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Compared Oxidant Antioxidant Balance in Cord Infants between Vaginal Delivery and Cesarean

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Abstract

Objective: oxidative stress plays an important role in a large number of neonatal diseases. The purpose of this study was to investigate the effect of mode of delivery on pro-oxidant antioxidant's balance in umbilical cord blood of the newborns. Methods & Materials: In this prospective study we investigated pro-oxidant antioxidant's balance in umbilical cord blood of 163 term neonates (80 born via normal vaginal delivery (NVD) and 83 born via elective caesarean section (CS)).For this purpose, we examined hydrogen peroxide ratio to uric acid in the serum samples collected from 2 groups. Furthermore, we followed the babies mentioned; in their newborn period and investigated those in terms of the need for hospitalization, the cause of admission, weight gain, jaundice and general condition. Results: Umbilical cord blood pro-oxidant antioxidant's balance was not significantly different between the two groups. The average pro-oxidant antioxidant's balance was59.18±64.043 in the Umbilical cord blood of normal vaginal delivery group,and50.56 ± 44.233 in the elective cesarean group (P value=0.929). Conclusion: Our results didn't show a significant relationship between umbilical cord blood pro-oxidant antioxidant's balance and type of delivery.

Keywords: Pro-Oxidant Antioxidant's Balance, Elective Cesarean Section, Oxidative Stress, Normal Vaginal Delivery.

Introduction

If the body is not able to neutralize or detoxify the harmful effects of free radicals, Oxidative stress occurs (Biswas et al., 2014). In fact, oxidative stress is the imbalance between the oxidative factors and the enzymes involved in removing the free radicals or reactive oxygen species (Jauniaux & Burton, 2016).

Free radicals such as superoxide (anionic oxygen radical), H2O2 and hydroxyl (OH) are agents that have one or more unpaired electrons and therefore have a high reactivity potential. They are produced during numerous chemical and metabolic processes in cell membrane, mitochondrion, and endoplasmic reticulum and can damage the proteins, lipids and DNA molecules and result in cell death through apoptosis or necrosis (Mutinati et al., 2014; Wilinska et al., 2015).

The mechanisms of human defense against oxidants system called antioxidant defense and they include enzymatic and non-enzymatic processes. Superoxide Dismutase (SOD), Glutathione Peroxidase (GPX) and Catalase play role in enzymatic antioxidant defense system (Alfadda AA, Salla, 2012; Bar-Or et al., 2015).

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The presence of appropriate oxygen gradient between the uterus and fetal blood circulation is essential for normal function of the placenta, because the early stages of development of the fetus occur in a Low oxygen environment and this physiological hypoxia protects the developing fetus against the harmful effects of reactive oxygen species. Inappropriate oxygen gradient can cause placental dysfunction and may lead to abortion, Preeclampsia, Intrauterine growth restriction (IUGR), and preterm labor (Jauniaux & Burton, 2016; Ramos & Witkin, 2016).

After delivery and transition from fetal to neonatal place, the newborn, is exposed to new conditions that prone it to damage by oxidative stress (Mutinati et al., 2014).

Oxidative stress affects various organs of the body, especially the epithelium of the lung, retina and brain blood vessels and plays an important role in the pathogenesis of many neonatal diseases, such as respiratory distress syndrome, bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity and periventricular leukomalacia (Wilinska et al., 2015; Ozsurekci & Aykac, 2011).

Because of the important role of oxidative stress in newborn diseases, so far, many studies have been down on it. Some of these studies have focused on the effect of mode of delivery on oxidative stress on mothers and their newborns. Concerning the effect of modes of delivery on oxidative stress in neonates and their mothers, contradictory results are available in published articles. some studies suggest that oxidative stress is higher in cord blood of neonates born via cesarean section as compared to those who born via normal vaginal delivery (Mutlu et al., 2011; Katzer et al., 2015; Nejad et al., 2016; Siddiqui et al., 2014; Hu et al., 2017; Ulubas et al., 2018; Noh et al., 2014) While other studies have achieved contradictory results (Inanc et al., 2005; Raijmakers et al., 2003; Cindrova-Davies et al., 2007; Vakilian et al., 2009). Also, some other studies show no significant relationship between mode of delivery and level of oxidative stress (Saphier et al., 2013).

