the pulmonary microvascular systems has not been reported. We therefore studied the effects of hypoxic- vs. normoxic ventilation in an in-vivo microcirculatory lung model.

Methods: 39 male White New Zealand rabbits were anesthetized using Thiopental (30mg/kg), Chloralose (50mg/kg) and Piritramid (0.3mg/kg). The animals were intubated and ventilated mechanically. Tidal volume and respiratory rate were adjusted to keep pH near 7.35 and pCO₂ at 35mm Hg. Airway pressure changes were monitored continuously. Arterial pressure (AP), pulmonary artery pressure (PAP) and left atrial pressure (LAP) were recorded via indwelling catheters. Rhythmic changes of pulmonary blood flow and cardiac output (CO) were measured. A transparent window was implanted into the right thoracic wall. At closed thorax conditions the pulmonary microcirculation was visualized using fluorescence videomicroscopy after i.v. injection of fluorescein-isothiocyanate (FITC) stained red cells. Videorecordings were performed on-line during prolonged inspiration of 2 seconds at alveolar pressures of 9 mm Hg. Videomicroscopic images of identical microvascular areas were recorded on videotape during normoxic and hypoxic (FIO₂: 0.3 vs. 0.12) ventilation. In arterioles (art), venules (ven) and alveoli (alv) vessel diameters (D_{art}; D_{ven}) red cell flux (F_{art}, F_{ven}, F_{alv}), red cell velocity (V_{art}, V_{ven}), microhematocrit (H_{art}, H_{ven}) and alveolar transit time (TT_{alv}) were

measured by off the video screens at magnifications of 1300x using a digital image processing unit. Prior to and after video recordings the stained red cell fraction was measured by a fluorescent analyzing cell sorter. Simultaneously blood gas analysis was performed. For statistical analysis the Wilcoxon matched pairs signed rank test was utilized.

Results: With both experimental conditions the airway pressure (9mm Hg), pH (7.40), CO₂ (35mm Hg) and the labeled red cell fraction (1.2%) remained constant. At an FIO₂ of 0.33 an arterial pO₂ of 135 ± 12 mm Hg (mean ± SD) was measured. The macrohemodynamic measurements revealed a PAP: 15 ± 2mm Hg; LAP: 3 ± 1mm Hg; CO: 157 ± 57ml/min; PVR: 77 ± 27mmHg/ml/min. During these conditions the following results were obtained from arterioles and venules with diameters ranging from 17 - 114 μm and 13 - 74 μm respectively: F_{art}: 619 - 3465 cells/s; F_{ven}: 392 - 2641; V_{art}: 387 - 1108 μm/s; V_{ven}: 230 - 1745 μm/s; H_{art}: 0.26 ± 0.04; H_{ven}: 0.26 ± 0.05.

During alveolar hypoxia (FIO₂: 0.13) an arterial pO₂ of 44 ± 5 mm Hg was achieved. The results are given in changes vs normoxic ventilation: PAP: +15%; PVR: +22%; LAP: -1%; CO: +2%; D_{art}: -20% D_{ven}: -19%; F_{art}: +42%; F_{ven}: +46%; F_{alv}: +72%; V_{art}: +59%; V_{ven}: +69%; H_{art}: +35%; H_{ven}: +39%; TT_{alv}: -33%. The changes of PAP, PVR and all microhemodynamic variables were significantly different from the values during normoxic ventilation.

Conclusions: The rise in red cell flux and red cell velocity in the pre- and postalveolar vessels as well as the red cell flux increase and the transit time reduction in the alveoli on the surface of the lung indicate a pronounced local flow increase during alveolar hypoxia. These results and the maintenance of the cardiac output strongly suggest a vertical redistribution of total pulmonary blood flow within the lung in favour of the apex. Furthermore the decrease of the arteriolar vessel diameter is a direct proof that the hypoxic vasoconstriction is induced by pulmonary arterioles. Moreover this model is a valuable experimental tool to study anesthetic and drug effects on hypoxic pulmonary vasoconstriction and on pulmonary macro- and microcirculation.

A586

TITLE: VOLATILE ANESTHETICS AND PLATELET AGGREGATION IN PIGS AND HUMANS

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Drugs that stabilize platelets and inhibit aggregation protect against coronary thrombosis and myocardial infarction. The effect of volatile anesthetics on platelet aggregation remains poorly understood. No prior study exists comparing aggregation in vitro in the presence of each anesthetic. The current study asked two questions: (a) Do halothane, isoflurane and enflurane inhibit aggregation of human platelets? Two concentrations of each anesthetic were tested in blood from each subject and four different aggregating agonists were employed. (b) Do the anesthetics inhibit aggregation of pig platelets? Pigs are commonly used in thrombosis research. It is important to know if anesthetic effects on platelet aggregation are similar in pigs and humans.

Platelet rich plasma was prepared from the blood of six awake, fasting humans and seven pigs and studied using a light transmittance aggregometer. Responses to adenosine diphosphate (ADP), epinephrine (epi), collagen and arachidonic acid (AA) were measured with and without the anesthetics (1% and 2%). Results indicate that in human plasma, 1% halothane inhibited aggregation evoked by 3 of 4 agonists and 2% halothane inhibited responses to all 4 agonists. Isoflurane and enflurane had less marked or minimal effect even at 2%

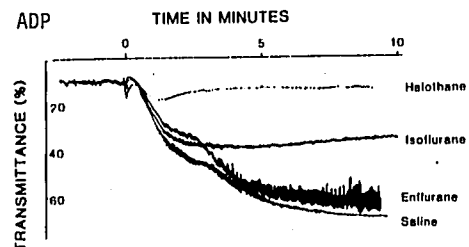
concentrations (Table). Results also indicate that pig platelet responses resembled those of human platelets.

In platelets from both pigs and humans, halothane has a consistent and marked stabilizing effect. Neither isoflurane nor enflurane exhibit this property. Whether or not this potentially beneficial halothane effect is manifest clinically in patients with coronary disease undergoing surgery is not known.

Anesthetics (2%) and aggregation in humans

agonist	control	halothane	isoflurane	enflurane
ADP	59±2	39±6*	65±9	59±7
EPI	57±6	36±7*	49±9*	48±3
Collagen	67±6	54±4*	67±5	64±3
AA	60±6	44±9*	59±7	58±6

values m ± SEM; light transmittance units, n = 6; *p<0.05 (↓ light transmittance = ↑ platelet aggregation)



Aggregation responses in an individual human (anesthetics = 2%). Halothane had greatest platelet stabilizing effect.