Serum lipid peroxidation levels in small-for-gestational-age babies

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SUMMARY: Ergin H, Kılıç İ, Karaduman Gürses D, Kılınç K. Serum lipid peroxidation levels in small-for-gestational-age babies. Turk J Pediatr 2001; 43: 215-217.

The levels of lipid peroxidation in sera of asymmetric small-for-gestational-age (SGA) babies at the second hour of life were investigated. Lipid peroxidation levels, measured as malondialdehyde (MDA), were 3.3 ± 1.1 and 3.9 ± 1.2 mmol/L in SGA and appropriate-for-gestational age (AGA) groups, respectively. The difference was not significant ($p>0.05$). This result may indicate that free radical scavengers are sufficient in SGA babies.

Key words: lipid peroxidation, Malondialdehyde, SGA, IUGR.

Fetal growth is affected by fetal growth potential during the first half of the pregnancy and by maternal environment and uteroplacental functions during the second half[1]. Various criteria are used in defining small-for-gestational-age (SGA) babies. SGA may be defined as birth weight below the 10th percentile for gestational age or more than two standard deviations below the mean for gestational age[2]. The ponderal index can be used to identify infants whose soft tissue mass is below normal for the stage of skeletal development. Thus, a ponderal index below the 10th percentile may be used to identify SGA infants[3,4]. The ponderal index is not affected by gestational age, race or sex, and is thus preferred to define SGA. In 20% of babies with SGA, fetal growth is affected at the very beginning of gestation (symmetric SGA). In babies with asymmetric SGA, especially during the third trimester of gestation, maternal complications such as preeclampsia, chronic hypertension, diabetes mellitus, chronic cardiac and renal diseases and factors related to the placenta and uterus disturb the uteroplacental blood flow. In 50% of babies with asymmetric SGA, the hypoxia risk is increased due to the impaired uteroplacental blood flow[5].

Free oxygen radicals that increase during the reperfusion phase after hypoxia in perinatal asphyxia are thought to be responsible for the organ damage[6]. Free radicals cause cell membrane injury by lipid peroxidation, and the aldehyde products cause intracellular and extracellular harm. Malondialdehyde (MDA), an aldehyde that appears during lipid peroxidation, is an indirect indicator of lipid peroxidation[7].

In this study, MDA levels, an indicator of lipid peroxidation, are searched in the sera of the babies with asymmetric SGA who were thought to have intrauterine chronic hypoxia and fetal malnutrition.

Material and Methods

Patients: Term babies of 38 weeks' or more than 38 weeks gestation according to the Dubowitz score[8], with no history of drug usage, illness, syndrome, chromosomal abnormality or intrauterine infection were selected for the study. All of the babies had arterial oxygen saturation of more than 95% and normal blood glucose concentration. In the determination of the babies with SGA the ponderal index (PI) = (body weight/length^3) x 100 was used; babies having PI under 10% were considered as asymmetric SGA[3,4].

The study was approved by the Medical Ethics Committee of Pamukkale University Hospital.

Collection and preparation of samples: The sera of the venous blood samples which were taken at the second hour after birth were separated and were stored at -70 °C for biochemical studies.

Determination of TBARS: In this study we used the thiobarbituric acid method for determination of lipid peroxidation. Although the thiobarbituric acid assay is not specific for MDA, measurement

of TBARS is an easy and reliable method which is used as an indicator of lipid peroxidation and free radical activity in biological samples. Lipid peroxidation in sera were determined using the method of Uchiyama and Mihara[9]. Tetramethoxypropane was used as the standard and the level of TBARS was calculated as micromoles of MDA per liter.

Statistics: Values are expressed mean ± SD. The Student's t test was used for statistical analysis. A $p < 0.05$ value was considered to represent a significant difference between the compared values.

