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A.A. Musaev

THE EFFECT OF GESTATIONAL AGE ON THE DEVELOPMENT OF NECROTIZING ENTEROCOLITIS

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Over the past 10 years, 208 children with necrotizing enterocolitis (NEC) have received our treatment. The control group consisted of 50 children whose gestational age was approximately similar to the main group. A case-control study was conducted to determine the role of the influence of gestational age on the development of NEC. 89 (42.8%) children with NEC and gestational age from 30 to 36 weeks had significantly lower percentiles of birth weight, umbilical cord pH, and a 1-minute Apgar score compared with 22 children from the control group of the same gestational age. On the contrary, there were no significant differences between 98 (47.1%) children with NEC and the control group (n= 24) aged 25-29 weeks, except that a small number of children with NEC received breast milk. 21 full-term infants in the main group and 5 infants in the control group appeared to have an obvious predisposing factor. The study proved that the predisposition to NEC depends on the gestational age. In the range of 25-29 weeks, all babies are at risk due to extreme prematurity. In the range of 30-36 weeks, asphyxia and children with stunted growth are at increased risk, while at full term, serious predisposing factors are apparently required.

Keywords: necrotizing enterocolitis, risk factors, gestational age.

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Introduction. Necrotizing enterocolitis (NEC) remains a severe and life-threatening disease that occurs in the neonatal period. In the USA in 2017, 9.9% of newborns were born before 37 weeks of gestational age, which are classified as premature [1]. Necrotizing enterocolitis is usually manifested by bloody stools, food intolerance, and a swollen, painful stomach. Necrotizing enterocolitis is the most common indication for urgent surgical intervention in premature infants. Complications of necrotizing enterocolitis of newborns include intestinal perforation with pneumoperitoneum, abdominal abscess, strictures, short bowel syndrome, septicemia, and death. Despite widespread numerous scientific and practical investigations, the etiology of the disease has not yet been definitively clarified. Some research groups believe that prematurity is almost the only perinatal factor in the development of NEC [2]. At the same time, in other studies that identify other risk factors for NEC, the risk of prematurity is not considered as the main factor of this disease. Hyaline membrane diseases are more common among NEC patients, but it is quite common among the control group of the examined patients [3]. Some authors point out that asphyxia is more common in patients with NEC [4] and usually umbilical vein catheterization is often performed in this category of patients [5]. The presence of such differences seems to underlie the differences among the surveyed population. Back in the 80s of the 20th century, a group of researchers did not detect NEC among the examined premature infants (body weight <1500-1750 gy); however, when analyzing the results of the examination of all newborns, the frequency of NEC detection increased[6].

Warner B.B., et all. in their studies indicate that risk factors for the development of necrotizing enterocolitis vary with birth weight [7]. The risk factors with the greatest prognostic significance are birth weight less than 1500 g, gestational age from 28 to 32 weeks, Apgar scores less than 3 points at birth [8].

An analysis of the literature data suggests that birth weight and gestational age are, to varying degrees, risk factors for the development of NEC [9]. In these case-control studies (retrospective comparison of two groups), comparison of birth weight was most often significant [10]. In one study that controlled for gestational age, only 23 patients had "late onset" NEC. Another group of researchers in their recent reports have provided new information on the etiology of NEC, demonstrating a very significant relationship between the absence or inverse end-diastolic flow velocity (AREDF) curves in the umbilical artery or fetal aorta and the subsequent development of NEC [11].

For the first time, a subgroup of preterm infants has been identified that

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appears to significantly increase the risk of developing NEC. Although these infants were very stunted on average, Malcolm et al., in their case-control studies in which infants were matched for gestational age and birth weight, concluded that the risk of NEC was associated with AREDF keeping up in growth [12]. However, in stunted children, an increased incidence of NEC can be expected; it is surprising that such an association has not been noted in many previous studies involving the identification of risk factors for NEC. Based on this, we decided to conduct a case-control study including indicators of gestational age with NEC.

The aim of the study was to determine the factor of gestational age in the development of necrotizing enterocolitis in newborns.

Material and methods. All 208 neonates who developed NEC were included in this retrospective (case-control) study. The control group consisted of 50 children whose gestational age was approximately similar to the main group.

