ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

CORRECTION OF INTESTINAL DYSBIOSIS IN HEMORRHAGIC DISEASE OF NEWBORNS

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Annotation: Early neonatal hemorrhagic disease begins in utero and occurs 5–7 days after birth in 0.25–0.5% of cases in healthy children under the influence of unfavorable internal and external factors, even after prophylactic administration of Vitamin K to newborns. The purpose of the work was to study the role of eubiotics in the correction of intestinal dysbiosis in hemorrhagic disease of newborns (GRDN). The results of clinical, conventional laboratory, paraclinical, and microbiological examinations of 22 newborns are presented. The use of eubiotics for hemorrhagic disease of newborns in order to correct intestinal dysbiosis, helps restore intestinal microflora, improves hemostasis and eliminates symptoms of bleeding.

Relevance. The problem of bleeding in newborns is associated with the characteristics of their hemostatic system. Circulatory disorders remain a pressing problem in pediatrics due to coagulation disorders due to deficiency of Vitamin K-dependent coagulation factors in children [4,6,7].

An analysis of the literature indicates that early neonatal hemorrhagic disease begins in utero and GRDN occurs in 0.25–0.5% of cases in healthy children 5–7 days after birth [5].

The lack of prophylactic administration of Vitamin K drugs to newborns can lead to the development of hemorrhagic disorders in the future due to the influence of unfavorable internal and external factors [8].

All newborns have a relative deficiency of vitamin K and its reserves at birth are very low. After birth, a small amount of Vitamin K comes in breast milk, and from 3–5 days of age its production by the intestinal microbiota begins [3]. Sources of vitamin K for newborns are breast milk, artificial milk formulas, or external Vitamin K intake through medications [1,2,5]. The concentration of Vitamin K1 in cord blood is less than 2 mg/ml.

According to studies, the intestinal microbial landscape in newborns with GRDN is altered and may be one of the causative factors.

Target. To study the role of eubiotics in the correction of intestinal dysbiosis in hemorrhagic disease of newborns.

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Material and research methods. The paper presents the results of clinical, generally accepted laboratory, paraclinical, microbiological examinations of 22 newborn children who were hospitalized during 2021-2023 in the neonatology and neonatal intensive care departments of the Children's Medical Center.

When diagnosing GRDN and determining the severity of the disease, ICD-10 was used.

Clinical examination of patients included: collection of conventional and clinical anamnestic data. Upon admission, a coagulogram, a general blood test, a general urinalysis, a coprogram were performed, and, if indicated, a biochemical blood test and instrumental studies (x-ray, electrocardiography, ultrasound of the abdominal organs and heart.). Neuroultrasound and brain KT were used to identify, localize and quantify intracranial hemorrhage in all children.

The intestinal microbiota in the dynamics of the disease was studied in the bacteriological laboratory of the Regional Clinical Medical Research Center and the Russian Scientific Center for Emergency Medicine using a common non-invasive generally accepted method of stool culture developed by R.V. Epstein–Litvak, F.A. Vilshanskaya modified by M.A. Akhtamova et al. [5,6] using domestic nutrient media and reagents.

Research results. The examined patients were divided into II groups depending on the method of therapy: Group I included 10 newborns with GRDN who did not receive eubiotics, Group II included 12 newborns with GRDN who received eubiotics against the background of standard treatment for the correction of dysbiotic intestinal disorders and treatment of GRDN.

The diagnosis was established on the basis of a detailed study of the anamnesis, objective data and the results of instrumental indicators (platelet count, coagulogram, ultrasound and neurosonography).

Analysis of the work showed that all sick newborns were from rural areas: 40.9% (9) patients were residents of the Kashkadarya region, 22.7% (5) newborns were from the Kushrabad region, 36.4% (8) children were from other regions.

In newborns with GRDN, when examining the intestinal microflora, in addition to bifidobacteria and lactobacilli (80.0%), fungi of the genus Candida (80.0%), Escherichia coli (70.0%) and enterococci (70.0%) were identified. The level of anaerobic flora, beneficial for the child, was reduced to 105 CFU/g, which indicated the influence of external and internal pathogenic factors on the development of dysbiosis.

A comparative analysis of the study of the microflora of newborns with GRDN undergoing traditional therapy showed that upon discharge from the hospital, the formation of the microbiota slightly improved, but did not normalize. Thus, the frequency of detection and the number of Staphylococcus aureus and saprophyticus, fungi of the genus Candida, decreased by one order of magnitude. The level of aerobes decreased, but did not reach normal values, i.e. the dynamics in improving microflora indicators was insignificant.

