ROLE OF THE IMMUNE DRUGS IN THE TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

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ABSTRACT — Authors on the basis of study of clinical laboratory data, hemodynamic indices, data on infectious complications in patients with acute lymphoblastic leukemia after Viferon use in complex therapy have achieved positive results. Chemotherapy and long-term antibiotic treatment bring to intestinal dysbiosis and application of Viferon provides the normalization of intestinal flora, reducing Candida genus fungi. Out of the 41 children patients, whose therapy course included Viferon, by the end of the 1st week positive dynamics observed, bowel passage restored, leveled down bloating, decreased endogenous intoxication syndrome.

KEYWORDS — Viferon, complex therapy, comprehensive treatment, intestinal microflora, prebiotics, lymphoblastic leukemia, children.

RELEVANCE

To date, the primary means of prevention and treatment of infectious complications of disease is antibiotic therapy. However, in some cases, it does not achieve the desired effect, prompting the search for new drugs and change tactics such patients.

At present, there are insufficient data on the state of intestinal microbiota in children with leukemia in different periods of the disease, and the effect of cytostatics on cross-species interaction on a modern cytostatic therapy [1, 3]. There is lack of information on clinical efficacy of immune drugs (Viferon) in the complex treatment of patients during the clinical and hematological deployed pattern for correction of intestinal microflora and preventive treatment of infectious complications in children with acute lymphoblastic leukemia (ALL).

Among the other interferon drugs special attention deserves Viferon containing, along with interferon alpha 2b recombinant human vitamins E and C [1].

Impact of Viferon components can significantly reduce the course doses and duration of antibiotic and hormone therapy [1, 2].

There are numerous studies that indicate the feasibility of using Viferon in children with infectious process, who frequently get sick after surgery in obstetrical practice. However, administration of this drug in patients with acute lymphoblastic leukemia after chemotherapy to prevent suppurative complications and improve intestinal dysbiosis in adjuvant therapy in the available literature is not reflected. Therefore, to improve the results of treatment in these patients we have studied the application of Viferon [2,4].

OBJECTIVE

The purpose of this study was to explore the clinical and bacteriological aspects of disorders of the intestinal flora and to determine the effectiveness of using Viferon in complex therapy in children with acute lymphoblastic leukemia.

SUBJECTS AND METHODS.

Work carried out on the basis of a comprehensive treatment of 76 children with acute lymphoblastic leukemia. During the period 2009–2012, the children were under hospital treatment of pediatric hematol-

ogy National Medical Center of the Republic of Tajikistan.

Microbiological examination was carried out in children with acute lymphoblastic leukemia of both sexes between the ages of 3 to 17 years. All the children came to the hospital during the expanded clinical and hematological picture (Table 1).

Among the examined there were 43 (56.5%) boys, 33 girls (43.5%). Of all patients 54% were urban dwellers (Table 2).

In 35 (46%) of 76 patients with observed adverse somatic background of: underweight from 10 to 25% — 11 (31.4%), chronic infection hearth (dental caries, tonsillitis, pyelonephritis) 17 (48,5%), retarded physical development in 7 (20.0%) children.

Diagnosis was based on complaints, clinical examination, laboratory and instrumental examination that included blood tests, urine and feces, myelogram, spinal fluid test, immunophenotyping, and chest X-ray, endoscopy with biopsy tissue and seeding microflora, ECG, ultrasound (liver , gall bladder, spleen, kidneys, adrenals, thyroid, testes, heart). According to the testimony consulted specialists - ophthalmologist, neurologist, endocrinologist, gastroenterologist, nephrologist, genetics, ear-nose-throat doctor, dentist.

To study the state of intestinal microbiocenosis and infectious complications 76 children with acute lymphoblastic leukemia were examined. A control group comprised 15 healthy children, who underwent the work-up of intestinal microbiota using the methods described above.

To determine the effect of cytostatics on bakteriocinogenic activity of E. coli used a modified method of determining bakteriocinogenic activity [3].

Assessment of the state of intestinal microbiocenosis by degrees carried out in accordance with the classification of I.B. Kuvaeva and K.S. Ladodo [2, 3].

