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Full Length Research Paper

The influence of mode of delivery on the levels of high-sensitivity C - reactive protein determined in umbilical cord blood

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Data suggest that the fetus responds to chronic hypoxia by higher umbilical cord blood high-sensitive CRP concentrations. In order to evaluate the effects of acute hypoxia on fetus, cord blood high-sensitive CRP concentrations according to the delivery mode were compared. High-sensitive CRP concentration was measured by an immunonephelometric method in umbilical cord blood samples from 45 newborns born by different delivery modes (15 newborns by vaginal delivery, 15 newborns by elective cesarean section and 15 newborns by emergency section delivery due to acute hypoxia). No significant differences in high -sensitive CRP concentrations were documented between the three groups of newborns. However, a moderate negative correlation was determined between cord blood pH, pO_2, and hs-CRP concentrations ($p<0.05$). In conclusion, the mode of delivery reflecting acute hypoxia did not influence cord blood high-sensitive CRP levels in newborns.

Key words: Inflammation, CRP, mode of delivery.

INTRODUCTION

C-reactive protein (CRP), a plasma acute- phase protein synthesized by hepatocytes, is present in the serum of healthy subjects in trace amounts. In response to some cytokines, CRP levels in blood rise up to 1000-fold during injuries, trauma, infection, burns, neoplasia and inflam-matory conditions (Ledu and Rifat, 2003; Sellmayer et al., 2003). CRP is a useful assay in the initial evaluation of early or late- onset bacterial infectious diseases in new-borns, and in monitoring its response to therapy (Labora-da et al., 2003; Yoon et al., 2003).

Recent data suggest that the fetus responds to chronic hypoxia by an inflammatory reaction. It is shown that small for gestational age (SGA) newborns have higher hs-CRP concentrations than appropriate-for-gestational age (AGA) neonates suggesting the presence of an in-flammatory process in SGA infants during the fetal life due to chronic hypoxia (Trevisanuto et al., 2007). In addi-tion, it is well-known that maternal diabetes increases the risk of intrauterine hypoxia, and in these pregnancies a negative correlation existed between cord serum CRP and umbilical artery pH and pO_2 (Loukovaara et al., 2004).

Could acute hypoxia, which develops a short time be-fore birth due to acute fetal distress affect the cord blood hs-CRP concentrations? Hence, the purpose of this study was to measure concentration of hs-CRP in umbilical cord blood serum depending on the delivery mode: spon-taneous vaginal birth or by cesarean delivery. This study was also conducted in order to compare the hs-CRP con-centrations in umbilical cord blood serum obtained during elective cesarean deliveries and emergency cesarean deliveries and to determine if there were any changes due to acute fetal distress.

Abbreviations: Hs-CRP, High sensitive; C-reactive protein; **SGA,** small for gestational age and **AGA,** appropriate-for-gestational age.

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Table 1. Characteristics of the neonates and their mothers depending on different types of deliveries.

	Vaginal Delivery Mean (SD)	Elective Cesarean section Mean (SD)	EmergencyCesarean section Mean (SD)	p
Mothers'				
Age (years)	24.60 (5.51)	28.27 (4.45)	27.93 (5.83)	0.021
Education (years)	5.3 (2.82)	6.13 (3.56)	5.60 (3.74)	0.941
Height (m)	1.58 (0.05)	1.61 (0.04)	1.57 (0.04)	0.183
Weight gain duringpregnancy (kg)	12.85(5.24)	13.77(3.06)	13.60 (4.97)	0.762
Blood pressure (mmHg)				
Systolic	118.00 (13.20)	108.67 (6.40)	127.00 (33.02)	0.004
Diastolic	74.67(8.34)	73.33 (4.88)	78.00 (14.76)	0.117
Newborns				
Gestational age (wk)	40.13(0.35)	38.80(1.26)	39.60 (1.45)	0.006
Birth weight (g)	3227.3(263.7)	3177.3(352.1)	3187.3 (624.6)	0.597
Birth length (cm)	49.00(1.25)	48.73(1.98)	48.50 (2.72)	0.134
Head circum (cm)	34.47(1.13)	34.47(1.20)	34.67 (1.96)	0.229
Mid arm circum (cm)	10.43(0.75)	10.10(0.54)	10.07 (0.94)	0.440
Ponderal index	2.74 (0.22)	2.74 (0.18)	2.76 (0.25)	0.586
1' Apgar	6.27 (0.88)	6.87 (0.92)	6.00 (1.65)	0.072
5' Apgar	8.93 (0.26)	8.93 (0.26)	8.60 (0.51)	0.056

P > 0.05 not statistically significant.