Methods & Materials

This prospective study was conducted in the Department of Obstetrics and Gynecology in Ghaem hospital, Mashhad, Iran between 2016 and 2018. This study was approved by the ethical committee for Clinical Research of Mashhad university of Medical sciences (Mashhad, Iran) and informed consents were taken from all participated mothers'.
inclusion criteria: the gestational age of 37-41 weeks, the health of the fetus, maternal health, the age of the mother of 18-38 years, the apgar score of the 5th minute >7.

163 healthy neonates with gestational age between 37-41 weeks were included for this study and were divided into 2 groups according the mode of their mother's delivery: group NVD (n=80) and group CS (n=83). Neonates having congenital malformations, metabolic disorders, congenital or perinatal infections or born by mothers having signs and symptoms of chorioamnionitis (such as fever, tachycardia (>120 bpm), uterine tenderness, foul-smelling or purulent vaginal discharge), premature rupture of membranes (PROM) or urinary tract infection during labor were excluded.

A total of 2 cc of umbilical cord blood were collected in a tube without anticoagulant. Samples were obtained immediately after parturition and were centrifuged at 2,000 × g for 10 min to isolate their sera, and then were stored at -70 °c till analysis. The pro-oxidant antioxidant's balance is measured by TMB in two different reactions.

The pro-oxidant antioxidant's balance (PAB) assay was performed, as previously described (Alamdari et al., 2007). We mixed varying proportions (0-100%) of 250μM hydrogen peroxide with 3 mM uric acid (in 10 mM NaOH) to prepare standard solutions and then, transferred the mix to a 96 well plate. Then we added 100 ml of 2 NHCl to this mixture and measure in an ELISA plate reader at 450 nm with a reference wavelength of 620 nm. 400 μM of TMB/DMSO (which was prepared with mixing of 16 mg TMB (3, 3, 5 and 5, tetra methyl benzidine) and 10 ml DMSO) was added in 20 ml of acetate buffer. 70 ml of chloramin T solution was added into this 20 ml and incubated for 2h in room temperature. A standard curve was prepared with the values of standard samples. We used Hk unit to express pro-oxidant antioxidant's balance, an arbitrary unit that shows hydrogen peroxide percentage in standard solutions.

All data were expressed as mean ± SD and analytic tests (Chi-squared test, Mann–Whitney test and t-test) were performed using SPSS version 16.0.P-value<0.05 was defined statistically significant.

Results:

A total of 163 neonates were enrolled in this study and categorized into 2 groups: 80 neonates born via normal vaginal delivery (NVD) and 83 neonates born via elective cesarean section (CS). Comparison general characteristics of participants of the 2 groups are shown in

Table 1. No significant differences were found in maternal age, gender of neonates and birth height between the 2 groups. (P- Value> 0.05)

There were statistically significant differences between 2 groups in gestational age, gravidity and mother's weight. (In sequence P-value=0.000, P- value= 0.008, P- value= 0.000). In NVD group, mean (± SD) gestational age was 39.75(± 0.932) weeks and in CS group, mean (± SD) gestational age was 39.06(±0.659) weeks. Gestational age in NVD group was about 1 week more than the other group. The gravidity was higher in women who chose elective CS than those who chose NVD. (P- Value= 0.008). Mothers' weight in NVD group was significantly lower than mothers delivering by elective CS.

In NVD group, mean (± SD) birth weight and head circumference were 3198.12(± 380.72) gram and 34.71(± 1.09) cm respectively and 3332.65(± 397.45) gram and 35.26(± 1.15) in CS group, significant differences were observed between 2 groups in birth weight (p-value=0.036) and head circumference (P-value=0.001).

As shown in Table 2, we followed the neonates in their newborn period and compared the 2 groups in case of weight gain, development, and jaundice and admission rate. There was no significant difference between 2 groups (P-value>0.05).

Umbilical cord blood pro-oxidant antioxidant's balance was not significantly different between the two groups. The average pro-oxidant antioxidant's balance was 64.043±59.18 in the Umbilical cord blood of normal vaginal delivery group, and 50.56 ± 44.233 in the elective cesarean group (P value=0.929)(figure 1).

