



## Improvement of therapy for escherichiosis in children infected with Epstein-Barr virus

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**Abstract. Background.** Escherichiosis remains one of the most common intestinal infections, especially among young children. Indigestion of essential nutrients, transient fermentopathy, imbalance of the symbiotic flora, which develop in escherichiosis in combination with general intoxication and water-electrolyte disturbances, can lead to unfavorable outcomes. One of the factors influencing the course of escherichiosis can be Epstein-Barr virus (EBV) infection in the child. Purpose of the research — improvement of treatment of children with escherichiosis and EBV infection in different periods of the disease. **Materials and methods.** We examined 74 children aged 2–3 years, who were treated at the Regional Children's Clinical Infectious Diseases Hospital in Kharkiv with a diagnosis of moderate-to-severe escherichiosis. A group of 36 children was selected, who received conventional therapy with early gradual restoration of nutrition according to the existing protocol, and the restoration of the qualitative and quantitative composition of food was carried out as soon as possible (first group). The second group was represented by 38 children, who received two-day prolonged gradual restoration of the diet: more gradual increasing the volume of food at each feeding and reducing the number of feedings per day. Children of the second group received drugs containing Lactobacillus, milk thistle extract and B vitamins (once daily with meals) from the first day. Ultrasound examination of the abdominal cavity was performed in all children. **Results.** Analysis of the main clinical, laboratory and instrumental parameters of patients in both groups during their stay in the hospital and one month after the discharge from the hospital revealed that in children of the second group, in whom rational diet therapy was applied, there was a reduction in the duration of bowel dysfunction, abdominal syndrome, flatulence; the parameters of the coprological test and the echosonography of the hepatic parenchyma were normalized more quickly. Patients on the optimal diet regained their weight in a shorter period. The proposed methods of improving the therapy made it possible to prevent exacerbation of escherichiosis in children of the second group at the early convalescence stages. **Conclusions.** Early detection of EBV infection in children with escherichiosis, correction of therapy enable early restoration of physiological processes in the intestine and bile system, normalization of digestion and absorption of nutrients, and generally has a positive effect on the course of the underlying disease.

**Keywords:** escherichiosis; Epstein-Barr virus; children; therapy

### Introduction

In the structure of acute bacterial intestinal infections (II) in infants one of the most common is escherichiosis. Pathogenic *E. coli* can cause not only inflammation of the gastrointestinal tract, but also leads to the generalized forms with urinary tract lesions (widespread use of diapers in children under one year contributes to this now), biliary system disorders and sepsis [1, 2]. Especially dangerous are enterohemorrhagic *E. coli*, which, in comparison with other strains, are more often as a factor of development of severe forms, lethal outcomes [3].

The main factors that lead to disruption of digestion and absorption of the main nutrients in bacterial II are the occurrence of an inflammatory process with damage of intestinal enterocytes and mucus secretion, disruption of the acid medium, enzymatic balance and motor function of the gastrointestinal tract, development of imbalance of symbiotic microflora [4–6]. The intensification of these pathological changes by fever, refusal to eat or loss of appetite, repeated vomiting and/or regurgitation, the phenomena of water-electrolyte disorders inherent in children with escherichiosis, contributes to the de-

velopment of prolonged bowel dysfunction, anemia and hypovitaminosis, irritable bowel syndrome, progressive weight loss [7].

The course of escherichiosis largely depends on the child's age, pathogenic properties of the pathogen, the state of the immune system, the presence of concomitant diseases. In recent decades, the herpes-viral infection (Epstein-Barr virus (EBV) among the young children) has a leading role in the socioeconomic importance, impact on the level and quality of life, prevalence among the population [8, 9]. Presence of persistent EBV infection with periodic activation and exacerbation of the process leads to suppression of the cellular immune response, expressed immunosuppressive state of the organism. As is known, one of the largest organs of the immune system, consisting of Peyer's plaques, lymphatic follicles, mesenteric lymph nodes, is the GALT-system (gut associated lymphoid tissue), whose main function is the recognition and elimination of antigens or the formation of immunological tolerance to them [10, 11]. Therefore, the development of bacterial inflammatory process in the mucosa of the gastrointestinal tract in children infected with EBV infection can enhance the dysfunction of immune-competent cells of the body, deepen immune disorders. Simultaneously with inflammatory process of the gastrointestinal tract, disorders of the main antigen-presented dendritic cells of the GALT system may occur, causing a breach of oral tolerance, formation of allergic sensitization, which enhances and supports bowel dysfunction [12, 13]. Diarrheal syndrome at escherichiosis in children with EBV can be prolonged by such factors as a violation of the functional state of the liver, dysfunction of the biliary system, the development of secondary pancreatic insufficiency, which together are the main components of the formation of malabsorption syndrome [14].

