The effect of cigarette smoking on IgE levels and circulating lymphocytes in cord blood

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Abstract

Mechanisms of smoking-induced morbidity and mortality include a lower birth weight, preterm delivery, and abruptio placentae. This study showed the effects of nicotine on cellular proliferation and elevated level of the immunoglobulin E in newborns. This analysis of cord blood markers was part of a larger study of maternal inflammatory response to smoking during pregnancy. Newborns of smokers and exposure to smoking mothers elevated level of the IgE. The proportion of CD4+ T cells in smokers compared to non-smokers mothers (p=0.02). There was no significant difference in the percent of CD8+ cells between smokers and all other subjects during pregnancy at the time-points analysed.

Key words: *pregnant women, cord blood, newborns, immunoglobulin E, lymphocytes T.*

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Introduction

Maternal tobacco use during pregnancy adversely affects prenatal and postnatal growth and increases the risk of immunity deficits in children. Nicotine easily crosses the placenta and is found in fetal blood at a maternal-fetal blood concentration ratio of 0.9 [1]. In adult cigarette smokers, the mean half-life of nicotine is 2.6 hours (95% CI, 1,7 to 3.5 hours) [2]. Nicotine and its metabolite cotinine have an influence on many different parameters of mother-fetus system in the child intrauterine development. Immune system of placenta is insufficient to stop many components of cigarette smoke [3]. Changes called out by these elements lead to premature delivery or lower birth weight. Newborns with hypotrophy often have oxygen deficiency in tissues, hypoglycemia, hyperbilirubineamia and changes in pulmonary system [4]. In cord blood there is a higher level of immunoglobulin E and proportions of lymphocytes CD4+ and CD8+ are changing [5]. More powerful allergens act on fetus immune system cells, escalating production of immunoglobulin E. These observations suggest that alterations in maternal immunological parameters can be associated with the mechanisms mediating preterm labour [6].

Materials and Methods

The questionnaires were filled by examined 79 women recruited from the Obstetries Department of the Mother and Child Institute in Warsaw. Closed questions were used, concerning women's smoking habits. At follow-up visits, women filled in a questionnaire, the infants were clinically examined. Among questioned women 27 were exposed to cigarette smoke, active or passive. During the labors there were 76 cord blood samples taken to the laboratory investigation. Determination of 79 newborns umbilical cord cellular response was measured by immunofluorescence cytometric methods. To test the subpopulation of CD4 and CD8 lymphocyte standard techniques of immunofluorescence were used. Blood was incubated at room temperature with specially prepared, diluted monoclonal antibody (Caltag Laboratories). Samples were read in FACScan flow cytometry with argon laser 488 nm (Becton Dickinson). Results were given as positive cell percent in investigated samples. Total IgE in cord sera was estimated by enzyme linked immunosorbent assay ELISA in cord blood samples the concentration of immunoglobulin E was determined with ELISA method by the ready to use ELISA kit – Alexon – Trend Ramsey (USA) according to the producer procedure.

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For the purpose of the investigation the agreement of Bioethical Commission of Mother and Child Institute in Warsaw was obtained.

Results

At the first stage of investigation the relation between the length of pregnancy and course of delivery at groups of women exposed and non - exposed to cigarette smoke during pregnancy was analysed (Table 1). Preterm delivery takes place more often in smoking women than non-smoking groups.

Concentration of IgE in cord blood of newborn babies exposed to cigarette smoke during prenatal life was fluctuated in a wide range and it was about three times higher than the IgE in cord blood of newborn babies without any earlier exposition to nicotine (Table 2).

The amount of active lymphocytes T in newborns cord blood exposed to cigarette smoke during prenatal life was much lower in comparison with lymphocytes isolated from cord blood of newborn babies without such environmental factor threat. Results of one percentage of lymphocyte subpopulation CD4+ and CD8+ are shown in Table 3.