MATERIALS AND METHODS

In this study plasma concentrations of hs-CRP and blood gases were determined in umbilical cord blood sample from 45 term AGA newborns born at Sadi Konuk Bakirköy Teaching and Research Hospital, Istanbul, Turkey between January 2007 and May 2007. The newborns were divided into three groups. The first group comprised 15 newborns, who were born by a vaginal delivery; the second group consisted of 15 newborns who were delivered by elective cesarean section; the third group consisted of 15 newborns that developed some fetal distress during labor and have under-gone emergency cesarean section delivery (Figueroa et al., 2005). Signs and symptoms of fetal distress were accepted as decreased movement felt by the mother, signs which include increased or decreased fetal, especially during and after a decreased variability in the fetal.

Elective caesarean delivery indications included prior caesarean section, placenta previa. Those newborns with a history of suspected or proven feto-maternal infection, and those with major anomalies were not included in the study. All newborns had been delivered at term, with rupture of membranes less than 6 h prior to delivery and have clear amniotic fluid. Also, maternal chronic inflammatory conditions were excluded.

Age, educational level, weight, height, and blood pressure of mothers were obtained. The mode of delivery, gestational age, birth weight, height and head circumference, 1' and 5' Apgar score was recorded for the newborns.

Both arterial and venous cord blood samples were obtained from neonates immediately after birth. Arterial cord blood gases were analyzed by "Bayer-Health Care Raid'' analyzer. For hs-CRP determination, venous blood samples were centrifuged; the samples were divided into serum aliquots and stored at –20 °C until the analysis was performed. Serum hs-CRP concentrations were measured in 3 ml specimens using nepholemetric method (Dade Behring) applied by PROSPEC which employs polystrene particles coated to monoclonal antibodies specific to human CRP. The exact measuring range depends upon the concentration of protein in each standard lot. Serum samples were matched against the same calibration curve ranged from 0,0060-5,0 mg /dl. The detection limit was 0, 02 mg/dl. Samples with concentrations higher than the calibration range were diluted automatically by the instrument. Two quality control samples were included in each assay series and the specimens were assayed in duplicates.

All the laboratory examinations were performed in Istanbul University Cardiology Institute Biochemistry Laboratory. The study was approved by the Local Hospital Ethics Committee, and written informed consent was obtained from the parents of newborns.

Statistical analysis was performed using the SPSS for Windows 10.0 statistical program. Clinical and anthropometric parameters of the study population were expressed by using mean and standard deviation (SD). The parameters among the groups were compared by ANOVA test. The differences between mean values of study and control groups were analyzed using chi-square test, Mann- Whitney-U test and Kruskal Wallis Test. A value of P<.05 was considered as significant. Pearson correlation analysis was used to determine the relationships between variables.

RESULTS

Data on the characteristics of mothers and newborns and the anthropometric measures of newborns are shown in Table 1. There were no statistical differences in maternal height, maternal weight gain during pregnancy among the three groups. Mothers who delivered by emergency cesarean section have higher systolic blood pressure than other delivery groups. Furthermore, there were no statistically significant differences among the groups in birth weight, birth height, head circumference, Apgar score, mid arm circumference and Ponderal index according to mode of delivery.

Data on venous cord blood serum and arterial blood

Table 2. Umbilical cord blood serum hs-CRP concentrations and blood gases analysis according to the type of delivery.

	Vaginal Delivery Mean(SD)	Elective Cesarean section Mean (SD)	Emergency Cesarean section Mean (SD)	p
hs-CRP (mg/dl)	0.026(0.041)	0.014(0.001)	0.015(0.001)	0.051
pH	7.31 (0.14)	7.34 (0.05)	7.34 (0.09)	0.981
pO_2 (mmHg)	22.30 (5.55)	28.04 (12.20)	34.47 (17.35)	0.064
pCO_2(mmHg)	47.38 (18.22)	47.82 (9.98)	40.69 (10.43)	0.223
HCO_3 (mmol/l)	20.04 (2.99)	24.82 (3.04)	20.78 (3.50)	0.001
BE (mmol/l)	-3.71 (3.15)	-0.71 (2.53)	-4.39 (3.55)	0.003
HgB (g/dl)	16.03 (1.18)	15.08 (1.40)	15.26 (1.09)	0.094

P > 0.05 not statistically significant.

Table 3. The correlation between the newborns characteristics and cord blood serum hs-CRP concentrations.

hs - CRP	Vaginal Delivery		Elective Cesarean section		Emergency Cesarean section	
	r	p	r	p	r	p
Gestational age (wk)	-0.102	0.728	0.242	0.385	-0.250	0.434
Birth weight (g)	0.042	0.887	-0.371	0.174	0.564	0.056
Birth length (cm)	-0.006	0.984	-0.309	0.263	0.251	0.432
Birth head circumference (cm)	0.128	0.663	-0.099	0.726	0.371	0.235
Mid arm circum (cm)	0.391	0.167	-0.008	0.978	0.368	0.239
Ponderal index	0.048	0.872	-0.030	0.917	0.740	0.006
1' Apgar	0.242	0.405	-0.241	0.386	0.047	0.886
5' Apgar	0.076	0.795	0.066	0.816	0.306	0.333

P > 0.05 not statistically significant.

gases according to the type of delivery are given in Table 2. As the table indicates. the hs-CRP serum concentrations were statistically similar among the groups (p=0.51) (Table 2). Also. in the cord blood gases analysis of pH and pCO_2 did not differ statistically significantly between groups. The variables of cord blood HCO_3 and BE were found to be statistically significantly higher in the group born by elective cesarean section delivery than those of vaginal (p=.001) and emergency section delivery (p= .003) (Table 2).

