Original Article

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Resistin in Cord Blood of Small for Gestation Age and Appropriate for Gestation Age Term Neonates

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Abstract

Objective: Placental hormones such as resistin, adiponectin, ghrelin and leptin are known to have considerable role in fetal growth and there are some articles published in this area recently. Nevertheless there is a shortage of data showing association between resistin level and fetal growth; that was why we decided to conduct a study to evaluate this association.

Methods: This study was approved by ethic committee of pediatric health research center and research vice chancellor of Tabriz University of Medical Sciences. In this case-control study we measured the insulin, glucose and resistin in the cord blood of neonates with gestational age of 37 weeks or more in Al Zahra tertiary hospital from March 2011 to March 2012. Thirty-nine appropriate for gestation age (AGA) neonates and 41 small for gestation age (SGA) neonates were studied.

Findings: The umbilical cord blood resistin level was not found to have significant correlation with the type of delivery [normal vaginal delivery (NVD) or cesarean-section (C-S)], neonate's gender, maternal age or body mass index (BMI). There was no significant difference in the levels of Insulin and glucose between AGA and SGA groups. Resistin level of blood cord in AGA group was 613.76±180.10 (range: 132.6-983.80 ng/ml) and in SGA group it was 1303.47±537.07 (range: 800.9-3001 ng/ml) (P<0.001). Neonates' weight in AGA group was 3162.82±407.92 g and in SGA group it was 2425.85±32.84 g (P<0.001).

Conclusion: In this study resistin level had reverse correlation with fetal weight in term neonates. The SGA neonates with growth insufficiency have higher resistin levels in their cord blood than AGA neonates with same gestational age. It is recommended to conduct more studies in future with larger population of patients to clarify the resistin role in neonatal birth weight.

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Introduction

Fetal growth depends on receiving nutritional materials from mother and endogenous reserves of maternal substrates that act as precursors of fetal tissues synthesis and source of fuel for oxidative metabolism of fetus. Also fetal growth depends on optimal endocrine environment. The

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most important hormones in fetal growth are insulin and insulin like growth factor (IGF)[1-3].

Insulin doesn't cross the placenta and its origin is from the fetus itself. Insulin increases the fat and glycogen stores of the fetus and stimulates the amino acids uptake and muscular protein synthesis. IGF1 and IGF2 are present since 15th week of gestation in fetus plasma and the level of fetal IGF1 is fairly correlated with fetus weight[4,5]. Other hormones such as leptin and adiponectin affect the insulin resistance, fat resources quality and fetal growth[6,7]. One of the hormonal factors that has been shown to have a role in fetal growth is resistin. Resistin, that is discovered in 2001, is secreted from adipocytes and mononuclear cells of Human being[8,9] and is a cysteine rich protein[10]. It deranges glucose hemostasis and its actions in peripheral tissues are opposite of insulin. It is also secreted from human placenta too and is supposed to act as energy source in gestational metabolism.

During pregnancy, energy metabolism changes, maybe due to increasing demand of energy in growing fetus, and great number of extracted hormones from placenta get partially resistant to insulin, caused by an unknown mechanism[11].

On the other hand, decreased sensitivity to insulin that is more common in SGA neonates may be seen in early life[7,12]. Recent studies that demonstrated the high levels of adiponectin and resistin in cord plasma approved the role of these adipokines in intra uterus fetus development[13,14]. Resistin is found in cord blood of fetuses since the 20th week of gestation and it has positive correlation with gestational age[11]. The increasing levels of resistin with increasing of gestational age may be only indicated the greater mass of fat in the late stages of gestation that leading to producing more hormone. Resistin levels were determined in macrosomic infants and compared between term and preterm newborn infants. Nevertheless there is a shortage of data showing association between resistin level and fetal growth.

The purpose of this study is to evaluate resistin level in cord blood of neonates at birth, and to detect the relationship between the levels of resistin and neonates' birth weight.

