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PATHOPHYSIOLOGIC IMPACT OF ENDOTHELIN-1 IN INFLAMMATORY LUNG DISEASE

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Introduction: Inflammatory lung diseases are often associated with enhanced vascular resistance and permeability. The aim of this study was to investigate whether endothelin-1 (ET-1) is involved in the pulmonary vascular reactions after PMN activation and after lipopolysaccharide (LPS) injection.

Methods and Results: The experiments were performed in isolated rabbit lungs which were perfused with a buffer solution containing 10% of autologous blood. PAP and lung weight reflecting edema formation were continuously registered. Intermittently perfusate samples were drawn to determine ET-1 concentrations. PMN were stimulated by the injection of FMLP (10^{-6} M; n=6), resulting in an immediate PAP increase (21.2 ± 1.8 mmHg). Pretreatment with the ET_A receptor antagonist LU135252 (10^{-6} M; n=6) significantly reduced the pressure reaction after PMN activation (p<0.01). In parallel, ET-1 was detectable in the perfusate 15 min after FMLP injection. In another series of experiments LPS from *Escherichia coli* (100 mg/ml; n=6) was added to the perfusate in the presence or absence of LU135252 (10^{-6} M; n=6). LPS injection induced a marked PAP increase (23.1 ± 3 mmHg) followed by a massive edema formation after 60 min. Pretreatment with LU135252 almost completely suppressed the pressure increase and edema formation due to endotoxin injection (p<0.05).

Conclusion: The current data demonstrate that ET-1 is essentially involved in inflammatory lung injury induced by PMN activation or LPS challenge, which can be attenuated by ET_A receptor antagonist.

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SUPERIMPOSING POSITIVE END-EXPIRATORY PRESSURE (PEEP) DURING PARTIAL LIQUID VENTILATION (PLV) IN EXPERIMENTAL LUNG INJURY

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Introduction: PLV presents a new way to assist ventilation by using a hybrid of liquid and gas techniques, in which a conventional gas tidal volume is superimposed on perfluorocarbon (PFC)-filled lungs. Mechanical ventilation with PEEP is a well established means to provide lung volumes in the acutely injured lung. We speculated that the efficacy of PLV might be improved by applying higher levels of PEEP.

Methods: 8 pigs (30 ± 4 kg) were submitted to pressure-controlled mechanical ventilation and surfactant depleted by repeated lung lavage (PaO_2 < 100 mmHg). PLV was accomplished by intratracheal instillation of 22.5 ml/kg PFC. Following instillation, pressure-controlled mechanical ventilation with PEEP 5 and 15 mbar was performed. Data are expressed as mean±SEM, statistical analysis was performed using Wilcoxon matched-pairs-test and ANOVA for repeated measures (p<0.05).

Results: Following induction of lung injury, PLV increased PaO_2 (50 ± 5 vs. 78 ± 9 mmHg) (p<0.05). Application of PEEP 15 mbar significantly reduced intrapulmonary shunt (Qva/Qt) and increased PaO_2 (236 ± 60 mmHg) (p<0.05). PLV induced a significant increase in dynamic resistance (R_{dyn}) that was reduced by PEEP (p<0.05 by ANOVA).

Conclusions: In experimental lung injury, gas exchange during PLV is augmented by co-applying higher levels of PEEP. Moreover, PEEP compensates for a PLV-associated increase in R_{dyn} and might enhance recruitment.

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PROCALCITONIN AS A MARKER FOR PULMONARY ASPIRATION

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INTRODUCTION: During the last few years procalcitonin (PCT) has been shown to be a useful marker for infectious diseases. Much higher plasma levels of PCT have been found in patients with bacterial compared to viral infections. Some believe that the neuroendocrine cells of the lung are the origin of PCT. We prospectively investigated if PCT plasma levels are elevated in patients with clinical signs of aspiration.

METHODS: After approval by the local ethics committee, we studied PCT plasma levels in patients with severe head injury. Blood samples were drawn from arterial lines 12, 24, 36 and 72 hours after trauma. PCT plasma levels were measured by chemiluminescence technique. Lung injury scores within seven days and Glascow coma scale scores at the day of admission were evaluated.

RESULTS: These are preliminary results from an ongoing study. Up to now seven patients have been enrolled in this investigation. Patients without aspiration showed plasma levels from 99 to 962 pg/ml. Highly elevated PCT levels (1040 - 8358pg), higher lung injury scores and lower Glascow coma scores were found in patients with clinical signs of aspiration.

CONCLUSION: As early as 12 hours after the traumatic event, PCT plasma levels are highly elevated in patients with clinical signs of aspiration. Whether PCT will serve as an prognostic screening marker for infectious complications due to aspiration remains to be evaluated by further results of this investigation.

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A WWW-BASED MULITCENTRIC STUDY FOR ARDS THERAPY ENTRY CRITERIA DEFINITIONS

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Introduction: Treatment of patients suffering from ARDS is a difficult task because of the lack of a unique definition and various forms of therapy. The extra-corporal carbondioxid removal ($ECCO_2$-R) is, at present, the ultimative therapy to treat patients with ARDS; however, there are no clear guidelines when this therapy is indicated. A knowledge-based computer system is being implemented to support the clinician in his/her decision to apply $ECCO_2$-R or not.

Methods: Entry criteria for $ECCO_2$-R should be established within the framework of an international study and formally modeled to be processed by a computer program. This step includes evaluation and testing of various meaningful criteria definitions. Here, inherent vagueness, uncertainty of the occurrence and limited availability of medical data are to be considered to establish a useful practical tool. This is done by using the theory of fuzzy sets.

Results: The study framework for entry criteria definition is available as WWW-application under following URL:
http://trulli.imc.akh-wien.ac.at/FuzzyARDS/.