Considering all the above, it is clear the importance of following a rational diet in the treatment of escherichiosis in children with EBV, improving the diet of children at different stages of the disease and timely correction of the diet depending on the severity and activity of pathological process [15–17]. The importance of diet in combination with rehydration therapy in the treatment of escherichiosis increases due to the prevalence of resistance of *Enterobacteriaceae* pathogens to antibiotics despite the success of the pharmaceutical industry [18, 19]. In the sources available to us, we did not find work devoted to the features of dietary therapy of escherichiosis in children infected by EBV. Earlier research conducted by us revealed the peculiarities of escherichiosis in children with EBV, which include prolonged fever, oropharyngeal hyperemia, lymphadenopathy, hepatomegaly, signs of liver parenchymal reaction, longer disease course, extension of dyspeptic phenomena, signs of hepatomegaly [20]. In our opinion, it is possible to improve the therapy of such children by improving of dietary therapy. It is rational for all parameters of nutrition (according to age, activity of persistent herpes-viral infection, severity of the main disease, disorders of liver function and bile-excreting system) will facilitate rapid regression of diar-

rheal syndrome, improve the general condition of the child, and shorten the stay in the hospital.

**Purpose of the research** — improvement of treatment of children with escherichiosis and infected with EBV in different periods of the disease.

## Materials and methods

Under our supervision there were 74 children of two-three years who were treated at the Regional Children's Clinical Infectious Disease Hospital in Kharkov with a diagnosis of moderate-severe forms of escherichiosis. An additional examination of children revealed the presence of a persistent EBV infection in them. The diagnosis of escherichiosis was established based on the clinical, epidemiological, bacteriological and serological studies. Persistent EBV infection was diagnosed when the patient had high titers of antibodies to the capsid antigen (EBV CA) IgG class in the dynamics of the disease (latent form). The results of studies of patients for other herpes viruses were negative. Medical treatment of children was carried out in accordance with approved clinical protocols (Order N 354 of 09.07.2004 "On the approval of protocols for the diagnosis and treatment of infectious diseases in children"). In the acute phase the daily amount of food was reduced on 1/3–1/4 of the physiological norm with increasing frequency rate to 7–10 feedings per day.

All children were divided into two groups. The first group included 36 children who received conventional therapy with early gradual restoration of nutrition, while the restoration of the qualitative and quantitative composition of food was carried out as soon as possible (in accordance with the existing protocol). The second group was represented by 38 children, who received two days prolonged gradual restoration of diet: more gradual increasing the volume of food at each feeding and reducing the number of feedings per day. Children of the second group received drugs containing Lactobacillus, Milk thistle extract and Vitamins group B (once daily along with meals) from the first day. The choice of this drug is due to the prevention of the intestinal dysbiosis resulting from the antibiotics therapy as well as the protection of liver cells. The liver's damage is possible as a result of acute escherichiosis and/or persistent EBV-infection. The use of drugs of combined effect is less expensive. It was recommended for parents of second group children to feed them more frequently, in small portions for two weeks in the period of early rehabilitation: up to 6 times a day not more than 150 ml depending on the age and nutritional value of products.

Statistical processing of the obtained data was carried out by means of Excel and Statistica 7.0 applications. The significance of differences between groups was determined using the t-test (Student's test).

## Results and discussion

We analyzed the main clinical, laboratory and instrumental parameters of patients of both group within pathological process and for one month after discharge from the hospital. It was revealed significantly longer preservation of the local manifestation of intestinal disorders

in children of the first group: diarrheal syndrome ( $5.83 \pm 0.24$  vs  $4.55 \pm 0.32$  days,  $p < 0.05$ ), abdominal pain ( $3.51 \pm 0.21$  vs  $2.41 \pm 0.15$  days,  $p < 0.05$ ), signs of flatulence ( $3.09 \pm 0.22$  vs  $2.01 \pm 0.18$  days,  $p < 0.05$ , respectively in groups). The coprological test revealed a longer presence of impurities of undigested food, increased amounts of fat and fatty admixtures at patients of the first group ( $6.44 \pm 0.27$  days vs  $4.29 \pm 0.29$ ,  $p < 0.05$ ), which indicates a transient dysfunction of the pancreas and is grounds for early use of drugs that improve the digestion and absorption of food (enzymes) to treat the children with escherichiosis who are infected with EBV. Rapid recovery of bowel function in children of the second group leads to positive dynamics of their body weight. The daily gain of body mass and its normalization occurred in much shorter period at patients of the second group ( $10.33 \pm 0.45$  vs  $6.84 \pm 0.57$  days, respectively,  $p < 0.05$ ). Thus, compliance with such a diet contributed to a better absorption of nutrients.