Against the background of a continued decrease in the level of anaerobes, the number of Bifidobacterium and Lactobacillus increased by 1-2 orders of magnitude and reached 109 in

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
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1 gram of feces, the quantitative content of Staphylococcus epidermidis decreased to 103 microbial bodies, Staphylococcus aureus and Proteus to 103, Candida - to 104, and the content of E. coli, Klebsiella and Citrobacter remained almost unchanged.

Studies have shown that in newborns with GRDN, the use of traditional therapy leads to only partial inhibition of pathological colonization and has a positive effect on the anaerobic flora.

Dysbiotic disturbances in the intestinal microflora of newborns with GRDN who did not receive eubiotics create conditions for the development of hemostasis disorders in them; therefore, correction of dysbiosis has prospects in terms of preventing GRDN.

To eliminate dysbiotic changes and restore eubiosis, which can ensure the full functioning of the gastrointestinal tract of the newborn, we carried out a therapeutic correction, which included the use of prebiotic, probiotic and synbiotic agents aimed at creating favorable conditions for the growth of normal intestinal microbiota.

Clinical examination data were compared with microbiological parameters.

We have included eubiotics in the arsenal of traditional therapeutic agents - enterol, lacto-zhi, linex, bifidumbacterin, lactobacterin, which contribute to the restoration of intestinal normal flora and conducted a comparative study of the intestinal microflora of group II, which, against the background of the traditional method of treatment, were prescribed eubiotics in an age-specific dosage.

Clinical phenomena of intestinal imbalance correlated with stabilization of the main symptoms of the pathological process, which confirmed the existence of a relationship between clinical and microbiological parameters.

When treated with eubiotics in newborns with GRDN, upon discharge, the formation of the intestinal microbiota significantly improved - the level of aerobes decreased by several orders of magnitude and almost reached normal values, the frequency of contamination and the level of Staphylococcus saprophyticus decreased, and Staphylococcus aureus, fungi of the genus Candida, hemolytic strains of Escherichia were not sown , which indicates the effectiveness of corrective therapy.

In newborns who received eubiotics upon discharge from the hospital, Bifidobacterium and Lactobacillus were found in all children and the level of anaerobic flora increased by 1-2 orders of magnitude, reaching borderline values (109 CFU/g), although it did not reach standard values, which may be due to their short course applications. Against the background of traditional therapy and the prescription of eubiotics, pathogenic microorganisms were sown less frequently - fungi of the genus Candida and Proteus, respectively, in 1.8 and 4 times lower quantities (102-3 CFU/g) than on admission. In patients using eubiotics, the quantitative content of Staphylococcus epidermidis and aureus decreased to 103 CFU/g. It should be noted that the frequency of inoculation of individual bacteria decreased significantly in group IIB compared to group IIA.

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AMERICAN ACADEMIC PUBLISHER
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Thus, in newborns with GRDN, with traditional treatment, there was an improvement in obligate microflora indicators, a decrease in the amount of opportunistic and pathogenic flora, however, upon discharge, their microbiological changes were not restored to normal values, whereas when eubiotics were prescribed, more significant changes were noted in positive side.

The results of the work showed that the inclusion of eubiotics in the complex therapy of newborns with GRDN has the best clinical and laboratory effect and contributes to the fastest clinical recovery and improvement of the intestinal microbiota.

The effectiveness of corrective therapy over time was assessed by clinical symptoms of the disease, which disappeared significantly earlier in patients of group II compared to group I.

In children who took corrective eubiotic therapy, restoration of stool and sucking was observed on the 5th day, an improvement in the general condition, the disappearance of cramping colic, rash and flatulence was noted on the 4th day, a decrease in melena was observed on the 5th day, and other symptoms lasted until discharge from the hospital.

The phenomena of dysbacteriosis stopped only as the main hemorrhagic syndrome stabilized, which gives grounds to indicate an indisputable connection between the underlying disease and dysbiosis. This confirms the fact that intestinal normal flora is one of the factors of hemostasis.

It is assumed that microbial imbalance aggravates the course of the underlying disease and provokes bleeding.

The effectiveness of corrective treatment ultimately manifested itself in the length of stay of patients in the hospital, averaging 6.6±0.3 bed days in patients in this group, which was significantly lower ($P<0.01$) than in Group I (7.1±0.4).

Thus, in newborns with hemorrhagic disease, conventional therapy does not stop intestinal colonization. Correction of intestinal microbial imbalance with eubiotics contributes to the partial restoration of the patient's microbiota. Despite this, the microbiotic imbalance that persisted at discharge in newborns with hemorrhagic disease on the background of the use of eubiotics is characterized by a deficiency of representatives of obligate and facultative microflora and is an indicator indicating a continuing disturbance of the microecosystem.

Conclusions. Thus, the use of eubiotics for hemorrhagic disease of newborns, correcting intestinal dysbiosis, helps restore intestinal microflora, improve hemostasis and eliminate the symptoms of bleeding.

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ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
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