Subjects and Methods

In a case control study, term healthy neonates with gestational age of 37 weeks or more were studied from March 2011 to March 2012. Forty neonates born at Al Zahra Hospital, a referral tertiary teaching hospital, with weight appropriate for gestational age (AGA) were randomly selected as control group according to random number list. At the same time 41 neonates who were small for gestational age (SGA) and their birth weight were less than %10 percentile for gestational age, selected randomly as case group. Cord blood sample was collected at birth. Neonates gestational age was determined by the neonatologist based on the first trimester ultrasound examination, neonatal physical examination and Ballard scoring.

The neonates with major congenital malformations and chromosomal disorders were excluded. Other exclusion criteria were: maternal diabetes, history of maternal treatment with levothyroxine or corticosteroids in recent pregnancy, documented chorioamnionitis, intrauterine infections (diagnosed by maternal seropositivity to TORCH infections and neonatal suggestive signs including microcephalia, cataract, microphthalmia and hepatosplenomegalia) and premature rupture of membranes more than 18 hours before delivery. The medical ethics committee of pediatric health center and research vice chancellor of Tabriz University of Medical Sciences approved this study (T/M 88/65). Parental written informed consent was obtained.

The measurement of resistin in cord blood was performed by Bender Med systems (Vienna, Austria) and by using primary and secondary antibodies by standard ELISA method.

Meanwhile insulin in the same cord blood was measured by using 0-1-Diaplus kite (United Status of America), by ELISA method and by using primary and secondary antibody method. The blood sugar was measured in the same line too. The analysis of data was performed by SPSS.14 software. The chi square test was used for qualitative variables and Student T test for quantitative variables and p value less than 0.05 was considered as significant.

Finding

Eighty newborn infants were enrolled in this study: 39 neonates in AGA group and 41 neonates in SGA group. The route of delivery was cesarean section in 20 neonates (51.3%) of AGA neonates and 20 (48.8%) of SGA neonates (p=0.82). Twenty cases (51.3%) in AGA group and 22 patients (55%) in SGA group (p=0.66) were female. The mean gestation age was not different among patients in two groups (37.3±1.8 in AGA group and 37.5±1.4 weeks in SGA group). The mean maternal age was 26.86±6.92 years in AGA group and 26.48±6.52 years in SGA group (p=0.8). The mean body mass index (BMI) of mothers in AGA group was 28.2±3.08 and in SGA group 28.33±4.83 (p=0.79). The mean blood sugar in AGA was 76.25±24.32 mg/dl and 72.73±23.4 mg/dl in SGA group. The mean body weight of neonates in AGA group was 3162.82±407.93 gr and 2425.85±338.4 gr in SGA group (p<0.001). The mean cord blood parameters are shown in table 1. The most common predisposing factor for SGA in studied patients was maternal preeclampsia [9 patients (21.9%)]. The mean cord blood resistin level in neonates delivered by cesarean section was 1002.44±555.24 ng/ml and in infants delivered vaginally was 932.03±510.3 ng/ml (p=0.55). The mean cord blood resistin level was 1018.96±621.36 ng/ml in male neonates and 922.73±441.72 ng/ml in females (p=0.45).

Discussion

According to results of this study, the amount of resistin in SGA neonates was significantly higher than AGA neonates, which may explain the role of resistin in birth weight control of neonates.

There are small numbers of studies explaining this correlation; in one study Wang et al have compared the amount of resistin and adiponectin of cord blood with neonatal birth weight and the weight of the placenta. They have studied the correlation between adiponectin and resistin levels in cord blood and maternal serum in macrosomic neonates. Their results indicated that the level of adiponectin and resistin in the serum of mothers of macrosomic neonates were less than mothers of appropriate weight neonates[15]. In normal pregnancies the amount of these two markers was considerably higher in macrsomic neonates but it was less than IUGR neonates. The cord adiponectin level has diversely correlated with neonatal birth weight, maternal BMI and placental weight but there was no correlation with maternal serum adiponectin.

