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Importance of Combinations of Risk Factors in the Development of Necrotizing Enterocolitis in Newborn Children

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The purpose of the study was to identify factors of increased risk of necrotizing enterocolitis among young children in Baku.

Materials and methods. Two observation groups were selected: the main observation group – children with necrotizing enterocolitis (128 children), the control observation group – healthy children (64 children). The children of the main group were divided into 2 groups: group 1 (n=83) – children with necrotizing enterocolitis who were treated conservatively and had no complications; group 2 (n=45) – children with necrotizing enterocolitis who had purulent-inflammatory complications and were treated surgically. In the course of the study, anamnestic and clinical laboratory research methods were used.

Results and discussion. A relatively high percentage of women aged 19–29 years and 30–39 years was established – 63.2 ± 4.3 and 20.3 ± 3.5%, respectively, in the main group of children, and 75.0 ± 5.4 and 14.0 ± 4.3% in the control group. In families of children born with necrotizing enterocolitis, 38.3% of mothers assessed their material and living conditions as unsatisfactory ($p<0.01$). It was revealed that the proportion of children with postnatal risk factors: < 1500 g of body weight at birth among children of the main group (63.2 ± 4.3%) is by 5 times more than among children of the control group (12.5 ± 4.2%, $p<0.05$). It was also found that the proportion of children with respiratory disorders significantly differs from each other in the compared groups (22.6 ± 3.6 and 3.2 ± 2.1%, respectively, $p<0.05$). The proportion of children who were administered artificial enteral nutrition with milk formula among children of the main group (75.0 ± 3.8%) was by 9.6 times higher than among children of the control group (7.8 ± 3.3%, $p<0.001$).

The results of our study also coincide with the results of the authors, who revealed a relationship with the course of pregnancy, childbirth, and necrotizing enterocolitis.

Conclusion. The results of the study showed that the most pronounced risk of necrotizing enterocolitis incidence is expected at the birth of children weighing 1500 g or less (prematurity of degrees 3–4), and usually such children predominate among newborns whose mothers were not observed by obstetrician-gynecologists in the antenatal period and, therefore, did not receive adequate treatment. Background medical and biological factors can be called such as the age of the mother, the state of health of the woman (the presence of genital and extragenital diseases) and the course of pregnancy (gestosis in combination with various pathologies).

Keywords: necrotizing enterocolitis, risk factors, young children.

Introduction. The most complex and least studied problem in neonatology is necrotizing enterocolitis (NEC). The vast majority of children with NEC are premature babies with a body weight less than 1500 g. According to various authors, NEC occurs at a frequency of 2–10 per 1000 premature babies with very low and extremely low birth weight [1, 2]. Surgical stages of NEC occur on average in 50% of sick children, mortality in this case reaches 20%, and with extensive intestinal necrosis it can reach 80–100%. The high mortality rate in NEC is the reason for the active study of this disease [3]. Investigating the causes of NEC, it is necessary to proceed from the factor of heterogeneity of pathology and its multifactorial etiology. Ischemic factors, feeding with hyperosmolar mixtures, malabsorption, forced amounts of food, and bacterial flora lead to the damage of the intestinal mucosa [4, 5]. In NEC, in almost all cases, there are factors of social, medical-organizational, and medical-biological nature, which are either a cause or an aggravating situation for the occurrence of NEC and fatalities [3, 6]. In connection with the abovementioned, the task was set to prove the significance of the combinations of these factors for a reliable study of the incidence rate.

The purpose of the study was to identify factors of increased risk of the incidence of necrotizing enterocolitis among young children in Baku.

Materials and methods. The study was carried out at the K. Faradzhov Research Institute of Pediatrics and at the Department of Children's Diseases-1 of the Azerbaijan Medical University. In accordance with the set purpose, two observation groups were selected: the main observation group – children with NEC (128 children), and the control observation group – healthy children (64 children).

The study was carried out in compliance with the basic provisions of the "Rules of ethical principles of scientific medical research with human participa-

tion", approved by the Declaration of Helsinki (1964-2013), ICH GCP (1996), EEC Directive No. 609 (dated 24.11.1986), Orders of the Ministry of Health of Ukraine No. 690 (dated 23.09.2009), No. 944 (dated 14.12.2009), No. 616 (dated 03.08.2012). Parents of each study patient signed an informed consent to participate in the study and all measures to ensure anonymity of patients were taken.

