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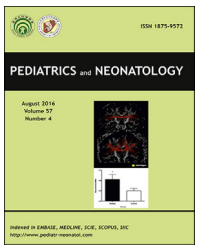

ORIGINAL ARTICLE

Neonatology Oxidative Status in Preterm Infants with Premature Preterm Rupture of Membranes and Fetal Inflammatuar Response Syndrome

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Background: The aim of this study, to determine an index of oxidative stress index in preterm infants less than 34 weeks gestational age with premature preterm rupture of membrane (PPROM) and fetal inflammatory response syndrome (FIRS).
Methods: This study was designed as a prospective study. Fifty-one premature infants less than 35 weeks of gestational age were included in the study. The umbilical cord blood concentrations of IL-6, TAC (total antioxidant capacity) and PON-1 (paraoxonase-1) levels and TOS (total oxidative stress) were studied. The oxidative stress index (OSI = TAC/TOS) was calculated in all of prematüre infants. PPROM was defined as rupture of membranes at least 24 hours before the onset of labor. FIRS was defined by an umbilical cord IL-6 level greater than 11 pg/mL. Premature infants included in the study were divided into 4 groups. Group 1 included preterm infants without FIRS and with PPROM ($n = 16$), while Group 2 included preterm infants without PPROM and with FIRS ($n = 9$), Group 3 consisted of premature infants with PPROM and FIRS ($n = 21$) and Group 4 included premature infants without PPROM or FIRS ($n = 5$).
Results: Umbilical cord TOS level was found to be higher in the preterm infants without FIRS and with PPROM (36.1 μmol H_2O_2 Equiv./L) compared to the preterm infants without PPROM or FIRS (11.9 μmol H_2O_2 Equiv./L) ($p = 0.03$). Umbilical cord PON-1 level was found to be lower

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in the preterms without FIRS and with PPROM (32 U/L), preterms without PPROM and with FIRS (30. 3 U/L) and the preterm infants with both PPROM and FIRS (48.6 U/L) compared to the preterm infants having no PPROM or FIRS (85.6 U/L) ($p = 0.001$).
Conclusion: High pro-oxidant capacity was found in PPROM and low antioxidant capacity in PPROM and FIRS.

1. Introduction

Premature preterm rupture of membranes (PPROM) is defined as the rupture of the amniotic sac at least 24 hours before the onset of labor in preterm infants with a gestational age of < 37 weeks.[1] In 60–70% of cases, PPROM is associated with maternal inflammatory response syndrome (chorioamnionitis, microbial invasion of the amniotic cavity) and/or fetal inflammatory response syndrome (FIRS) (funisitis).[2,3] FIRS occurs due to activation of the innate immune system of the fetus with or without PPROM.[4] FIRS is defined either clinically by an umbilical cord blood concentration of IL-6 greater than 11 pg/mL or histologically by findings of funisitis.[5,6] PPROM is responsible for almost one-third of preterm births,[7] whereas FIRS is responsible for high morbidity and mortality among preterm infants.[8–10] Oxidative stress is defined as an increased pro-oxidant status due to an imbalance between pro-oxidant and antioxidant agents.[11,12] Premature aging of the fetal membranes due to increased oxidative stress may play a role in the pathophysiology of PPROM.[13,14] The involvement of oxidative stress in the pathogenesis of FIRS is unknown. Increased oxidative stress and lower antioxidant capacity have been reported in maternal blood and vaginal washing fluids in PPROM.[15,16] There are a limited number of studies on preterm infants which demonstrate the relationships between oxidative stress and either PPROM or FIRS. In this study, umbilical cord blood oxidative stress markers [total antioxidant status (TAS), total oxidative stress (TOS), paraoxonase-1 (PON-1)] were evaluated in preterm infants with PPROM and/or FIRS.

2. Methods

2.1. Patients and study design

In total, 5254 babies were born in Zeynep Kamil Maternity and Children Training and Research Hospital between August 2009 and January 2010, with 550 hospitalized in the neonatal intensive care unit and 154 born at less than 37 weeks' gestation. Of these, 63 preterm infants aged under 34 weeks' gestation were eligible for the study. IL-6 and/or oxidative stress markers were not studied in the umbilical cord blood samples collected from 12 preterm infants. Thus, 51 preterm infants aged under 34 weeks' gestation were included.

2.2. Definition

PPROM was defined by the occurrence of amniotic fluid leak more than 24 hours before the onset of labor. ROM was diagnosed by sterile speculum examination with a combination of vaginal pooling and nitrazine and ferning tests. FIRS was diagnosed by the finding of umbilical cord blood levels of IL-6 > 11 pg/mL.[6] Oligohydramnios was defined as an amniotic fluid index < 5 cm. Respiratory distress syndrome was diagnosed with the association of clinical presentation and characteristic radiological findings described by Giedion et al.[17] Bronchopulmonary dysplasia was diagnosed by an oxygen need at 36 weeks of postmenstrual age.[18] Retinopathy of prematurity was defined according to The International Classification of Retinopathy of Prematurity.[19] Early onset neonatal sepsis was defined as any systemic bacterial infection documented by a positive blood culture and the presence of symptoms or clinically highly suspected sepsis (presence of symptoms and elevated C-reactive protein and/or affected white blood cell count) during the first 72 hours of life. Intraventricular hemorrhage was diagnosed by ultrasonography and classified as described by Volpe.[20] In our clinic, transcranial ultasound of premature patients with the birth weight < 1500 g is routinely obtained in the 1st, 3rd, and 7th days of life.

2.3. Blood sampling and biochemical studies

2.3.1. Cord blood concentrations of total antioxidant capacity (TAC, mmol trolox equiv/L), TOS (μmol H_2O_2 equiv/L), PON-1 (U/L), IL-6 (pg/mL)

Samples (2 mL) of umbilical cord blood were drawn into the tubes with EDTA following birth. Blood samples were centrifuged for 3 minutes at 5000 rpm, and plasma samples were stored at −80°C. Serum TAC and TOS levels were measured, as described by Erel.[21] Erel's method for serum TAC level measurement is based on the bleaching of the characteristic color of a more stable 2,2,2-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) radical cation by antioxidants. The results were expressed in mmol trolox equivalents/L. Erel's TOS measurement is based on the oxidation of ferrous ion to ferric ion in the presence of various oxidative species and the measurement of the ferric ion by xylenol orange. The results were expressed in mmol H_2O_2 equivalents/L. Oxidative stress index [arbitrary unit = TOS (μmol H_2O_2 equiv/L) / TAC (mmol trolox equiv/L)] was calculated as the percent ratio of TOS to TAC.[22] PON-1 (U/L) activity was measured spectrophotometrically

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