Results

Malondialdehyde (MDA) levels as mean ± SD of 32 term SGA babies in the study group and in 19 term appropriate-for-gestational age (AGA) babies in the control group were 3.3 ± 1.1 and 3.9 ± 1.2 mmol/L, respectively. No maternal illness or special diet during pregnancy was found in the obstetrical charts or reported by the mothers. There was no statistically significant difference between the mean values of the two groups ($p > 0.05$). As Table I shows, there were no statistically significant differences between gestational age, sex, Apgar score, length or head circumference.

Table I. Perinatal data of SGA and control groups (median ± SD)

	SGA	Control
n	32	19
Male	17	10
Female	15	9
Gestational age (weeks)	39.7 ± 0.9	39.7 ± 0.9
Birth weight (g)	2350 ± 212	3326 ± 291
Length (cm)	48.2 ± 1.4	49.8 ± 1.3
Head circumference (cm)	34.1 ± 0.9	34.9 ± 0.8
Apgar score (5 min)		
Median	9	10
Range	(7-10)	(7-10)

There were no statistically significant differences between the groups.

SGA: small-for-gestational-age.

Discussion

In 20% of babies with SGA, fetal growth is likely to be affected from the early stages of gestation (rapid cell proliferation stage); a proportional retardation is seen in weight, length and head circumference, and the PI is found normal[5]. In the etiology of this group, termed symmetric, chromosomal abnormalities, dysmorphic syndromes, congenital metabolic diseases, drug usage and intrauterine infections can be present[1].

Since a fetus gains 85% of its body weight during the second half of pregnancy, any impairment of uteroplacental blood flow during this period will definitely disturb food and oxygen transfer to the baby[5]. Also, in a fetus undergoing chronic hypoxia, protein/amino acid metabolism fails and the fetal weight decreases[10]. Although the length and head circumference are protected, because of the inadequate weight gain, these babies are termed asymmetric SGA, and their ponderal indexes are found lower. In 50% of asymmetric SGA babies, the intrauterine chronic hypoxia risk has increased because of their impaired uteroplacental blood flow[5].

Free oxygen radicals are known to be involved in cellular damage. They contribute to various organ injury at the stages of initiation and/or progression. Organ dysfunction induced by free radicals may be a major component of hypoxic ischemic disease of the heart, intestines, liver, kidney and brain.

Free oxygen radicals appear at mitochondrias when oxygen is not completely saturated with cytochrome oxidase enzyme during hypoxia and ischemia. Other sources are prostaglandin synthesis from arachidonic acid and xanthine and uric acid formation from hypoxanthine reactions during active phagocytosis[11]. It has been reported that free oxygen radicals are produced during the reperfusion phase following hypoxemia, and that hyperoxia increases free oxygen radical production[6]. Animal studies show that activities of antioxidant enzymes in the fetal lung and other tissues are lower than at term[12-14]. A recent study by Phylactos et al.[15] show that this is also the case for humans, at least in erythrocytes. By using a sensitive technique they demonstrated that preterm infants with gestational age between 29 and 34 weeks had only 50% activity of Cu/Zn superoxide dismutase in cord erythrocytes compared with term babies. The activity of this enzyme in erythrocytes increased toward the expected day of delivery, however, it was still lower than in term AGA babies. In newborn rabbits, short-term malnutrition caused a decrease in the enzymes (superoxide dismutase) that metabolize the free radicals in the intestine[16]. Similarly, we believe that in SGA babies with fetal malnutrition, the enzymes

inactivating free oxygen radicals might be decreased. There has been no study performed in SGA babies on this subject.

Ishimoto et al.[17] in 1997, investigated the involvement of oxygen-derived free radicals in the pathogenesis of intrauterine growth retardation (IUGR) in rats induced by ischemia of the uterine horn. The placental levels of lipid peroxidates were significantly increased and IUGR was induced. Pretreatment with superoxide dismutase and catalase inhibited the increase in placental lipid peroxidates and prevented IUGR. Results indicate that oxygen-derived free radicals may be important in the development of postischemic uteroplacental hypoperfusion and of ischemia-reperfusion induced IUGR in the rat.

