Title: MICROHEMODYNAMIC CHANGES IN THE PULMONARY MICROCIRCULATION DURING HYPOXIC PULMONARY VASOCONSTRICTION

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Introduction: An enormous amount of reports has accumulated describing macrohemodynamic changes and redistribution of blood flow within the pulmonary circulation induced by alveolar hypoxia. In contrast, data determining the pulmonary microcirculation are meager, yet. The microhemodynamic changes during hypoxic pulmonary vasoconstriction (HPV) reported so far, include the direct and indirect measurements of arteriolar vasoconstriction (2,3), the increase of vascular resistance in pulmonary arterioles observed in isolated lung preparations (4) and the increase in the transit time of fluorescent dyes in the subpleural vessels of an intact lung preparation (6). It was our aim to measure the effects of alveolar hypoxia on the pulmonary microcirculation in more detail in an in-vivo preparation under closed thorax conditions.

Methods: 10 healthy male Sprague-Dawley rats were tracheotomized and ventilated mechanically during pentotal-anesthesia (50 mg/kg b.w.). The tracheal tube was connected to a pressure-transducer to detect airway-pressure changes. Catheters were advanced into the ascending aorta, vena cava superior and - for detecting the transpulmonary pressure gradient - into the pulmonary artery and the left atrium. To achieve access to the pulmonary microvascular bed, a window was implanted into the right thoracic wall after partial resection of the fourth rib. The circular window (diameter: 1cm) consisted of a teflon membrane attached to the thoracic wall by polyacryl adhesives. The pulmonary microcirculation was visualized using fluorescence microscopy after i.v. application of fluorescein-isothiocyanate (FITC)-labelled red cells.

Controlled ventilation was adjusted to normalize arterial blood gas values. Hypoxic ventilation was induced by addition of nitrogen to the inspired gas until an arterial pO_2 of 40 mm Hg was attained.

With both experimental conditions fluorescence videomicroscopy was performed within the window area by recording identical microvascular segments on videotape using a high-sensitivity tv-camera attached to the microscope. For videorecordings ventilation was interrupted for a maximum period of 20 - 25 sec. at an alveolar pressure of 9 mmHg. The videotapes were later analyzed offline by frame-to-frame-analysis at magnifications of 1200x using previously taped calibrations. The following microhemodynamic parameters were analyzed: microvessel diameter (d), red blood cell velocity (v), red cell flux (F), microhematocrit (H_{micro}) and the transit time of labelled red cells from a terminal arteriole to a postcapillary venule. For statistical analysis the Wilcoxon matched pairs signed rank test was used. Values are expressed as mean $\pm$ SD. $p < 0,05$ (*) and $p < 0,01$ (**) were considered statistically significant.

Results: Data with normoxic (FiO_2 : 0,2 - 0,3) and hypoxic ventilation ($p_a O_2$: 40 mmHg; FiO_2 : 0,12 - 0,14) are given. Pulmonary artery pressure (PAP): 20,0 $\pm$ 2,5 / 27,1 $\pm$ 4,3 (mmHg), left atrial pressure (LAP): 2,1 $\pm$ 0,8 / 2,2 $\pm$ 0,9 (mmHg), alveolar pressure (P_{alv}): 9,2 $\pm$ 2,7 / 9,9 $\pm$ 2,4 (mmHg).

At zone 2 conditions ($PAP > P_{alv} > LAP$) we were able to study 46 pulmonary arterioles and 11 venules. The micorhemodynamic data with alveolar hypoxia are given as percent changes of the values with normoxic ventilation:

	d	v	F	H_{micro}
		(% of control)		
Arterioles				
d: 65-45 µm (n=9)	-18**	40**	42**	41**
45-25 µm (n=17)	-9	36**	44**	24**
25 µm (n=20)	0	31**	41**	6
Venules				
d: 21-54 µm (n=11)	2	27	24	-7

90 % of the vessels between 45 - 65 um and 50 % of those 25 - 45 um were constricted during hypoxic ventilation, whereas no changes in microvessel diameter in venules and smaller arterioles were measured.

The transit time of labelled cells during hypoxia (0,47 $\pm$ 0,40; n=80) was significantly reduced as compared to normoxia (0,80 $\pm$ 0,25; n=85).

Conclusion: The red cell transit time , so far estimated by analyzing a dye transit in the pulmonary circulation (6), has been directly measured in the present study. Its significant reduction and the marked increases in red cell velocity and red cell flux support the hypothesis that a redistribution of blood flow in favour of the apical parts of the lung occurs during alveolar hypoxia of the whole lung. Although the transit time of the red cells reaches nearly the lower limit for red cell oxygenation (6) the time for O_2 uptake is sufficient since oxygenation starts already in arterioles (1). As in-vitro studies demonstrated an increase in viscosity and resistance with increasing tube hematocrit, we conclude that the significant increase in H_{micro} in terminal arterioles contributes significantly to the increase in pulmonary vascular resistance during alveolar hypoxia.

References:

1. Conhhaim CL and Staub NC: Reflection spectrophotometric measurement of O_2 uptake in pulmonary arterioles of cats. J. Appl. Physiol. 48: 848-856, 1980.
2. Goetz AE, Berger R, Conzen PFM, Hobbhahn J and Brendel W: Direct measurement of the site of hypoxic pulmonary vasoconstriction by fluorescence videomicroscopy. Anesthesiology 65: A501, 1986
3. Marshall C and Marshall B: Site and sensitivity for stimulation of hypoxic pulmonary vasoconstriction. J. Appl. Physiol. 55: 711-716, 1983
4. Nagasaka Y, Bhattacharya J, Nanjo S, Gropper MA and Staub NC: Micropuncture measurement of lung microvascular pressure profile during hypoxia in cats. Circ. Res. 54: 90-95, 1984
5. Wagner PD: Diffusion and chemical reaction in pulmonary gas exchange. Physiol. Rev. 257-312, 1977
6. Wagner WWJr, Latham LP, Gillespie MN and Guenther JP: Direct measurement of pulmonary capillary transit times. Science 218: 379-380, 1982