BRADYKININ IN ISCHEMIA-REPERFUSION INJURY OF THE RAT LUNG

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Introduction: Recent studies described possibilities to reduce lung damage after intestinal ischemia by application of a selective bradykinin receptor antagonist (HOE 140). In contrast, it has been shown that the preischemic application of bradykinin (BK) reduced ischemic damage of the myocardium.

Material and methods: To evaluate the effects of bradykinin in lung ischemia-reperfusion injury we used a standardized in vivo ischemia-reperfusion model of the right rat lung. Ischemia of 60 min was induced by cross-clamping of the right hilus followed by 120 min of reperfusion. During reperfusion the left hilus was ligated. In group 1 (n=5) animals were sham operated without induction of ischemia under ligation of the left lung hilus. Group 2 (n=5) was operated as described, group 3 (n=5) received 100µg BK before reperfusion, group 4 (n=5) was given a B2-agonist before reperfusion and group 5 (n=5) was given 100µg HOE140 before reperfusion intravenously. Monitoring of blood pressure and arterial oxygenation were performed during ischemia and reperfusion. Blood and lung tissue samples were collected after each experiment. As a marker of endothelial damage angiotensin-converting-enzyme activity (ACE) in serum and RT-PCR of ACE and angiotensin-2 in lung tissue were determined in all groups.

Results: N=2 HOE140 treated animals died within 30min of reperfusion. During reperfusion significantly higher PaO_2-values ($P<0.01$) were observed in BK treated animals of group 3 (214 ±22 mmHg) and sham operated controls of group 1 (233 ±26 mmHg) compared with groups 2 (132 ±13 mmHg) and 5 (125 ±50 mmHg; $P<0.01$). Serum ACE activity after reperfusion was significantly lower in groups 1 (3.5 ±0.5 IU/l), 3 (3.8 ±1.1 IU/l) and 4 (2.2 ±0.5 IU/l; $P<0.05$) *vs.* group 2 (4.8 ±0.9 IU/l), whereas group 5 (6.2 ±5.4 IU/l) did not differ from group 2. mRNA expressions of ACE was lower in groups 1 and 3 compared with group 2 ($P<0.01$). AT-2 mRNA expression did not show any differences between the investigated groups.

Conclusions: A significantly lower ACE-activity and expression and a significantly higher oxygenation after BK application in group 3 strongly suggest its positive influence on ischemic preconditioning of the pulmonary endothelium. Positive effects of application of bradykinin-receptor antagonists could not be proved in this study.