We believe that in SGA babies with fetal malnutrition, the enzymes inactivating free oxygen radicals might be decreased, and that lipid peroxidates might be important for the pathogenesis of IUGR. We could find no study performed in SGA babies on this subject in the relevant literature. However, in this study we did not find a statistically significant difference in MDA levels of SGA and AGA babies at the second hour of life. Lipid peroxidates may have been decreased by free radical scavengers after birth. The role of free oxygen radicals in SGA babies has not been studied in detail. Further studies are required to determine whether oxygen-derived free radicals are involved in the pathophysiology of human IUGR.

REFERENCES

1. Crouse DT, Cassady G. The small for gestational age infant. In: Avery GB, Fletcher MA, Macdonald MG (eds). Neonatology Pathophysiology and Management of the Newborn (4th ed). Philadelphia: JB Lippincott Company; 1994: 369-398.
2. Battaglia FC, Lubchenco LO. A practical classification of newborn infants by weight and gestational age. J Pediatr 1967; 71: 159-163.
3. Tümerdem Y, Ayhan B. Yenidoğanlarda intrauterin gelişmenin değerlendirilmesinde ponderal indeks. Tıp Fak Mecmuası 1988; 51: 549-556.
4. Cole TJ, Henson GL, Tremble JM, Colley NV. Birthweight for length: ponderal index, body mass index or Benn index. Ann Hum Biol 1997; 24: 289-298.
5. Kliegmann RM. Intrauterine growth retardation: determinants of aberrant fetal growth. In: Fanaroff AA, Martin RJ (eds). Neonatal-Perinatal Medicine: Diseases of the Fetus and Infant (5th ed). St Louis: Mosby Year Book; 1992: 149-185.
6. Granger DN, Rutili G, McCord JM. Superoxide radicals in feline intestinal ischemia. Gastroenterology 1981; 81: 22-29.
7. Öztürk MA, Büyükpatır A, Doğan P, Köse K. Asfiktik yenidoğan bebeklerde ve annelerinde antioksidan aktivite. Çocuk Sağlığı ve Hastalıkları Dergisi 1996; 39: 665-675.
8. Dubowitz L, Dubowitz V, Goldberg C. Clinical assessment of gestational age in the newborn infant. J Pediatr 1970; 77: 1-10.
9. Uchiyama M, Mihara S. Determination of malonaldehyde precursor in tissues by thiobarbituric acid test. Anal Biochem 1978; 86: 271-278.
10. Attaix D, Aurousscau B, Manghebati A. Contribution of liver, skin and skeletal muscle to whole-body protein synthesis in the young lamb. Br J Nutr 1988; 60: 77-84.
11. Saugstad OD. Hypoxanthine as an indicator of hypoxia: its role in health and disease through free radical production. Pediatr Res 1988; 23: 143-150.
12. Frank L, Groseclose EE. Preparation for birth into an O_2-rich environment: the antioxidant enzymes in the developing rabbit lung. Pediatr Res 1984; 18: 240-244.
13. Hayashibe H, Asayama K, Dobashi K, Kato K. Prenatal development of antioxidant enzymes in rat lung, kidney and heart: marked increase in immunoreactive superoxide dismutase, glutathione peroxidase, and catalase in kidney. Pediatr Res 1990; 27: 472-475.
14. Saugstad OD. Mechanisms of tissue injury by oxygen radicals: implications for neonatal disease. Acta Paediatr 1996; 85: 1-4.
15. Phylactos AC, Leaf AA, Costeloe K, Crawford MA. Erythrocyte cupric/zinc superoxide dismutase exhibits reduced activity in preterm and low birth weight infants at birth. Acta Paediatr 1995; 84: 1421-1425.
16. Dobbing J. The later growth of brain and its vulnerability. Pediatrics 1974; 53: 2-6.
17. Ishimoto H, Natori M, Tanaka M, Miyazaki T, Kobayashi T, Yoshimura Y. Role of oxygen-derived free radicals in fetal growth retardation induced by ischemia-reperfusion in rats. Am J Physiol 1997; 272: H701-H705.