One of the features of escherichiosis in children with EBV is hepatomegaly. We revealed preservation of hepatomegaly in all children until discharge from the hospital. However, the dynamics of liver size reduction was more significant in children of the first group, in whom the liver was reduced on  $1.06 \pm 0.24$  cm compared to  $1.85 \pm 0.37$  cm in patients of the second group, although the difference was not significant,  $p > 0.05$ . More significant changes were found by echosonography of the liver. Preservation of the parenchymal reaction of the liver with an increase of its echogenicity until discharge from the hospital was noted only in 12 patients of the second group, while among the children of the first group this feature was found in 24 patients. Long-term maintenance of the main clinical symptoms in the patients of the first group resulted in the prolongation of the stay of these children in the hospital ( $10.89 \pm 0.51$  vs  $8.27 \pm 0.32$  days, respectively,  $p < 0.05$ ).

Follow-up observation for one month has shown an exacerbation in five children of the first group which were characterized by moderate bowel dysfunction on day  $4.38 \pm 1.34$  after discharges from the hospital. Parents noticed the deterioration of stool consistency and increased its frequency rate, which required correction of therapy. There were no such manifestations among the patients of the second group. After one month of observation the echosonography of liver was performed and hepatomegaly was found in 10 patients of the second group without signs of parenchymal organ reaction and in 22 patients of the first group with preservation of parenchymal liver reaction in 8 children.

Thus, our obtained data indicate that rational diet therapy remains the main component of treatment of children with escherichiosis not only in the acute period, but also at the stages of rehabilitation. Early detection of EBV infection among children with escherichiosis, correction of patients' therapy creates conditions for restoring physiological processes in the intestine and bile excretory system, facilitates the speedy normalization of digestion and absorption of nutrients, and generally has a positive effect on the course of the disease.

## Conclusions

1. Children with escherichiosis who are infected with EBV require long-term gradual recovery in feeding regime in the acute period.

2. Adherence to the nutritional care in combination with drugs containing *Lactobacillus*, Milk thistle extract and vitamins B in children with escherichiosis and infected with EBV facilitates the restoration of their clinical, laboratory and instrumental indexes.

3. Saving of mode frequent and small portions feeding during early rehabilitation at patients with escherichiosis and infected with EBV, prevents the development of bowel dysfunction and has positive impact on the liver restoration.

The procedure was done strictly in compliance with the Helsinki Declaration after approval from the Regional Ethical Review Board at Kharkiv National Medical University.

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**Conflict of interest.** The authors declare no conflict of interest.

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### Усовершенствование терапии больных эшерихиозом детей, инфицированных вирусом Эпштейна — Барр

**Резюме. Актуальность.** Эшерихиоз остается одной из распространенных кишечных инфекций, особенно среди детей раннего возраста. Развивающиеся при эшерихиозе нарушения пищеварения основных нутриентов, транзиторная ферментопатия, дисбаланс симбиотической флоры на фоне общеинтоксикационного синдрома и водно-электролитных нарушений могут приводить к неблагоприятным последствиям. Одним из факторов, влияющих на течение эшерихиоза, может быть инфицированность ребенка вирусом Эпштейна — Барр (ВЭБ). **Цель работы** — усовершенствование терапии детей, больных эшерихиозом и инфицированных ВЭБ, на разных этапах заболевания. **Материалы и методы.** Обследовано 74 ребенка в возрасте 2–3 лет, лечившихся в Областной детской клинической инфекционной больнице г. Харькова с диагнозом «эшерихиоз средней тяжести». Выделена группа из 36 детей, которым проводилась общепринятая терапия с ранним постепенным восстановлением питания, при этом в соответствии с существующим протоколом восстановление качественного и количественного состава пищи осуществляли в максимально возможно короткие сроки (первая группа). Вторую группу составили 38 детей, которым восстановление питания проводили постепенно, с задержкой увеличения объема пищи на каждое кормление и уменьшения кратности кормления на один-два дня. Детям второй группы с первых дней лечения назначали препараты, содержащие одновременно