Among the main group, in 89 (42.8%) children with NEC, in 21 (42%) newborns of the control group, the gestational age was from 30 to 36 weeks; with a gestational age of 25-29 weeks in the main group there were 98 (47.1%) infants with NEC and 24 (48%) infants in the control group. 21 (10.1%) term infants with NEC were in the main group and 5 (10%) in the control group.

The diagnosis of NEC was made on the basis of clinical signs such as the presence of biliary aspirates or vomit, bloating, lethargy of the newborn, detected by x-ray examination of intestinal pneumatosis with or without gas in the portal vein, and/or pathological signs detected during laparotomy or autopsy materials of deceased patients.

Pneumoperiteunum without intestinal pneumatosis, without obvious signs of perforation of the wall of a hollow organ, was not considered a strong symptom indicating HEC [13]. These diagnostic criteria served as the basis for establishing the diagnosis in the examined 133 newborns.

The control group consisted of newborns selected from the ICU register, born at the closest time and with the same gestational age as the infant with NEC. Infants who died earlier compared to NEC infants were excluded from the control group.

The results of ultrasound confirming the duration of pregnancy for the antenatal period were analyzed. Based on such indicators as height, weight, head and chest circumference, a centile table was compiled. We calculated the centile of the body mass of a newborn, taking into account gestational age, using standard methods [14]. The required data for the study is taken from the computerized database of the neonatal intensive care unit. UNC 84%.

Statistical analysis. Statistical processing was carried out using Microsoft Excel 2010, Statsoft Statistica 10.0. Certain indicators were taken into account as the arithmetic mean and standard deviation (M ± σ) for indicators with a normal distribution and as a median Me (25%; 75%) for signs with a distribution that deviated from normal.

In the studied groups with a normal distribution of the trait, the difference in the variation series was assessed by Student's t test; with a distribution that does not correspond to the normal difference between the samples - using the nonparametric U test (Wilcoxon-Mann-Whitney).

During the comparison and probabilistic assessment of differences between groups with a small (<30) number of options, White's W-test was used. In groups and subgroups, the significance of differences in frequencies was assessed using Pearson's $\chi 2$ test with Yates' correction. The odds ratio, 95% confidence interval, the degree of influence of factors, Pearson's and Fisher's coefficients were calculated. When evaluating the effectiveness of each method of therapy, the McNemar criterion was used. In all cases, the differences were considered statistically significant at $p < 0.05$.

The study was performed in accordance with Good Clinical Practice and the principles of the Declaration of Helsinki.

The study was approved by the Regional Ethics Committee of the Scientific Research Institute of Pediatrics named after K. Farajova, Protocol No. 11 dated 06/25/2018. All parents of patients received full information about the study and signed an informed consent to voluntarily participate in it.

Results and Discussion. 208 cases of NEC were identified. These newborns had a mean birth weight of 1418 g (mean birth weight centile 37%) and a mean gestational age of 30.4 weeks. 30 (14.4%) neonates with NEC died.

The median gestational age of the deceased infants was 28 weeks, the oldest was 34 weeks, while the median for surviving infants was 31 weeks. A total of 85 children (40.9%) were operated on, of which 46 (54.2%) survived. During the diagnosis of NEC, blood cultures performed in 50 (24%) cases gave an increase in microflora: Klebsiella spp. was detected in 24 newborns, Staphylococcus epidermicus - in 8, Eschericha coli - in 8, Clostridium spp. in 5, Enterobacter spp. - in 3 and streptococcus haemolyticus - in 2 newborns.

Before the onset of symptoms of NEC, in all cases, the child was fed. The median age at onset of NEC was 11 days (mod-5 and median 9). A significant negative correlation was found between gestational age and day of onset of NEC (r=-0-35, p=0.002).

Of the 208 newborns, 187 were preterm and 13 were 21 term infants; because term infants had predisposing factors, they were analyzed separately from preterm infants.

Premature newborns. Overall, children with NEC had significantly lower birth weights than control children (p<0-001). They were significantly more stunted, as evidenced by a lower mean centile birth weight (p<0-001), or a higher proportion of infants below the 10th percentile (p = 0-01, odds ratio (OR) 3.6 (95%), confidence interval (CI) ranged from 1.3 to 9.7.

