First Vienna Shock Forum

Part A: Pathophysiological Role of Mediators and Mediator Inhibitors in Shock

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REACTION PATTERN OF ALVEOLAR CELLS IN THE POSTTRAUMATIC LUNG FAILURE*

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INTRODUCTION

The acute respiratory distress syndrome (ARDS) is still one of the life threatening organic complications which might occur as a consequence of pulmonary and extrapulmonary diseases like e.q. sepsis, polytrauma, burns or shock. It ist caused by an initial disturbance of the capillary and alveolar barrier function (HAMMERSCHMIDT et al. 1980) which later is followed by a proliferative parenchyma (BLEYL 1979). The broncho-alveolar lavage (BAL) can be used as a diagnostic tool to detect early cellular and humeral alterations in ARDS (HUNNINGHAKE et al. 1979, JOKA et al. 1985).This is independent of the etiology of the immunologic process.

Our scientific interest is focussed on the following questions:

1. to determine the extent and limitation of the capillary and alveolar barrier dysfunction.
2. To investigate the interdependant interaction of pathogenetic factors based on the alveolar cell response

* This work was supported by the "Deutsche Forschungsgemeinschaft" project II B 6.

METHODS AND MATERIALS

In multi injured patients with uniform initial criteria (PTS) (OESTERN et al. 1985) clinical progress (cardio pulmonal monitoring) (LEWIS et al. 1979) was compared with biochemical parameters in serum and BAL. The following factors were determined: complement fragments,intracellular marker-enzymes (Elastase, Myeloperoxidase, Laktoferrine, Alpha-1-PI, LDH, etc.) leukotrienes and further selected proteines. The oxidation potential as an indirect measure of the cell activity was determined by the luminol-enhanced chemoluminescence (WILLIAMS et al. 1981, CHENUNG et al. 1983).

RESULTS

19 polyinjured patients have been examinated prospectively. The severity of trauma has been defined by the common initial trauma score (PTS 30 points). BAL has always been performed under the same conditions immediately after the trauma and once per day. However to investigate the pathomechanismen of the ARDS it is necessary to define this failure on clinical criteria. In our studies the extravascular lung water (ELVW) was the most essential criterion to detect capillary leakage. In addition patients were divided in group with (group AB) or without (group CD) increase of lung water to evaluate the measured clinical and biochemical parameters respectively. This was based on the experience that an ELVW exceeding 1o ml/kg KG leads to significant respiratory alterations associated with ARDS. The wedge-pressure served as an expression for an insufficiency of the left heart to exclude left ventricular failure.

The same difference in regard to the alveolo-arterial oxygen pressure difference (AaDO2), the oxygenation quotient and the dynamic compliance were seen for the ARDS/non-ARDS group. The accompanying pulmonary vascular hypertension in case of ARDS was evidenced by the progress of the mean pulmonary artery pressure. However the increase of lung water above 10 ml/kg KG occured before the alterations of respiratory and hemodynamic values. 40 % of the ARDS-group (n=5) died as a result of a respiratory failure, whereas the mortality in the group without increase of the lung water (n=14) was only 11 %.

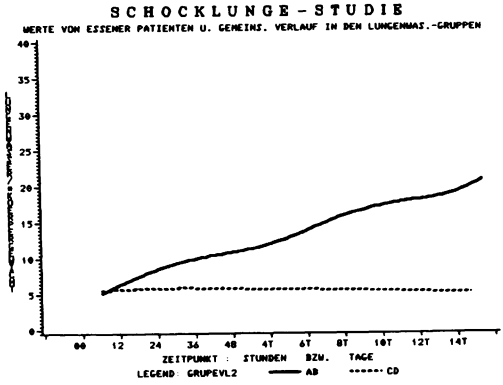

Figure 1. Cours of extravascular lung water group AB (ARDS) compared to group CD (non-ARDS). Statistically evaluated by C.REINSCH 1969

Plasmatic and cytobiological alterations were classified in the same way. The influx of neutrophiles into the alveolar unit was in accordance with data described in the literature (TATE et al. 1983). In the group without ARDS normal inflammatory response of the cells was seen.This was suggested by data found in the chemoluminescence-assay with purified alveolar neutrophiles (high PEAK, short PEAK-time). Alveolar neutrophiles of patients with ARDS were characterized by low PEAK and long PEAK-time during the chemoluminescence response. Simular results were obtained for blood as well as alveolar neutrophiles in one patient. In this case the release of LTB4 was inhibited.

