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α-2-MACROGLOBULIN LEVELS IN EARLY RESPIRATORY DISTRESS SYNDROME*

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The vasoactive products of uncontrolled protease activity can play an important role in the pathogenesis of respiratory distress syndrome in newborn infants. In this study α-2-macroglobulin, which has antiproteolytic activity, was studied in the first few hours of life in preterm infants with and without respiratory distress syndrome. Mean plasma α-2-macroglobulin levels were found to be similar in both groups. These findings implicated that α-2-macroglobulin has no significant role in the pathogenesis of respiratory distress syndrome. *Key words: α-2-macroglobulin, fibrinolysis, respiratory distress syndrome, newborn infants.*

Pulmonary vascular damage is frequently encountered in newborn infants with respiratory distress syndrome (RDS)[1-4]. It has been postulated that the vasoactive products of uncontrolled protease activity can play an important role in the pathogenesis of RDS[5]. Proteinases appear in the circulation during blood clotting, fibrinolysis, and activation of the complement system. These proteinases can be inactivated by one or more of the several proteinase inhibitors in the blood. Alpha-2-macroglobulin is one of these proteinase inhibitors[5]. It has been shown that alpha-2-macroglobulin levels were significantly lower in infants with respiratory distress syndrome compared with control[6,7]. Therefore, we investigated plasma alpha-2-macroglobulin levels in preterm infants within the first few hours of life, in order to evaluate its role in the development of RDS.

Material and Methods

Thirty-five infants were included in the study. All neonates received vitamin K_1 (1 mg) intramuscularly upon delivery. Respiratory distress syndrome was

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considered to be present if all the following diagnostic criteria were fulfilled: symptoms of respiratory distress within one hour after birth and present for at least 24 hours, need for respiratory support including mechanical ventilation, and typical findings on lung x-ray and arterial blood gas analysis. None of the infants with RDS had any other disease.

Blood samples for alpha-2-macroglobulin (single radial immunodiffusion method, NOR-Partigen, Behring, Germany)[8] testing were obtained from a peripheral vein within six hours after birth, and mixed with 3.8 percent trisodium citrate in amounts according to individual hematocrit levels. The tubes were centrifuged at 3000 rpm for 10 minutes within 30 minutes of collection. The plasma was stored at –20 °C and analyzed within a month.

Results

Among 35 infants, 15 developed RDS; 20 infants with stable clinical conditions served as the control group. No significant statistical difference between the two groups was found for gestational age or birth weight. The mean plasma alpha-2-macroglobulin levels were found to be similar in both groups ($p>0.05$ by Mann-Whitney U test, Table I).

Discussion

Alpha-2-macroglobulin forms 1:1 complexes with various proteolytic enzymes, and inhibits several proteolytic enzymes in coagulation and fibrinolysis. It inhibits thrombin more slowly than antithrombin III, but acts as a rapidly acting antiplasmin[9-11]. The sites of production and biodynamics of this inhibitor are

Table I: Plasma Alpha-2-macroglobulin Levels in Preterm Infants with and without RDS

	Infants without RDS (n = 20)	Infants with RDS (n = 15)
Gestational ages (weeks)	32.1 ± 2.1 (27-35)	32.4 ± 1.7 (29-34)
Birth weight (g)	1614 ± 439 (1030-2460)	1851 ± 602 (830-2680)
alpha-2-macroglobulin (mg/dl)	116.68 ± 30.52 (44.00 – 183.30)	104.76 ± 34.37) (39.20 – 162.00)

Mean ± SD, ranges in parentheses. In all comparisons $p>0.05$ by Mann-Whitney U test.

unknown, although its production and secretion by fibroblasts, mononuclear phagocytes, platelets, and endothelial cells have been demonstrated in cell culture[12].

The concentration of alpha-2-macroglobulin in plasma ranges from 130 to 325 mg/dl[9]; however, neonatal levels are higher than those in adults[13,7]. In this study, alpha-2-macroglobulin levels in premature infants who did not develop RDS ranged between 44-183 mg/dl (116.68 ± 30.52).

A reduced fibrinolytic state has been shown in the early stages of RDS[3]. A hypercoagulable state, defective fibrinolysis, hypoproteinemia, and systemic and pulmonary edema are common features observed in RDS[5]. The characteristic pathological finding of RDS is hyaline membranes in the lung. Hyaline membranes are formed by coagulation of several proteins following parenchymal and vascular damage[14].

This study was designed to determine the role of alpha-2-macroglobulin in the pathogenesis of RDS. Low levels of protease inhibitors have been found on the first day of life in infants with respiratory distress syndrome[6,7]. These findings indicate that reduced alpha-2-macroglobulin levels may play a role in the reduction of fibrinolytic activity observed in the early stages of RDS. In contrast to these authors[6,7], our findings suggest that alpha-2-macroglobulin levels are unchanged in the early stages of RDS and that it probably has no role in the hemostatic abnormalities which arise during RDS pathogenesis.

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