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Comparison of interleukin-10 and interleukin-13 in cord blood of infants born by vaginal delivery and caesarean

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Background: Modification of the immunological balance based on the mode of delivery has been recently suggested. The present study assessed the levels of IL-13 and IL-10 in umbilical cord blood of infants born through normal vaginal delivery and infants born with cesarean section.
Methods: This pilot study was performed on 42 neonates born at Rasool-e-Akram hospital between May 2013 and May 2014 categorized into two groups born by vaginal delivery (n = 21) and those who born by cesarean section (n = 21). The cord blood levels of IL-13 and IL-10 were measured by ELISA technique.
Results: No difference was observed between the two groups with normal vaginal delivery and cesarean delivery in the level of IL-13 in umbilical cord blood (1.42 ± 0.23 versus 1.40 ± 0.22, respectively, p = 0.785). The mean level of IL-10 in umbilical cord blood in the group with vaginal delivery was 6.35 ± 2.54 and in another group with cesarean section was 5.69 ± 2.42 with no significant difference (p = 0.393). According to the multivariate linear regression analyses, no difference was found between the two groups of the mode of delivery in the level of IL-10 (beta = -0.454, SE = 0.802, p = 0.575) and also in the level of IL-13 (beta = 0.012, SE = 0.076, p = 0.877). None of the indicators including gestational age, mother's age, sex of neonate, number of live births, history of abortion, and number of parity could predict increased level of the interleukins in umbilical cord blood.
Conclusion: Mode of delivery may not be an indicator for altering cord blood levels of IL-13 and IL-10.

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Comparison of interleukin-10 and interleukin-13 in cord blood of infants born by vaginal delivery and caesarean

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ABSTRACT

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Conclusion: Mode of delivery may not be an indicator for altering cord blood levels of IL-13 and IL-10.

Keyword: Delivery; Interleukin-10, Interleukin-13; Cord blood.

Introduction

In recent decades, the rate of cesarean section is increasing in most parts of the world [1] and Iran is no exception of this upward trend [2]. The number of live births by caesarean section in developed countries and in developing countries is rising [3]. In contrast, the results from different studies show that the risk of maternal death during cesarean delivery is 3 times higher than that of the vaginal delivery [4]. In addition, cesarean delivery method can be a dangerous procedure not only for the mother but also for the neonates even for many years after birth [5]. Recently, it has been found the incidence of asthma and atopy in childhood may be increased by cesarean section delivery [5]. Asthma and atopy are associated directly with the child's immune system. The role of immunoglobulin, such as immunoglobulin E and some other cytokines such as interferon-gamma (INFγ) in the etiology of asthma has been established [6]. The main pathophysiological basis of allergic asthma is producing some cytokines secreted by T helper cells [7]. A large number of cytokines have been identified as triggers of allergic asthma [8-10] that among them the critical role of interleukins 13 and 4 secreted by T helper cells II is more taken into consideration [5]. Interleukin-13 appears to have the ability to induce and begin all processes of allergic asthma and plays its role independent of immunoglobulin E and eosinophil [5]. Besides, interleukin-10 (IL-10) belongs to the group of type 2 cytokines that its effect is mainly based on activation of the T helper cells type I and II. These cells are the main cells in cellular immunity that particularly regulate IgE production in asthma condition. It seems that IL-10 is a main suppressor of the production of other inflammatory cytokines [4].

Recent studies have shown different levels of serum immunoglobulin in both asthmatic and atopy children compared to non-affected ones [3]. Recent evidences have also suggested that cytokines play an important role in delivery process and thus affects the immune system of the

newborn [4]. In addition, the effect of mode of delivery on production of cytokines has been also revealed [7]. Due to the increasing trend of cesarean section in our country and also the relationship between the incidence of asthma and atopy and the mode of delivery, we aimed to assess the level of IL-13 and IL-10 in umbilical cord blood of infants born through normal vaginal delivery and infants born with cesarean section.

