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# PLASMA THROMBOMODULIN LEVELS IN EARLY RESPIRATORY DISTRESS SYNDROME*

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**SUMMARY: Yurdakök M, Yiğit Ş, Aliefendioğlu D, Dündar S, Kirazlı Ş. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Plasma thrombomodulin levels in early respiratory distress syndrome. Turk J Pediatr 1998; 40: 85-88.**

**Infants with respiratory distress syndrome (RDS) undergo hemodynamic alterations in both the pulmonary and systemic vascular beds that predispose these infants to microvascular damage. In addition, disseminated intravascular coagulation (DIC) is frequently encountered in preterm infants with advanced RDS. In preterm infants with RDS, the plasma status is not known. Therefore, we studied plasma thrombomodulin levels in 25 preterm infants who did or did not develop RDS within the first few hours of life. The mean plasma thrombomodulin levels were found to be similar in the two groups (8.12 ± 10.20 ng/ml vs. 18.30 ± 22.77 ng/ml, respectively, $p > 0.05$ by Mann-Whitney U test). It seems that plasma thrombomodulin levels are normal in the earlier stages of RDS before the occurrence of severe vascular damage and DIC due to hypoxemia.** *Key words: newborn infant, thrombomodulin, respiratory distress syndrome.*

The vascular endothelium is metabolically active in the regulation of coagulation. The vascular endothelial cells produce various important antithrombotic substances, such as plasmin activators, heparin-like enzymes and others. Thrombomodulin (TM) is one of these endothelial products. It neutralizes thrombin-clotting activity and accelerates the thrombin-catalyzed activation of protein C, thereby limiting clotting activity. Although TM is mainly found on endothelial cell surfaces, it is also present in the circulating blood. This soluble form of TM appears to be active in its endothelial form[1].

Respiratory distress syndrome (RDS) is an important cause of hypoxemia in preterm infants. Infants with RDS undergo hemodynamic alterations in both the pulmonary and systemic vascular beds that predispose these infants to microvascular damage, increased capillary permeability and pulmonary interstitial

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edema. In addition, DIC is frequently encountered in preterm infants with advanced RDS[2]. An increase in TM levels, in both hypoxemia and DIC, point to endothelial cell damage[3]. In the setting of adult RDS, proteases released from leukocytes may be responsible for the release of TM into the circulation[4]. Disseminated intravascular coagulation (DIC) also significantly increases the soluble TM level. In DIC syndrome, activated proteolytic enzymes in the coagulation-fibrinolysis system may induce the release of TM[5].

In preterm infants with RDS, the TM status is not known. We previously reported (in preterm infants who developed RDS) normal plasma fibrinogen, antithrombin III, protein C, tissue plasminogen activator[6], thrombin-antithrombin III complex and prothrombin fragment 1.2[7], but lower D-dimer and higher plasminogen activator inhibitor (PAI)[6] and von Willebrand antigen (vWF-Ag) levels[8] within the first few hours of life, as compared to the control group. According to these findings, DIC is not a prominent event in early (or developing) RDS. higher D-dimer, PAI and vWF-Ag levels are probably related to abnormalities in the fibrinolytic system due to lung damage and local platelet activation in RDS.

Therefore, we studied plasma TM levels in 25 preterm infants who did or did not develop RDS within the first few hours of life.

## Material and Methods

Blood samples for fibronectin testing were obtained by umbilical artery catheterization within six hours after birth and were immediately mixed with 3.8 percent trisodium citrate according to the hematocrit level. The tubes were centrifuged at approximately 3,000 rpm for 10 minutes within 30 minutes of collection. The plasma was stored at -20 °C for less than one month before the procedure. The plasma TM levels were measured by a one-step sandwich enzyme-linked immunosorbent assay (ELISA) using polyclonal antibody (Diagnostica Stago, Asnieres, Cedex, France) raised against human TM[9].

## Results

Among the 25 infants, 10 who were in stable clinical condition served as the control group. Fifteen developed RDS, which was considered to be present if all of the following diagnostic criteria were fulfilled: symptoms of respiratory distress within one hour after birth and present for at least 24 hours, 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.

The mean plasma TM levels were found to be similar in the two groups ($P > 0.05$ by Mann-Whitney U test; Table I).

Table I: Plasma Thrombomodulin Levels in Preterm Infants with or without RDS (mean ± SD)

| | Controls (n = 10) | Infants with RDS (n = 15) |
|---|---|---|
| Gestational age (weeks) | 32.4 ± 2.1 (30-36) | 29.9 ± 2.7 (26-34) |
| Birth weight (g) | 1704 ± 558 (1120-3050) | 1397 ± 652 (520-2650) |
| Plasma thrombomodulin (ng/ml) | 18.30 ± 22.77 (0.00-66.10) | 8.12 ± 10.20 (0.00-35.17) |

## Discussion

Normal plasma TM levels are not clearly defined even in healthy adults. Results appear to be highly dependent on the ELISA method used for measuring the TM concentration. With the method used in the present study, the normal values of TM were found to be 30-40 µg/L[3]. Although Aurrousseau et al.[10] reported that the TM plasma levels were markedly increased at birth in healthy children (up to 110 ng/ml), normal values of endothelium-derived coagulation variables in infants and children are less obvious. In this study, we found normal plasma TM levels in preterm infants who did and did not develop RDS in the first six hours of life. It seems that plasma TM levels are normal in the earlier stages of RDS before the occurrence of severe vascular damage and DIC due to hypoxemia. However, further studies are required to determine the plasma TM status in the later (or developed) stages of the disease.

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