The correlation between the newborn anthropometric characteristics and cord blood serum hs-CRP concentrations are shown in Table 3. Moderately positive correlation was found between Ponderal index and hs-CRP values only in emergency cesarean section delivery group newborns (r=0.74; p<0.01).

The correlation between the cord blood serum hs-CRP concentrations and blood gases analyses are shown in Table 4. In elective cesarean section delivery group. a moderate negative correlation was determined between pH and hs-CRP cord blood concentrations (r=-0.54. p<0.05). On the other hand. in the emergency cesarean delivery group. a moderate negative correlation was determined between cord blood pO_2 and hs-CRP concentrations (r = -0.62. p<0.05).

DISCUSSION

CRP has long been used as a sensitive marker for infectious diseases. C-reactive protein is the best –known member of the acute phase protein group. Indications for a quantitave analysis of serum CRP include rheumatic and other inflammatory disorders and cellular necroses. An elevated CRP level indicates acute inflammation after acute event 4 to 8 h. Elevated level of the acute phase reactant C-reactive protein (CRP) is a very sensitive marker of acute inflammatory reactions.

Hs-CRP yields a more sensitive measure even at very low concentrations. Serum levels of hsCRP in umbilical cord blood are close to the detection limit and lower than in the other age groups investigated. This study compares hs- CRP concentrations in umbilical cord serum according to different types of deliveries (vaginal delivery ;elective and emergency cesarean section). It was found that the types of delivery. vaginal or cesarean section did not affect the response of hs-CRP. Also. it was found that the hs-CRP concentrations in cord blood were not affected in acute fetal distress in emergency cesarean section deliveries. However. a moderate negative correlation was determined between pH. pO_2 and hs-CRP cord blood concentrations.

Table 4. Correlation between cord blood serum hs-CRP and blood gases analysis according to the type of delivery.

	Vaginal Delivery		Elective Cesarean section		Emergency Cesarean section	
	r	p	r	p	r	p
pH	0.158	0.588	-0.537	0.039*	-0.558	0.059
pO_2 (mmHg)	0.040	0.892	0.012	0.965	-0.616	0.033*
pCO_2(mmHg)	-0.069	0.814	0.510	0.052	0.527	0.078
HCO_3(mmol/l)	0.315	0.273	0.299	0.278	0.103	0.750
BE (mmol/l)	0.297	0.302	0.212	0.448	-0.143	0.657
Hgb (g/dl)	-0.618	0.018*	0.388	0.153	0.593	0.042*

P > 0.05 not statistically significant.

The effects of chronic hypoxia on acute phase response have been studied in SGA newborns cord blood by several investigators (Trevisanuto et al., 2007). They demonstrated that in SGA infants. hs-CRP concentrations are higher than in AGA neonates suggesting the pre--sence of an inflammatory process in this group of patients during fetal life. Also. maternal diabetes increases the risk of chronic intrauterine hypoxia. Data suggest that negative correlation existed between cord serum CRP and umbilical artery pH and pO_2 in these pregnancies (Loukovaara et al.. 2004).

To our knowledge. influence of different delivery modes and acute fetal distress on hs-CRP levels has not been studied in newborns. Our data on a small group of newborns suggest that the fetus does not respond to acute fetal distress by elevation of cord blood hs-CRP concentrations or may be there is not enough time for hs-CRP values being affected by acute hypoxia during which acute fetal distress develops a short time before birth.

However. our findings revealed that a moderate negative correlation was determined between pH and hs-CRP cord blood concentrations in elective cesarean section group. and also a moderate negative correlation was found between cord blood pO_2 and hs-CRP concentrations in emergency cesaren group. This might support the theory that. if the fetus was not delivered by emergency cesarean section and acute hypoxia persists for longer time. fetus would respond with an inflammatory reaction. such as in chronic hypoxia.

In our study. none of the mothers have had infection or inflammatory status that affected the hs- CRP values due to our exclusion criteria. Therefore. our data reflect the normal values of hs- CRP in umbilical cord blood in AGA term newborns. Our results are similar with cord blood hs- CRP concentration in AGA neonates (Trevisanuto et al.. 2007; Lannergard et al.. 2005).

In conclusion. acute hypoxia determined by the route of delivery does not result in an acute inflammatory condition reflected by hs-CRP levels. Our findings show that the kinetics of the acute-phase proteins hs-CRP cannot be correlated with acute fetal distress regardless of the type of delivery. While no significant difference was observed between the different modes of delivery groups. our data were limited to a small number of samples. Further sampling is required to reach a more concrete conclusion.

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