лактобактерии, экстракт расторопши и источник витаминов группы В (один раз в сутки одновременно с приемом пищи). Всем детям проводили ультразвуковое исследование органов брюшной полости. **Результаты.** Анализ основных клинических, лабораторных и инструментальных параметров пациентов обеих групп за время пребывания в стационаре и на протяжении одного месяца после выписки выявил, что у детей второй группы на фоне применения рациональной диетотерапии отмечалось сокращение длительности дисфункции кишечника, абдоминального синдрома, метеоризма, быстрее нормализовались показатели копроцитограммы и данные эхо-соноскопии печеночной паренхимы. Пациенты, находившиеся на оптимальной диете, восстанавливали свой вес за более короткий период. Предложенные методы усовершенствования терапии позволили предотвратить обострение эшерихиоза у детей второй группы на этапах ранней реконвалесценции. **Выводы.** Раннее выявление инфицирования ВЭБ среди детей с эшерихиозом и проведение коррекции терапии больных создают условия для скорейшего восстановления физиологических процессов в кишечнике и желчевыводящей системе, нормализации пищеварения и всасывания питательных веществ, в целом положительно влияют на течение основного заболевания.

**Ключевые слова:** эшерихиоз; вирус Эпштейна — Барр; дети; терапия

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### Вдосконалення терапії хворих на ешерихіоз дітей, інфікованих вірусом Епштейна — Барр

**Резюме. Актуальність.** Ешерихіоз залишається однією з поширених кишкових інфекцій, особливо серед дітей раннього віку. Порушення травлення основних нутрієнтів, транзиторна ферментопатія, дисбаланс симбіотичної флори, що розвиваються при ешерихіозі, на тлі загальноінтоксикаційного синдрому і водно-елек-

тролітних порушень можуть призводити до небажаних наслідків. Одним із факторів, що впливає на перебіг ешерихіозу, може бути інфікованість дитини вірусом Епштейна — Барр (ВЕБ). **Мета роботи** — удосконалення терапії дітей, хворих на ешерихіоз та інфікованих ВЕБ, на різних етапах захворювання. **Матеріали та ме-**

**тоди.** Обстежено 74 дитини віком 2–3 роки, які лікувалися в Обласній дитячій клінічній інфекційній лікарні м. Харкова з діагнозом «ешерихіоз середньої тяжкості». Виділено групу з 36 дітей, яким проводилася загальноприйнята терапія з раннім поступовим відновленням харчування, при цьому відповідно до існуючого протоколу відновлення якісного і кількісного складу їжі здійснювали в максимально можливо короткі терміни (перша група). Другу групу становили 38 дітей, відновлення харчування яким проводили більш поступово, із затримкою збільшення обсягу їжі на кожне годування і зменшення кратності годування на один-два дні. Дітям другої групи з перших днів лікування призначали препарати, що містять одночасно лактобактерії, екстракт розторопші і джерело вітамінів групи В (один раз на добу одночасно з прийомом їжі). Усім хворим було проведено ультразвукове дослідження органів черевної порожнини. **Результати.** Аналіз основних клінічних, лабораторних та інструментальних параметрів пацієнтів обох

груп за час перебування в стаціонарі і протягом одного місяця після виписки виявив, що в дітей другої групи на тлі застосування раціональної дієтотерапії відзначалося скорочення тривалості дисфункції кишечника, абдомінального синдрому, метеоризму, швидше нормалізувалися показники копроцитограми і дані ехосоноскопії печінкової паренхіми. Пацієнти, які перебували на оптимальній дієті, відновлювали свою вагу за більш короткий період. Запропоновані методи удосконалення терапії дозволили запобігти загостренню ешерихіозу в дітей другої групи на етапах ранньої реконвалесценції. **Висновки.** Раннє виявлення інфікування ВЕБ у дітей з ешерихіозом та проведення корекції терапії хворих створюють умови для швидкого відновлення фізіологічних процесів у кишечнику і жовчовивідній системі, нормалізації травлення і всмоктування поживних речовин, загалом позитивно впливають на перебіг основного захворювання. **Ключові слова:** ешерихіоз; вірус Епштейна — Барр; діти; терапія