In order to prevent infectious complications children with acute lymphoblastic leukemia were divided into 2 groups randomly assigned to the major groups: 41 children received a combined therapy of probiotic lactoflor and Viferon suppositories 1 time per day, 35 children received standard therapy without immune correction.

Viferon administered to children simultaneously with the start of treatment with cytostatics protocol ALL BFM 90.1. Group received comprehensive treatment (+ Viferon lactoflora) for 4 weeks, then the two groups of children have been re-examined using bacteriological methods. [4] The effectiveness of the drug used was assessed by the dynamics of intestinal microbiota disturbances, level of bactericidal activity and persistent properties of E. coli, the clinical course of infection seen in a catamnesis for 12 months.

RESULTS AND DISCUSSION

We analyzed the medical history, clinical and functional parameters obtained from long-term (2-3 years) observation of 41 children with acute lymphoblastic leukemia.

Revealed that 69,3 ± 7,9% of children with ALL manifestation of the disease was observed in age from 1 to 7 years. Established family history of cancer pathology in the family at 24 ± 2,7% of children. Analysis of anamnestic data revealed that intestinal dysbiosis in the first year of life (before disease in acute leukemia) was observed in 26 children (66,7 ± 7,6%). Of these, a violation intestinal microbiota degree I-II was detected in 23 people (88,5 ± 10,1%), III-IV degree — in 3 (11,5 ± 1,2%). Intestinal dysbiosis is more common in children whose mothers during pregnancy suffered anemia, toxemia I and II half, obstructed labor ($p < 0.05$). These children are more likely than children who did not have the manifestations of intestinal dysbiosis in the first year of life, there were frequent colds (15,3 ± 1,7%, $p < 0.05$), violations of the chair (80,7 ± 9 2%, $p < 0.01$), abdominal pain (26,9 ± 2,9%, $p < 0.05$).

At the same time there is a significant increase in the level of B-lymphocytes (SD19) — the absolute amount of 0.7 t / l, relative - 24,8 ± 2,7% ($p < 0.05$). In the leucocyte count showed a sharp decline in the number of neutrophils: segmented neutrophils accounted for 10,4 ± 1,1% ($p < 0.01$), eosinophils — 0,6 ± 0,1% ($p < 0.01$). All children showed a significant reduction in monocyte — average - 0,4 ± 0,1% ($p < 0.001$), indicating a pronounced inhibition of cells that perform phagocytic function. Phagocytic index (FI) was reduced and reached 40,8 ± 4,6% ($p < 0.05$).

In children with acute lymphoblastic leukemia in first acute period revealed significant changes in indicators immunograms as a reduction in the total number of white blood cells, neutrophils and monocytes, as well as reducing AF These changes indicate a high risk of infectious complications in children with acute lymphoblastic leukemia during the expanded clinical-haematological picture.

It should be noted that in the context of chemotherapy and prolonged antibiotic therapy is disrupted intestinal dysbiosis and application Viferon provides the normalization of intestinal flora, reducing the fungi of the genus Candida. Of the 41 patients of the main group of children whose therapy included Viferon, by the end of the 1st week, there was a positive dynamics, restore intestinal passage, leveled bloating, decreased endogenous intoxication syndrome.

Thus, in children inclusion of Viferon in the complex treatment of acute lymphoblastic leukemia in comparison with traditional treatment was accompanied by a reduction in the length of exacerbations of

Table 1. *The distribution of patients by age and sex (in absolute terms and as a percentage)*

Sex	Age				Total (%)
	3-7	7-10	10-14	14-17	
Boys	12	14	10	7	43 (56.5)
Girls	6	8	8	11	33 (43.5)
Total	18	22	18	18	76 (100)

Table 2. *The distribution of patients by age and comorbidity*

№	Nosology	Age			
		3-7	7-10	10-14	14-17
1	Pneumonia	3	1	-	-
2	Bronchitis	3		2	1
3	Tonsillitis	1	4	3	1
4	Pyelonephritis	3	1	1	3
5	Dental caries	6	1	1	1

1.5 times, longer remission in 2.0 times, reducing the number of relapses per year by 1.5 times.

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