Activating clotting and inflammation as part of the aetiology of the neonatal respiratory distress syndrome (RDS)

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Apart from the well known etiologic factors surfactant deficiency and immaturity of the lung parenchyma there is increasing evidence that activation of clotting and inflammation are of importance in the course of neonatal respiratory disease in premature infants. Low anti thrombin III levels in plasma have been described as well as intra alveolar depositions of fibrin in preterm infants suffering from RDS. The concept of involvement of an inflammatory process was supported by the findings of increase of complement, increase of the number of alveolar macrophages and increase of release products of polymorph nuclear cells in tracheal aspirates.

To assess whether the activation of clotting and inflammation occurs simultaneously we studied preterm infants with RDS and preterm infants without RDS. In the first five days of life we could demonstrate significantly higher levels of factor XII, the thrombin/anti-thrombin III complex in the plasma of RDS infants. The platelet count was decreasing during these first five days as an indication of consumption by the formation of (micro) thrombi. Simultaneously we measured lower counts of polymorph nuclear cells in the blood and an indication of increased production of elastase-1. In addition we found release of platelet activating factor (PAF) and increase of serum complement (1,2).

Our next study was designed to investigate the association of activation of clotting and inflammation on lung injury. For this purpose we ventilated preterm rabbits and measured protein leak into the alveolar space as indication of lung injury. We found that leakage of protein in the lungs of preterm rabbits (28 days of gestation) is correlated significantly with activation of clotting and increase of complement and polymorph nuclear cells in plasma (3).

In another clinical study we compared two groups of patients with RDS that differed with respect to the severity of the lung disease. We assessed clotting and inflammatory parameters as in the previous studies and subsequently we related these values to peak inspiratory pressure, FiO2 and ventilator efficiency index. Most clotting parameters and inflammatory mediators were higher in the group of infants with severe RDS compared to moderate RDS. In addition we could demonstrate significant correlations of these parameters with the severity of RDS of the patients (4).

In conclusion: Activation of clotting and inflammation are important factors that contribute to the development of the respiratory distress syndrome in preterm infants. Additional studies are necessary to elucidate the sequence of events in the first hours after birth in these infants and to investigate whether therapeutic interventions can be instituted to mitigate the clinical course of RDS.

References:
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