The cord blood level of resistin have positively correlated with maternal serum resistin and negatively correlated with neonatal birth weight, BMI and placental weight. More even maternal serum resistin level has diversely correlated with neonatal birth weight.

These researchers concluded that resistin and adiponectin have important role in weight control and maybe in incidence of macrosomia[9]. In another study the resistin level was determined in term AGA neonates at birth time and it demonstrated high levels without change in the first 4 days of life[16].

In one study by Pak-Cheng et al in Hong Kong, resistin level was measured in preterm neonates and the results were compared with anthropometric indices and leptin and insulin levels. The results of their study demonstrated that the levels of resistin in term neonates were more than preterm ones and was correlated with leptin levels .The both levels of resistin and leptin have increased along with duration of pregnancy and were also correlated with anthropometric indices[17].

According to Cortelazzi study the level of resistin in fetus aged 28-41 weeks was more than adults but there was not any difference between

Table 1: The values of resistin and insulin in cord blood

Variable	AGA group (n=39)	SGA group (n=41)	P value
Resistin, ng/ml	613.76(180.1) (Range:132.6-983.8)	1303(537.07) (Range:800.9-3001)	<0.001
Insulin, µU/ml	5.93(1.05) (Range:1.1-29.7)	4.7(0.6) (Range:0.6-19.8)	0.98

diabetic and non-diabetic mother's fetuses[11]. The higher level of resistin in normal deliveries may be indicated that these hormones are increased due to stress or inflammation accompanied with normal delivery stages[18]. The high level of resistin was also correlated with high blood sugar.

This study in serum resistin level didn't indicate significant difference between NVD and C-S delivered infants. It may be because of gestational age of studied neonates when all neonates were term. We also didn't find any meaningful correlation between blood sugar and leptin levels in these two groups of neonates.

In the present study we achieved the same results about diverse correlation of resistin with neonatal birth weight. According to the results of study conducted by S.C. Cho and coworkers from Korea, high levels of resistin besides its effect on energy homeostasis in fetus, may have an important role in weight control by its effects regulating adipogenesis with negative feedback. The result of their study revealed that cord blood resistin level has positive correlation with maternal serum resistin and negative correlation with neonate's birth weight. Another study from Korea by Cho GJ et al about correlation between cord blood and maternal serum resistin level has the same results as the above study and there was negative correlation between resistin level with neonates' weight and positive correlation with maternal serum levels of resistin[19]. They did not find any correlation between resistin and insulin levels; so did we. In another study in China by Ng PC and et al[14] comparing resistin level in preterm and term neonates and also comparing it to leptin, insulin and anthropometric indices, they found that resistin has higher levels in terms than pre-terms and it is correlated with cord's leptin level and two hormones are correlated with gestational age and anthropometric indices. In the same study resistin level in vaginal delivery was higher than cesarean section delivered ones. The correlation between resistin and leptin and anthropometric indices demonstrated that these two hormones are gestational age related. The high levels of resistin in term neonates inhibited hypoglycemia at birth. These studies indicated that placental hormones (such as adiponectin, leptin, ghrelin and resistin) control adipogenesis and have important role in regulation of fetal metabolism of energy, adipogenesis and control of fetal growth. Our study demonstrated the role of resistin in the reduction of fetal growth in comparison of two groups AGA and SGA neonates and revealed that SGA neonates had significantly higher resistin levels than AGA group.

Another study showed that resistin level in preterm neonates with premature rupture of membranes (PROM) was significantly higher than babies without PROM that may be as a result of the effects of fetal inflammation on resistin levels[20]. We did not find distinct correlation between resistin and the method of delivery and also with cord's blood sugar. One of the limitations in this study was lack of data in preterm neonates and subsequent resistin measurement in neonatal period. The future study needed with greater samples for clarifying the existing problems.

Conclusion

The results of this study indicated that resistin level has diverse correlation with fetal weight gaining and also with comparable duration of pregnancy. The SGA neonates with insufficient growth has higher resistin in their cord blood than AGA ones.

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Conflict of Interest: None

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