Infants until 30 weeks of pregnancy. Differences in birth weight centile between children with NEC and control group were most noticeable in children of 30-36 weeks of gestation, while among children of 25-29 weeks of gestation, this difference was less significant.

An interesting result was the absence of identifiable risk factors in this age group among infants with NEC, other than increased mortality. However, in the NEC group, factors that were indeed significant were common among infants receiving only infant formula (p=004, OR=4-0, CI=-11 to 14-1), and were found to be less common among infants. with NEC who received only expressed breast milk (p = 003, OR = 0.29, CI = 0.09 to 0.87).

Birth weight and birth weight percentiles in infants with NEC were significantly lower than in controls (p<0.001), and there was a marked increase in the proportion of NEC infants with significant growth retardation (<10 percentile: p=0.02, OR=6.0, CI=1.3 to 26.8, <3rd centile: p=0.03, OR=9.0, CI=1.1-71.0).

Children with NEC born at 25-29 weeks of gestation compared with the control group had significantly lower pH in the arterial blood of the umbilical cord (p=0.05) and Apgar levels in 1 minute (p=004, OR=500, CI = -1.1 to 22.8), but there was no significant difference in feed composition.

Term infants. The 21 full-term infants in the main group who developed NEC had a mean (SD) birth weight of 3121

(469) g, a median birth weight percentile of 46 (33) and a gestational age of 38 (1) weeks.

In 11 cases, the onset of NEC coincided with exchange transfusion (9 through the umbilical venous catheter and 2 through the peripheral vein). In 6 and the newborn was a deep asphyxia at birth (pH of the umbilical cord reached 6.96 and 6.97). UNC 62%

Group with spontaneous perforation. There were 14 infants with NEC who developed pneumoperitoneum but did not show pneumotosis on x-ray. Their mean gestational age was 26 weeks. Five out of 14 did not feed at all and only one had birth asphyxia. The proposed mechanism in these cases is perforation in the area of focal ischemia, possibly due to embolism [15].

This study includes a fairly large number of children with NEC who were subjected to a matched case-control survey design. Comparison by gestational age allowed us to get an idea of its impact on the development of NEC.

The obtained results proved a certain nature of the change in risk factors depending on the duration of pregnancy. It turned out that the main risk factor for the development of NEC is prematurity itself, where the incidence was 10% during 25 weeks of infants, falling to 0-03% at normal gestation. The group with a gestational age of 25-29 weeks was distinguished by the absence of an identifiable risk factor.

The occurrence of NEC in this group Clarko and Miller [16] suggest the interaction of such pathological factors as the composition of the diet and the nature of the bacteria in the distal intestinal mucosa and does not depend on perinatal risk.

The only perinatal factor with the incidence of NEC was largely associated with the feeding of the child with expressed breast milk, that is, whether the child received expressed milk or not. This opinion was confirmed in studies by Eibl et al., in which they found that a mixture of immunoglobulin A/G present in expressed breast milk contributes to a significant reduction in the incidence of NEC [17]. The protective effect against the development of NEC induced by expressed breast milk is supported by other prospective studies. UNC 87%.

As can be seen from Table 2, children with NEC with a gestational age of 30-36 weeks were significantly more stunted than the control group and had a higher incidence of asphyxia, as evidenced by a decrease in pH in the umbilical cord arterial blood (p = 0.05) on the Apgar scale in 1 minute.

Fazilova A.Sh.,et all. their studies proved that there was no significant association between NEC and growth retardation, since only 46% of children with NEC had low gestational ages [18].

At the same time, in this study, 38% of infants in the control group, comparable in birth weight, also had a low gestational age, as a result of which the comparison of these groups did not give stunting as a significant difference.

Kleigman et al. [19] found no association between gestational age and NEC incidence despite the fact that 27% of their NEC cases were below the 3rd centile; at the same time, among the control group of infants weighing <1500 g, there is a higher gestation and among 22% of infants out of 553 children, NEC was detected below the 3rd centile. As a result, a comparison of the results obtained in these two populations did not give a clear confirmation that neither gestational age is a risk factor.