Children of the main group were divided into 2 groups: group 1 (n=83) – children with NEC who were treated conservatively and who had no complications; group 2 (n=45) – children with NEC who had purulent-inflammatory complications and were treated surgically (peritonitis with ileus, sepsis and pneumonia, anastomotic failure). In the course of the study, anamnestic methods such as collection of a family history and anamnesis of the life of children based on a survey of mothers and analysis of medical documentation (history of childbirth, case histories of newborns, outpatient development cards) and clinical and laboratory research methods such as an objective examination of children with a description of somatic and neurological status based on the examination data of functional diagnostics and laboratory examination were used. Statistical processing of the obtained results of the study was carried out by conventional methods of variation statistics.

Results and discussion. The basis for the birth and further development of a healthy child is formed in the intrauterine period. There are various medical-organizational and social factors that do not allow to organize high-quality medical supervision with timely and adequate correction of the course of pregnancy. In the control group of children, in more than half of the cases (54.7 ± 6.3%) mothers visited the antenatal clinic for the first time before the 12th week of pregnancy. A small part (7.8 ± 3.4%) were registered at a gestational period of 20–26 weeks. As it turned out, even in the control group of children, timely monitoring of pregnant women is not fully ensured. In the main group of children with NEC, in 9.0 ± 4.0% of cases, mothers were either not observed in antenatal clinics or were registered after 27 weeks of pregnancy. Moreover, a comparison of these groups of children according to the structure of the gestational period at the first visit to the antenatal clinic showed the existence of significant differences between them (χ^2= 87.5; p<0.0001).

Noteworthy is the relatively high specific weight of women aged 19–29 and 30–39 years old – 63.2 ± 4.3 and 20.3 ± 3.5% in the main group of children, and 75.0 ± 5.4 and 14.0 ± 4.3% in the control group, respectively. When analyzing the social factors of the studied families, a statistically significant difference in material and living conditions was found. In the families of children born with NEC, 38.3% of mothers rated their material and living conditions as unsatisfactory (p<0.01). In recent years, both in prosperous and disadvantaged families, there has been a change in the age composition of pregnant and parturient women: the proportion of women under 18 years is increasing and the number of women of older age groups is decreasing. It is obvious that the age of the mother as an integral criterion of biosocial demographic behavior remains a factor of the increased risk of morbidity in children, although its role is decreasing. The distribution of the surveyed groups of children according to the health status and the course of pregnancy of their mothers during the antenatal period of their development is presented in **Table 1**.

The proportion of children with postnatal risk factors: body weight at birth < 1500 among the children of the main group (63.2 ± 4.3%) is by 5 times higher than among the children of the control group (12.5 ± 4.2%, p<0.05). The specific weight of children with respiratory distress syndrome in the compared groups differ significantly from each other (22.6 ± 3.6 and 3.2 ± 2.1%, respectively, p<0.05). The proportion of children who received artificial enteral feeding with milk formula among the children of the main group (75.0 ± 3.8%) was by 9.6 times higher than that among the children of the control group

Table 1 – Distribution of the surveyed groups of children according to the health status and the course of pregnancy of the mother

Indicators	Main group (n=128)		Control group (n=64)		χ^2	p
	abs.	%	abs.	%		
Postnatal risk factors: birth weight < 1500	81	63.2 ± 4.3	8	12.5 ± 4.2	31.84	0.00001
Respiratory distress syndrome	29	22.6 ± 3.6	2	3.2 ± 2.1	7.07	0.1063
Need for mechanical ventilation	22	17.2 ± 3.3	7	10.9 ± 3.8	2.66	0.00001
Artificial enteral feeding with milk formula	96	75.0 ± 3.8	5	7.8 ± 3.3	55.43	0.0002
Antenatal risk factors: Chronic fetoplacental insufficiency	59	46.1 ± 4.4	4	6.2 ± 2.9	36.23	0.0002
Chronic intrauterine fetal hypoxia	16	12.5 ± 2.9	3	4.6 ± 2.7	1.56	0.2580
Intrauterine growth retardation	62	48.4 ± 4.4	7	10.9 ± 3.8	27.38	0.00001
Appointment of glucocorticoids	-	-	54	84.4 ± 4.6	93.21	0.00001

(7.8 ± 3.3%, p<0.001). Complicated courses of pregnancy were most often observed in mothers of children of the main group. In mothers of this group of children, chronic fetoplacental insufficiency was noted in 46.1 ± 4.4% of cases, chronic intrauterine fetal hypoxia – in 12.5 ± 3.9% of cases, and intrauterine growth retardation – in 48.4 ± 4.4% of cases. These pregnancy complications in mothers of the control group of children were relatively rare (6.2 ± 2.9; 4.6 ± 2.7 and 10.9 ± 3.8%, respectively).

