The Turkish Journal of Pediatrics 1996; 38: 195-197

PLASMA PLASMINOGEN LEVELS IN EARLY RESPIRATORY DISTRESS SYNDROME*

*Murat Yurdakök MD***, *Şule Yiğit MD****, *Berkan Gürakan MD*****
*Semra Dündar MD******, *Şerafettin Kirazlı MD*******

SUMMARY: Yurdakök M, Yiğit Ş, Gürakan B, Dündar S, Kirazlı Ş, (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Plasma plasminogen levels in early respiratory distress syndrome. Turk J Pediatr 1996; 38: 195-197.

The serum plasminogen status in 35 preterm infants with or without respiratory distress syndrome (RDS) was determined in the first few hours of life. Blood smaples for plasminogen testing (Synthetic chromogenic substrate method; Stachorm PLG. Diagnostica Stago) were obtained from a peripheral vein within six hours after birth. Among 35 infants, 20 infants who were in stable clinical condition served as the control group. Fifteen developed RDS with clinical, laboratory and radiological findings. The mean plasma plasminogen levels were found to be similar in the two groups ($p > 0.05$ by Mann-Whitney U test). These findings are discussed along with our previous findings showing normal tissue plasminogen activator (tPA) but lower D-dimer and higher plasminogen activator inhibitor (PAI) levels within the first few hours of life in preterm infants who later developed RDS compared to the control group. *Key words: newborn infant, plasma, plasminogen, respiratory distress syndrome.*

Disseminated intravascular coagulation (DIC) is frequently encountered in preterm neonates with advanced respiratory distress syndrome (RDS)[1]. However, we previously reported normal plasma fibrinogen, antithrombin III (AT-III), protein C and tissue plasminogen activator (tPA), but lower D-dimer and higher plasminogen activator inhibitor (PAI) levels within the first few hours of life in preterm infants who later developed RDS compared to the control group[2].

The assays commonly used in the diagnosis of DIC, i.e., prothrombin time, activated partial thromboplastin time, fibrinogen or fibrin degradation products (FDP), are insensitive and nonspecific. Evaluation of the plasminogen level is also important in the biological interpretation of the serum level of FDP including D-dimers in cases of DIC. If the concentration of plasminogen is very low in these patients, the degradation of fibrin will be deficient; thus a low level of FDP cannot rule out DIC[3].

* From the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.
** Professor of Pediatrics, Hacettepe University Faculty of Medicine.
*** Research Assistant in Neonatology, Hacettepe University Faculty of Medicine.
**** Neonatologist, Başkent University Faculty of Medicine, Ankara.
***** Professor of Internal Medicine, Hacettepe University Faculty of Medicine.
****** Medical Technician in Hematology Laboratory, Hacettepe University Hospital.

Therefore, we studied the serum plasminogen status in 35 preterm infants with or without RDS in the first few hours of life in an effort to determine the etiology of reduced D-dimer levels.

Material and Methods

All neonates received vitamin K1 1 mg intramuscularly upon delivery. Blood samples for plasminogen testing (Synthetic chromogenic substrate method; Stachorm PLG, Diagnostica Stago, Asnieres-Sur-Seine, France)[4] were obtained from a peripheral vein within six hours after birth, and were mixed with 3.8 percent trisodium citrate in an amount selected according to the hematocrit levels. The tubes were centrifuged at 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.

Results

Among 35 infants, 20 infants 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 fullfilled: 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 plasminogen levels were found to be similar in the two groups ($p > 0.05$ by Mann-Whitney U test; Tabel I).

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

	Controls (n: 20)	Infants with RDS (n: 15)
Gestational age (weeks)	32.1 ± 2.1	32.4 ± 1.7
Birth weight (g)	1614 ± 439	1851 ± 602
Plasminogen (%)	55.28 ± 33.12	41.43 ± 19.24

Plasminogen levels are expressed as a percentage of control.
In all comparisons, $p > 0.05$ by Mann-Whitney U test.

Discussion

D-dimers are the end-products of fibrinolysis which results from the conversion of an inert plasma proenzyme (plasminogen) into a proteolytic enzyme (plasmin)[5]. Reduced D-dimer levels found in the previous study[2] within six hours after delivery in preterm infants who developed RDS could not be explained by the normal plasminogen levels found in this study. However, reduced D-dimer levels may be due to an increase in the clearance of FDP or over-consumption in DIC. FDPs,

even large FDPs containing the D domain, are removed from the circulation by clearance mechanisms in the liver, kidney, and reticuloendothelial system. In addition, FDP products and their complexes profoundly impair the hemostatic process and are presumably a major cause of hemorrhage in DIC and fibrinolysis by inhibiton of coagulation and impairment of platelet functions[5].

Normal plasminogen levels in the early stages of RDS could be explained by normal levels tPA, of which converts plasminogen into plasmin[2]. However, the presence of increased PAI levels without any increase in tPA levels remains to be elucidated. Both tPA and PAI are isolated from many cells, including the endothelium[5]. The increased levels of PAI in the previous study may be related to endothelial damage during RDS, because increased von Willebrand antigen levels, which is a reliable marker for systemic and/or lung endothelial damage, were found in the early stages of RDS[6].

These abnormalities seen in the early stages of RDS are presumably different from those found in the later stages of the disease. Further studies are needed to clarify the changes in the hemostatic system in earlier and later stages of RDS.

REFERENCES

1. Stark CR, Abramson D, Erkan V. Intravascular coagulation and hyaline-membran disease of the newborn. Lancet 1968; 1: 1180-1181.
2. Yurdakök M, Oran O, Dündar S, Tekinalp G, Kirazlı Ş. Reduced fibrinolytic state in early respiratory distress syndrome. Am J Hematol 1993; 42: 233-234.
3. Feinstein DI. Diagnosis and management of disseminated intravascular coagulation: the role of heparin therapy (Review). Blood 1982; 60: 284-287.
4. Silverstein RM. The determination of human plasminogen using N^{α}-CBZ-L-Lysine p-nitrophenyl ester as subtrate. Anal Biochem 1975; 65: 500-506.
5. Bithell TC. Blood coagulation. In: Lee GR, Bithell TC, Foerster J, Athens JW, Lukens JN (eds) Wintrobe's Clinical Hematology, (9^{th} ed) Vol 1. Philadelphia: Lea and Febiger; 1993: 566-615.
6. Yurdakök M, Gürakan B, Ergin H, Kirazlı Ş. Increased von Willebrand factor antigen in early respiratory distress syndrome. Am J Hematol 1995; 49: 95-96.