Table 1: Characteristics of neonates and their mothers

	NVD (n=80)	CS (n=83)	P value
Maternal age (years)	**29.01± 4.704**	**30.30± 5.142**	**0.108**
Gestational age (	39.75±0.932	**39.06±0.659**	**0.000**
Gravidity	**2.43±1.22**	**2.94±1.12**	**0.008**
Mothers weight (Kg)	**68.44±6.79**	**77.59±11.54**	**0.000**
Gender of neonates	41/39 (m/f)	35/48 (m/f)	**0.406**
Birth weight (g)	**3198.12±380.72**	**3332.65±397.45**	0.036
Birth height (cm)	**51.05±2.04**	50.61±2.22	**0.120**
Birth head circumference (cm)	34.71±1.09	**35.26±1.15**	**0.001**

Table 2: characteristics of followed neonates in their newborn period

	NVD (n=80)	CS (n=83)	P value
Weight gain (g)	887.57±279.8	1044.27±578.9	**0.056**
Development	100% normal	98.7% normal	**0.342**
Jaundice	56.1% no jaundice	40.2% no jaundice	**0.092**
Admission rate	2.9%	9%	0.125

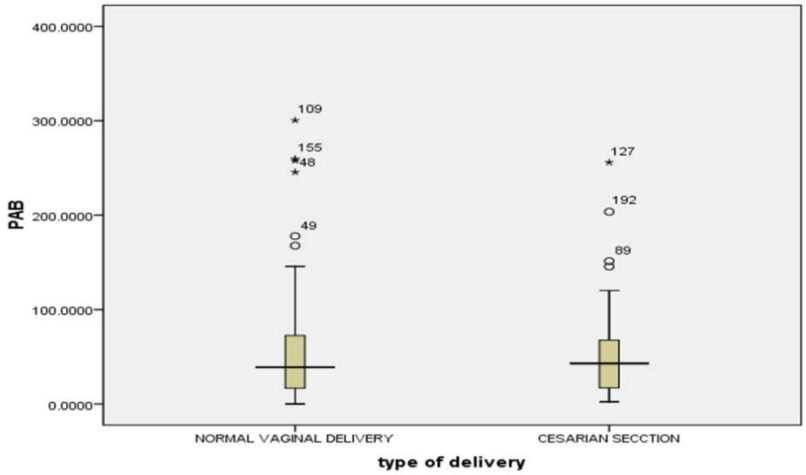

Fig. 1: Umbilical cord blood pro-oxidant antioxidant's balance

Discussion

In physiological conditions, there is a balance between antioxidants and pro-oxidants and Free radicals are neutralized by antioxidant defense system (Biswas et al., 2014). Different types of stress (e.g. transition a fetus from mothers uterus to neonatal environment)increase the production of free radicals and, therefore, Causes disturbances of the pro-oxidant antioxidant's balance and This can lead to damage to various tissues by oxidation of proteins, lipids, polysaccharides and DNA molecules (Mutlu et al., 2011, Perry wt al., 2005).

Pro-oxidant antioxidant's imbalance result in oxidative stress, which plays an important role in a large number of neonatal diseases and also affects on progression of certain cardiovascular disease, Alzheimer disease, stroke and certain types of cancer in adulthood (Mattson & Wan, 2005).
To asses antioxidant status of newborns, glutathione peroxidase, superoxide dismutase, riboflavin, vitamin E, zinc, selenium and other plasmatic factors can be measured (Buonocore & Groenendaal, 2007).We found no statistically significant relationship between mode of delivery and levels of oxidative stress in umbilical cord blood of newborns enrolled in this study. our results were differ from (Hu et al., 2017) and their studies showed that placental inflammatory response and oxidative stress, is closely related to the type of delivery and elective cesarean group had higher expression of inflammatory cytokines as compared to those who terminated pregnancy with vaginal delivery.

Our finding is consistent with the result of Saphier et al. , and velminsky (in Karvina) studies, their result showed no major differences were found between normal vaginal delivery and elective cesarean section in the level of neonatal oxidative stress (Saphier et al., 2013; Veleminsky et al., 2016).
As discussed so far, contradictory results are available about effects of mode of delivery on oxidative stress markers in newborns. And this, suggests that more studies are still required about this issue.

Conclusion:

based on our assays, we can say there was no significant difference between pro-oxidant antioxidant's balance in the cord blood of neonates who born via cesarean section compared to those born via normal vaginal delivery, And in this study, the level of oxidative stress in newborns did not have a significant relationship with mode of delivery.

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