Analyzing comparative materials on the distribution of two groups of children according to different characteristics (gestational period at the first visit of a pregnant woman to the antenatal clinic, the age of the pregnant woman, the mother's health status and the course of pregnancy, the quality of health during the neonatal period and the degree of maturity of children at birth, the presence of background pathology, etc.), it can be noted that the considered indicators are factors of increased risk of NEC disease in children. Our results are consistent with those of various authors who have studied the risk factors for NEC and found that low birth weight is the most frequently mentioned significant risk factor for NEC in newborns in the modern literature, which is consistent with studies describing the highest incidence of NEC among infants with the lowest body weight at birth. These authors also show that severe RDS was a significant risk factor for the development of NEC [2]. Mechanical ventilation, newborn weight, and maternal age have also been associated with an increased risk of NEC [2, 7, 8].

Other researchers consider hypotension during the week of life as an independent risk factor for the development of NEC, as circulatory disorders during this period of life can lead to impaired gastrointestinal blood flow, and, consequently, to a high incidence of necrosis [6, 8, 9].

The results of our study also coincide with the results of the authors [10, 11, 12], who found a relationship with the course of pregnancy, childbirth, and NEC.

Conclusion. The results of the study showed that the most pronounced risk of NEC incidence is expected at the birth of children weighing 1500 g or less (prematurity of degrees 3–4), and usually such children predominate among newborns whose mothers were not observed by obstetrician-gynecologists in the antenatal period and, therefore, did not receive adequate treatment. The age of the mother, the state of health of the woman (the presence of genital and extragenital diseases) and the course of pregnancy (gestosis in combination with various pathologies) can be called background medical-biological factors.

Perspectives of further research. In the future, it is planned to study the molecular pathways of the development of necrotizing enterocolitis in newborns.

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ЗНАЧЕННЯ ПОЄДНАНЬ ФАКТОРІВ РИЗИКУ В РОЗВИТКУ НЕКРОТИЧНОГО ЕНТЕРОКОЛІТУ У НОВОРОДЖЕНИХ ДІТЕЙ

Ісмайлова С. Д.

Резюме. *Мета дослідження.* Виявити фактори підвищеного ризику захворюваності на некротичний ентероколіт серед дітей раннього віку в м. Баку.

Матеріали та методи. Було відібрано дві групи спостереження: основна група спостереження – діти з некротичним ентероколітом (128 дітей), контрольна група спостереження – здорових дітей (64 дітей). Діти основної групи були поділені на 2 групи: група 1 (n=83) – діти з некротичним ентероколітом, що лікувалися консервативно і мали ускладнення; група 2 (n=45) – діти з некротичним ентероколітом, які мали гнійно-запальні ускладнення та лікувалися оперативно. У ході дослідження застосовувалися анамнестичні та клініко-лабораторні методи дослідження.

Результати. Встановлено відносно високу питому вагу жінок у віці 19-29 років та 30-39 років – відповідно 63,2±4,3 та 20,3±3,5% в основній групі дітей, та 75,0±5,4 та 14 ,0±4,3% у контрольній групі. У сім'ях дітей, народжених з некротичним ентероколітом, 38,3% матерів оцінили свої матеріально-побутові умови як незадовільні (p<0,01). Виявлено, що питома вага дітей з постнатальними факторами ризику: <1500 г маси тіла при народженні серед дітей основної групи (63,2±4,3%) у 5 разів більша, ніж серед дітей контрольної групи (12,5±4,2) %, p<0,05). Також встановлено, що питома вага дітей з порушеннями дихання суттєво відрізняється один від одного в порівнюваних групах (22,6±3,6 та 3,2±2,1% відповідно p<0,05). Питома вага дітей, яким вводили штучне ентеральне харчування молочною сумішшю, серед дітей основної групи (75,0±3,8%) була в 9,6 раза вищою, ніж серед дітей контрольної групи (7,8±3,3%, p <0,001).

Висновки. Результати дослідження показали, що найбільш виражений ризик захворюваності на некротичний ентероколіт очікується при народженні дітей масою тіла 1500 г і менше. Фоновими медико-біологічними факторами можуть бути названі такі як вік матері, стан здоров'я жінки та перебіг вагітності.

Ключові слова: некротичний ентероколіт, фактори ризику, діти раннього віку.

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