Methods

This pilot study was performed on 42 neonates born at Rasool-e-Akram hospital between May 2013 and May 2014. After explaining a detailed description of the study to parents or legal guardians of infants, the written consent was taken from them. The neonates were categorized as the two groups including neonates born by vaginal delivery (n = 21) and those who born by cesarean section (n = 21). We included term and near term pregnancies that were terminated with a normal vaginal delivery or planned cesarean section. The exclusion criteria were the presence of any abnormal symptoms during the first examination of children, preterm delivery, parental immunodeficiency diseases, starting of active phase of labor in cesarean group, chorioamnionitis or any maternal infections and maternal history of asthma and atopy. After coordinating with the laboratory of the hospital, 10cc of umbilical cord blood was extracted from immediately after the completion of the third stage of labor. After centrifugation, the serum was stored in a refrigerator at -20 ° C. Finally, the samples were transferred to the laboratory and the cord blood levels of IL-13 and IL-10 were measured by ELISA kits. Baseline information including gender, family history of asthma or atopy, mode of delivery, number of parity or gravidity, history of still birth

or abortion, mother's age, and history of any maternal disorders within pregnancy were asked and recorded in study checklists.

Data were analyzed using IBM SPSS statistical software version 21.0 (Armonk, NY: IBM Corp.). Quantitative variables were presented as mean ± standard deviation, and categorical variables were presented by absolute frequencies and percentages. Continuous variables were compared using t test. Whenever the data did not appear to have normal distribution, Mann-Whitney U test was used. Categorical variables were compared using chi-square test. Fisher exact test was used when more than 20% of cells with expected count of less than 5 had been observed. The multivariate logistic regression model was employed to determine difference in the level of interleukin between the groups with the presence of confounders. P values of ≤ 0.05 were considered statistically significant.

Results

Baseline characteristics and clinical data are shown in table 1. The two groups with vaginal delivery and cesarean section were similar in mean gestation age, age of mother, sex of neonate, number of live births, history of abortion, number of parity, and also number of gravidity. None of the groups had previous history of asthma or atopy. The mean level of IL-10 in umbilical cord blood in the group with vaginal delivery was 6.35 ± 2.54 and in another group with cesarean section was 5.69 ± 2.42 with no significant difference (p = 0.393). Also, no difference was observed between the two groups with normal vaginal delivery and cesarean delivery in the level of IL-13 in umbilical cord blood (1.42 ± 0.23 versus 1.40 ± 0.22, respectively, p = 0.785). In the group with vaginal delivery, no significant correlation was found between the level of IL-10 and IL-13 (r = -0.252, p = 0.271). Similarly, in another group with cesarean section, the level of IL10 was not correlated with IL-13 (r = -0.123, p = 0.595). Regarding association between the level of

interleukins in umbilical cord blood and sex of neonate, it was shown no difference between male and female neonates in the levels of IL-10 (6.45 ± 3.45 versus 5.84 ± 2.01, p = 0.577) and IL-13 (1.34 ± 0.26 versus 1.44 ± 0.20, p= 0.238). Also, gestational age was not correlated with the levels of IL-10 (r = 0.241, p = 0.124) and also the level of IL-13 (r = -0.149, p = 0.349). According to the multivariate linear regression analyses (Tables 2 and 3), no difference was found between the two groups of the mode of delivery in the level of IL-10 (beta = -0.454, SE = 0.802, p = 0.575) and also in the level of IL-13 (beta = 0.012, SE = 0.076, p = 0.877). In this regard, none of the indicators including gestational age, mother's age, sex of neonate, number of live births, history of abortion, and number of parity could predict increased level of the interleukins in umbilical cord blood.

Discussion

According to our analysis, the level of IL-10 and IL-13 is not influenced by the mode of delivery. The effects of the method of delivery on the cord blood level of these cytokines led to contradictory results in previous observations. Similar to our finding, Tutdibi showed that the concentration of IL-10 receptor antagonist was not different between elective cesarean section and vaginal delivery [9]. In another study by Blanco-Quirós *et al.* [10], the type of delivery (vaginal versus caesarean) did not influence cord blood IL-10 results. According to the observations by Bakheit *et al*. [8], concentration of IL-10 in the peripheral and placental sera was higher in vaginal delivery, while cord IL-10 was not significantly different in the two groups. Regarding association between mode of delivery and cord blood level of IL-13, Ly *et al.* [11] showed that cesarean section was associated with increased levels of IL-13. Also, in multivariate