Discussion

The results of our study are in agreement with previous epidemiological studies that reported that active smoking is associated with preterm delivery [7]. The present study was made to elucidate the relation of smoking to causes of very

Table 1. Length of pregnancy and course of delivery at investigated groups

Investigated group	Type of delivery				
	Preterm		At term		p
	Spontaneous delivery (%)	Surgical delivery (%)	Spontaneous delivery (%)	Surgical delivery (%)	
Mothers exposed to cigarette smoke (active smokers) during pregnancy (n=8)	12.5	20	62.5	7.5	0.9
Mothers exposed occassionally to cigarette smoke (passive smokers during pregnancy (n=19)	10.55	10.55	52.63	26.27	0.9
Mothers who have never been exposed to cigarette smoke during pregnancy n=52	3.84	5.77	86.53	3.86	0.6

Table 2. Concentration of IgE in newborns cord blood

Investigated group	IgE [IU/ml]				
	Minimum value	Maximum value	Arithmetical mean	Median	Standard deviation
Cord blood of newborns exposed to cigarette smoke n=27	0.10	2.30	0.69*	0.64	0.48
Cord blood of newborns not exposed to cigarette smoke n=52	0.05	0.41	0.23*	0.18	0.19

**p=0.03*

Table 3. CD4/CD8 lymphocyte index in newborns cord blood

Investigated group	Index CD4/CD8				
	Minimum value	Maximum value	Arithmetical mean	Median	Standard deviation
Newborns born by mothers exposed to cigarette smoke (active smokers) (n=8)	0.95	2.1	1.3*	1.2	0.6
Newborns born by mothers exposed periodically to cigarette smoke (passive smokers) (n=19)	1.29	2.5	2.0*	2.1	0.3
Newborns born by mothers who have never been exposed to cigarette smoke (n=52)	1.15	2.7	1.9	2.0	0.4

**p=0.02*

preterm birth. The data get from the questionnaires showed that percentage of premature delivery was higher in women who were exposed to cigarette smoke (active or passive smokers) and observed differences apply to delivery in both groups were significantly important ($p<0.05$). The most widely accepted hypothesis to account for the role of smoking on fetal development is that carbon monoxide and/or nicotine induce fetal hypoxia. Carbon monoxide is known to decrease the oxygen-carrying capacity of haemoglobin. Fetal haemoglobin has a higher affinity for carbon monoxide than adult haemoglobin and the impact on the fetus is more severe than on the mother, since fetal tissues receiveeven less oxygen [8]. Bernard et al. [9] showed that specifically sensitive lymphocyte T (CD4+) of the fetus stimulated by the proper allergen produce cytokines, typical of atopic profile of lymphocyte Th 2 (Il-4, IL-13). A lower index of helper lymphocyte (CD4) to suppressor lymphocyte (CD8) in newborns cord blood correlates with a higher amount of IgE. The growth of IgE level in cord blood is the effect of allergen and fetus lymphocyte B contact and could be, in the opinion of many experts, recognized as the entry criteria in disease diagnosis [10-12].

Entzel et al. [13] showed that endurance of Th 2 lymphocyte answer and associated with it, the production of immunoglobulin E present in cord blood is not the deciding factor in allergy development in children, it shows only the atopic phenotype. It is only when additional factors start working such as allergens and adjuvants, which results in development of nonspecific over-reactivity and releases allergy effects in new-borns.

In examinated groups concentration of IgE in cord blood was higher than 30 IU, what is regarded as the potential allergy threat and was found in 60% of newborn babies in the groups exposed to cigarette smoke.Concentration of total IgE is the result of influence of many different factors which are regulated by a complex mechanism in the immunological system. Lymphocyte B activation and its transformation in plasmacyte are in progress because of the combination of a receptor with interleukin 4 or interleukin 13 and directly contact with lymphocyte B with lymphocyte T CD4. Such a prepared plasmacyte after gen recombination is responsible for synthesis ε immunoglobulin chain [14]. The increase of IgE concentration in cord blood not always correlated with atopy. It could be found in patients with congenial immunology deficiencies, children with parasite infection, born with low birth weight, with cancer disease or newborns from smoking mothers. Similarly as a higher level of serum IgE does not confirm allergy, also the proper concentration of IgE does not exclude this disease [15].

Nowadays many authors in their works on allergy showed that valuation of property of serum IgE can play a helping role, but it could not be explicitly recognized as the diagnostic base of allergy disease [16]. The executed analysis of the results of our own research seems to confirm this opinion. It is why there was not only IgE concentration examined but also there was the examination of CD4 and CD8 lymphocyte subpopulation.

Cord blood taken during the delivery is a good and easily available source of morphotic blood elements, soluble antibodies whose analysis during pregnancy or congenial disorders may contribute to earlier prevention of allergy in new-born children.

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