Pediatrics and Neonatology (2015) 56, 95—100

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.pediatr-neonatol.com

ORIGINAL ARTICLE

Investigation on Malondialdehyde, S100B, and Advanced Oxidation Protein Product Levels in Significant Hyperbilirubinemia and the Effect of Intensive Phototherapy on these Parameters

Dilek Sarici [a,*], Tamer Gunes [a], Cevat Yazici [b], Mustafa Ali Akin [a], Levent Korkmaz [a], Seyma Memur [a], Selim Kurtoglu [a], Mehmet Adnan Ozturk [a], Serdar Umit Sarici [c]

[a] *Division of Neonatology, Department of Pediatrics, Erciyes University Faculty of Medicine, Kayseri, Turkey*
[b] *Department of Biochemistry, Erciyes University Faculty of Medicine, Kayseri, Turkey*
[c] *Division of Neonatology, Department of Pediatrics, Ufuk University Faculty of Medicine, Ankara, Turkey*

Received Dec 5, 2013; received in revised form May 25, 2014; accepted Jun 19, 2014
Available online 26 September 2014

Key Words
advanced oxidation protein product;
hyperbilirubinemia;
intensive phototherapy;
malondialdehyde;
S100B protein

Background: The parameters of oxidative stress [advanced oxidation protein products (AOPPs), malondialdehyde (MDA), and S100B] and the effect of intensive phototherapy (PT) on these parameters have not been studied extensively in newborns with significant hyperbilirubinemia (SH). We aimed to measure the levels of MDA, S100B, and AOPPs in newborns with SH, and to compare newborns with healthy control newborns without hyperbilirubinemia on the basis of these parameters of oxidative stress. In addition, we investigated the effect of intensive PT on these parameters during the treatment of SH and report our findings for the first time in the literature.

Methods: The study was performed in newborns ($n = 62$) who underwent intensive PT because of SH. Newborns without jaundice constituted the control group ($n = 30$). Both groups were compared with respect to demographic characteristics and biochemical (laboratory) parameters including MDA, AOPPs, and S100B. MDA, AOPPs, and S100B were also compared before and after intensive PT in the PT group. In the study group, a correlation analysis of demographic characteristics; MDA, AOPP, and S100B values; and changes occurring in MDA, AOPPs, and S100B values due to the effect of intensive PT was performed.

* Corresponding author. Division of Neonatology, Department of Pediatrics, Erciyes University Faculty of Medicine, Talas Yolu, Melikgazi, 38039, Kayseri, Turkey.
E-mail address: drdilekcoban@yahoo.com.tr (D. Sarici).

http://dx.doi.org/10.1016/j.pedneo.2014.06.006

Results: Serum total bilirubin, S100B, and MDA levels in the PT group before performing PT were significantly higher than those in the control group. In newborns receiving PT serum total bilirubin, MDA and AOPP levels decreased significantly after intensive PT. In correlation analysis, a statistically significant negative correlation was found only between the amount of bilirubin decrease with PT and AOPP levels after PT in the study group.
Conclusion: Whether the significant decrease in MDA levels, which was higher prior to PT, is due to the decrease in serum bilirubin levels or due to the effect of intensive PT itself remains to be determined in further studies. The decrease in AOPP levels after PT implies that intensive PT has protective effects on oxidative stress.

1. Introduction

In neonatology, free radicals and their products, lipid and protein peroxides, have been thought to be responsible for the pathogenesis of many conditions such as retinopathy of prematurity, bronchopulmonary dysplasia, intracranial hemorrhage, periventricular leucomalacia, sepsis, necrotizing enterocolitis, and hypoxic ischemic encephalopathy.[1] Bilirubin, at physiologic concentrations, protects neonatal red blood cells against oxidative stress. However, increased bilirubin concentrations are associated with significant cytotoxicity,[2] and significant hyperbilirubinemia (SH) may cause an increase in free radicals and their products.[2–4] On the other hand, phototherapy (PT) itself, which is the most commonly used treatment modality in SH, may also result in the release of reactive nitrogen and oxygen species, and photolysis products are cytotoxic and associated with the production of free oxygen radicals.[5] Ostrea et al[6] reported that the exposure of red cell suspension to PT light in the presence of a sensitizer (bilirubin) resulted in oxidative injury to the red cell membrane. Recently, *in vitro* fluorescent light has been shown to cause a decrease in red blood cell ATPase activity and an increase in lipid peroxidation, and it has been hypothesized that specific areas of the membrane, mainly the lipid/protein interface, are differently affected.[7] Various studies investigated the relationship between PT and/or SH and malondialdehyde (MDA) levels with conflicting results.[3,4,8–15]

Advanced oxidation protein products (AOPPs) are formed during oxidative stress,[1] and they are defined as novel parameters of oxidative stress.[16] There is a limited number of studies about AOPPs during the neonatal period, most of which have been conducted to investigate various free radical-mediated diseases.[1,17,18] However, to our knowledge, no studies have investigated the relationship between AOPPs and neonatal hyperbilirubinemia and/or PT.

S100B protein levels in cerebrospinal fluid, plasma, or serum have been used increasingly as biomarkers to evaluate the presence and severity of intraventricular hemorrhage, hypoxic ischemic encephalopathy, and brain damage.[19–21] Levels of S100B protein in neonatal SH were investigated in only one study,[22] and to our knowledge, the effect of PT has not yet been determined.

Thus, we aimed to measure the levels of MDA, S100B, and AOPPs in newborns with SH, and to compare these newborns with healthy control newborns without hyperbilirubinemia on the basis of these parameters of oxidative stress. In addition, we investigated the effect of intensive PT on these parameters during the treatment of SH for the first time in the literature.

2. Patients and methods

This study was performed on term and near-term ($\geq$35 weeks) newborns who underwent intensive PT because of SH between February 2011 and April 2013. A diagnosis of SH was made if the serum total bilirubin levels of the newborns were above the levels on age (hour)-specific bilirubin curves determined on the basis of risk status and gestational age of the newborns.[23,24] All infants were exposed (completely unclothed, with their eyes and genitals covered) to continuous PT that was interrupted only for feeding, cleaning, and blood sampling. The infants' weight and temperature were closely monitored during PT.

Sex, type of delivery, weight, length, and head circumference at birth, gestational age, age on admission, and maternal age of the newborns were recorded. Infants with any congenital malformation, prematurity ($<$35 weeks' gestation) or postmaturity, maternal diabetes, birth asphyxia, sepsis, or hemolytic-type hyperbilirubinemia due to blood group (Rh or ABO) incompatibility were excluded from the study. The study group comprised 62 newborns.

Intensive PT was chosen as the PT of choice in the treatment of SH, according to the guidelines of the American Academy of Pediatrics.[23] For PT, an intensive PT unit consisting of high-intensity gallium nitride light-emitting diodes (light spectrum = 450–470 nm and irradiance $\geq$ 35 $\mu W/cm^2/nm$; Bilicrystal IV. 2; Medestime S.A. Charleroi, Belgium) was used. The system was placed over the infants, at a distance of 40 cm. The irradiance was maintained above 35 $\mu W/cm^2/nm$ during PT and measured weekly. PT was stopped if serum bilirubin levels fell at least 5 mg/dL below the limits defined necessary for starting PT.

A control group (n = 30) was constituted by the newborns who had no jaundice, and were about to be discharged or came to the first control visit after hospital discharge. Blood samples from these cases were obtained during venipuncture performed for metabolic screening or various other reasons (such as control of thyroid function