Among full-term infants, NEC is rare (0-03%). Among our examined infants among full-term children, NEC developed in 21 cases; they had mean birth weight, mean birth weight percentile and gestational age of 38 weeks. In these newborns, an association was found between NEC and exchange transfusion and asphyxia at birth.

Our study confirms that gestational age is one of the risk factors for the development of NEC, in which susceptibility to NEC is inversely proportional to gestational age.

In full-term infants, NEC requires significant disruption of the gastrointestinal tract and immune system to develop, while in infants <30 weeks of gestation, NEC most often occurs in the absence of well-defined ischemia. In infants at 30 weeks' gestational age and full term, factors such as growth retardation and asphyxia become increasingly important in the development of HEC.

Conclusion. 1. Newborns at risk of NEC include all infants <30 weeks of gestational age, and term infants with severe asphyxia, shock, exchange transfusion, or polycythemia.

2. Breast milk helps reduce the risk of NEC, especially in children 25-29 weeks of gestational age.

The authors declare no conflict of interest in the submitted article

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Z.V. Gasimova, V.A. Veliyeva, O.F. Gasimov, I.A. Gafarov

LOWER THIRD MOLAR IMPACTION FORECAST BASED ON ANGULATION OF THEIR AXIS ON PANORAMIC X-RAYS

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The aim of the study was to evaluate the diagnostic value (sensitivity and specificity) of lower third molar bud impaction in 121 patients aged 7 to 23 years who presented to an orthodontic clinic with complaints of different malocclusions. All patients underwent multiple panoramic radiographs during orthodontic treatment, specifically: before treatment initiation, after completion of phase 1 therapy, after fixed appliance therapy, and during the retention period.

A retrospective analysis was conducted on a total of 1,085 lower third molar buds across 551 panoramic radiographs obtained from patients with maloclusions before, during, and after orthodontic treatment, as well as during the retention phase.

The study revealed that starting from the age of 14, the inclination angle of lower third molar buds allow prediction of their impaction rate with a sensitivity of 64.8±6.5% and a specificity of 71.4±6.0%. As age increases, higher sensitivity and specificity enable impaction rate prediction even with smaller angles (less than 40°).

The application of these diagnostic methods can enhance the effectiveness of preventive measures for pathological conditions associated with delayed tooth eruption.

Keywords: lower third molars, impaction, eruption dynamics on panoramic radiographs

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Introduction. It is well known that the lower third molars impaction (LTM) is one of the most common pathologies in patients with maloclusions [2,4,18,27]. Studies show that as age increases, the angulation of LTM germs changes, and often, after orthodontic treatment, their pressure on the lower dental arch leads to relapses and crowding in the anterior region of the mandible [1,17,24]. At the same time, a group of authors believes that the eruption of LTM does not affect crowding and does not lead to relapses of maloclusions [13,28].

Classical diagnostics for detecting LTM germs and their angulation was based on radiographic examination—orthopantomography (Panoramic X-ray) [3,8,16]. For a more detailed study of the germ position and their relationships, computed tomography (CT) is subsequently performed [14]. However, due to the high radiation dose associated with CT, repeated dynamic examinations are not feasible. Therefore, orthopantomography remains a relevant diagnostic method, allowing for a comprehensive assessment of this anatomical region over time and tracking changes in the angulation of LTM germs, their subsequent eruption, or impacted position [5,19,21].

The aim of this study was to assess the diagnostic significance (sensitivity and specificity) of retained lower third molar germs in patients presenting to an orthodontic clinic with complaints of malocclusion.

Materials and Methods. Our study included 121 patients with various maloclusions (MO). Among them, 54 were male (44.6%) and 67 were female (55.4%). Pearson's Chi-Square test revealed no significant gender-based differences (p=0.589). In total, 550 orthopantomograms of these 121 patients were analyzed, and the dynamic changes in the angulation of 1,085 LTM were examined in relation to age.

Statistical Processing. The statistical analysis of the results was carried out using variation methods (Mann-Whitney U-test), dispersion analysis (F-Fisher and FS-Fisher-Snedecor), and ROC analysis (calculation of cut off points, sensitivity, and specificity of the test) in the IBM SPSS Statistics 26 software package. The null hypothesis was rejected at $p < 0.050$ [20].

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