The alveolar influx of granulocytes was associated with an intraalveolar increase of elastase. Elastase-Proteinase-inhibitor complex was comparatively higher in BAL than in plasma. In addition the amount of this complex in BAL correlated with the severity of the lung failure. The encymatic activity of elastase could only be detected in severe cases.

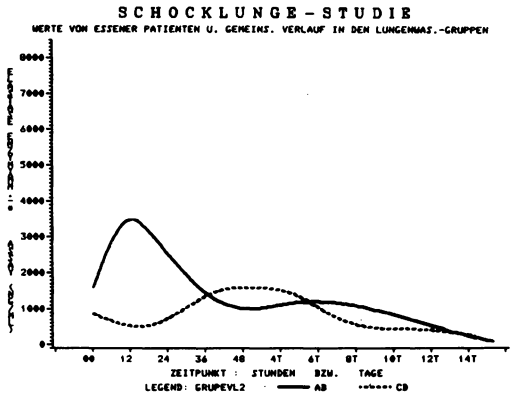

Figure 2. Concentrations of Elastase-Proteinase-inhibitor complex in BAL of patients with and without lung water increase (group AB/CD).

High concentration of leukotrienes could be measured in the ARDS-group during the first hours after trauma.

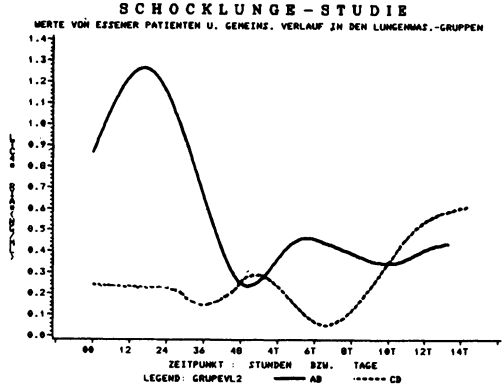

Figure 3. Courses of the leukotriene in BAL based on clinical classification (group AB/CD)

Significant differences were found in C3A during the first four days. C3A occurs one day before granulocytes influx.

A further chemotactic stimulus could be originated from the intraalveolar proteolytic potential. In contrast to

blood, we found an overall increase of total protein in ARDS-group during the onset of ARDS.Up to the 4th day all proteins in lavage were significantly increased. Two different types of proteins where found in the lavage fluid: those of vascular origin (Albumin,Alpha-1-Proteinase-Inhibitor,Alpha-2-Makroglobulin) as well as those of cellular origin from invading mobile cells (LDH,Elastase etc.).

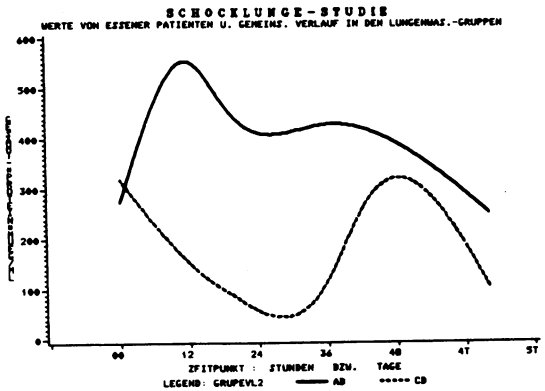

Figure 4. Courses of broncho-alveolar lavage Total Protein based on clinical classification (group AB/CD).

High amounts of IGG (above 3,5 mg/dl) and IGA during the first hours after trauma are commonly associated with an increase of the lung water at the 4th day. The intraalveolar presence of myoglobin strongly suggested an capillary leakage. In patients without ARDS (group CD) serum specific proteins or macro-proteins were undetectable after 36 hours.

DISCUSSION

The alveolar capillary unit can be damaged by many inflammatory active mediators. This damage causes the process of inflammation. Its cardinal symptoms are edema and transmigration of neutrophiles. We could describe the intraalveolar cell influx. A group specific response pattern of alveolar neutrophiles was demonstrated in luminol-enhanced chemoluminescence. During the onset of ARDS an enhanced level of intracellular enzymes (COCHRANE et al. 1983) was associated with a bad cell response. The latter could be due either to a downregulation of the tested cells, as was suggested for several mediator-cell interactions, or to

cell death. In any case the breakdown of the physiologic regulation systems in alveolar capillary unit is the pathophysiologic background of progressive lung failure. We assumed that the extravasation of proteins and the intraalveolar release of proteolytic potentials (PARSON et al.1985) served as a "second stimulus" for lung damage. This would be an explanation for the decisive increase of lung water occuring four days after trauma. In addition the influx of protein may be the reason for a direct surfactant damage or a fault in surfactant phospholipid synthesis. This leads to the complete ARDS (PISON et al. 1986)

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