analyses, cesarean section was associated with an increment of 79.4 pg/ml in secretion of IL-13. The paradoxical findings in the studies could be affected by various confounding factors. First, the presence of the history of asthma or allergic disorders in the mother could potentially affect the present increased levels of IL-10 and IL-13 in cord blood. On the other hand, lack of significant changes in the levels of these cytokines in our study might be affected by the absence of this history in our studied mothers. Second, it has been well shown that the frequency of cesarean section is frequently higher in preterm neonates who are more susceptible to various allergic and atopic disorders leading increased level of interleukins. In fact, because at present it suggests that cesarean is performed due to individual wishes not clinical judgment, cesarean section is not specified to preterm situation.

A few studies have focused an association between cesarean section and increased neonatal secretion of IL-13 and also IL-10. In this regard, our findings can provide a potential immunologic basis for previous reports of an association between cesarean section and clinical conditions related to increase in cytokines such as atopy or asthma [12-19]. The observed association between mode of delivery and neonatal immune responses may be explained by absent or reduced labor in children delivered by cesarean section [5, 20]. The process of labor may directly influence neonatal immune responses, thereby influencing cytokine secretion at birth. Although a relationship between labor and neonatal secretion of IL-13 and IL-10 has not been shown, the stress of labor has been associated with decrease of some immunological cell types such as T lymphocytes and CD4+ T helper cells [21], and also increased some other cells such as neutrophils [22, 23], and natural killer (NK) cells [24, 25] in cord blood. This evidence can also explain some observed relationships between cesarean section and increased susceptible to increase in cytokines and other immunological factors in cord blood. Mohammad Nabavi et al,

were found a significantly higher level of IgE in cord blood of neonates delivered via cesarean section [26, 27]. However, immunological status may differ at older age not due a difference in these cytokines, but due to some other factors such as IgE at birth.

Conflicts of interest

None declared.

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Ethical issues

The use of experimental on the human was approved by the committee of the Iran University of Medical Sciences. This study was also entirely adhered to the declaration of the Helsinki in 2008.

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Table 1: Baseline characteristics between the two groups with vaginal delivery and cesarean.

Variable	Vaginal delivery	Cesarean section	P-value
Gestational age	38.52 ± 0.98	38.43 ± 0.60	0.706
Mother's age	30.76 ± 4.99	31.81 ± 4.65	0.486
Male gender	6 (28.6)	6 (28.6)	1.000
Number of live birth			0.100
1	13 (61.9)	7 (33.3)	
2	8 (38.1)	12 (57.1)	
3	0 (0.0)	2 (9.5)	
History of abortion	2 (9.5)	3 (14.3)	0.999
Number of parity			0.268
1	12 (57.1)	7 (33.3)	
2	7 (33.3)	12 (57.1)	
3	2 (9.5)	2 (9.5)	
Number of gravidity			0.624
1	9 (42.9)	6 (28.6)	
2	9 (42.9)	11 (52.4)	
3	3 (14.3)	4 (19.0)	

Table 2: Multivariate linear regression model to assess difference in IL-10 level between the groups with vaginal delivery and cesarean section.

Variable	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Mode of delivery	-0.454	0.802	-0.093	-0.566	0.575
Gestation age	0.379	0.557	0.123	0.680	0.501
Mother's age	-0.108	0.082	-0.209	-1.309	0.199
Sex of neonate	-0.403	0.835	-0.074	-0.482	0.633
Live births	0.094	1.075	0.022	0.087	0.931
Abortion	1.586	1.176	0.210	1.348	0.186
Parity	-0.716	0.990	-0.190	-0.723	0.474

Table 3: Multivariate linear regression model to assess difference in IL-13 level between the groups with vaginal delivery and cesarean section.

Variable	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Mode of delivery	0.012	0.0760	.027	0.155	0.877
Gestation age	-0.013	0.053	-0.048	-0.250	0.804
Mother's age	0.001	0.008	-0.017	-0.099	0.922
Sex of neonate	0.091	0.079	0.186	1.141	0.262
Live births	-0.137	0.102	-0.365	-1.346	0.187
Abortion	0.008	0.112	0.011	0.068	0.946
Parity	0.087	0.094	0.256	0.923	0.362