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CHRONOPHARMACOLOGICAL APPROACH TO TREATMENT ANEMIA IN PATIENTS

JUVENILE RHEUMATOID ARTHRITIS

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Resume.

Anemia in patients with juvenile rheumatoid arthritis (JRA) aggravates the severity, course and prognosis of the underlying disease. Due to this The purpose of the study was to study the frequency and type of anemia in patients with JRA, to test and evaluate the effectiveness of chronotherapy with iron supplements in patients with JRA. Of the examined 129 patients with JRA, 99 (76.7%) were diagnosed with anemia. The effectiveness of chronotherapy has been proven maltofer in 57 patients with JRA, characterized by a significant improvement not only in blood counts, but also by accelerating the decline in JRA activity.

Key words: *JRA, iron deficiency anemia (IDA), chronotherapy, maltofer , effectiveness.*

Relevance of the problem. One of the most common extra-articular manifestations in JRA patients is anemia, the effectiveness of treatment of which largely determines the prognosis of the underlying disease. In this regard, to optimize the treatment of JRA, timely treatment of anemia is an important condition. In addition, while numerous studies have been conducted on the

prevalence and type of anemia in adult patients with rheumatoid arthritis (RA) [3,9], there is little information on this issue in children [4,10]. The opinion of most researchers agrees that anemia of chronic disease (ACD) most often prevails in RA patients, the combination of ACD and IDA is in second place, with a total prevalence of anemia from 30 to 70% [6]. Others have suggested that in

groups of patients with well-controlled disease, IDA may be more common. In a study conducted in the UK in 2011, patients with RA were found to have more IDA than ACD [2]. Regardless of the type of anemia, according to the unanimous opinion of researchers, treatment of anemia should begin with treatment of the underlying disease [3,6,11].

Therapy of juvenile rheumatoid arthritis is a rather complex problem, regardless of the use of new, effective drugs. The main goal in the treatment of JRA is to achieve long-term remission and ensure a normal quality of life. These tasks are much more complicated in the presence of an extra-articular manifestation of JRA - anemia. On the other hand, long-term drug therapy poses a threat of drug - induced side effects, aggravating the severity of anemia, on the effectiveness of treatment, which depends on the prognosis of the disease [3]. In this regard, to optimize the treatment of

JRA, timely treatment of anemia is an important condition.

For the treatment of IDA in patients with JRA, there is a wide choice of drugs, but the method of application remains not fully resolved and requires further research. The ratio of risks and benefits of the chosen treatment option does not always meet the standards of safe therapy and this requires the search for new and at the same time effective methods of treatment. This is fully consistent with the method chronotherapy of the disease [8,9]. There are single works on the use of chronotherapy nimesulide in JRA patients [5,7]. Despite the growing interest in this method of treatment [1,9], there are no works on the use of chronotherapy for IDA in patients with JRA in the available literature, which was the basis for choosing this scientific direction of research.

Purpose of the study. To study the frequency and type of anemia in patients with JRA, to test and evaluate the effectiveness of chronotherapy with iron preparations for IDA in patients with JRA.

Material and methods. A retrospective analysis of 502 case histories of patients with JRA over a 5-year period (2017-2021) was carried out, the incidence and type of anemia in JRA patients were established. 129 children aged 3 to 18 years were subjected to a complete clinical and laboratory examination, for the first time a chronopharmacological approach to the treatment of IDA in patients with JRA was applied, and the effectiveness of ferrotherapy was evaluated. In addition to traditional clinical and laboratory studies, a blood test was performed for rheumatoid factor, C-reactive protein, erythropoietin, ferritin, serum iron, hemoglobin equivalent in reticulocytes RET-He, IL 6, joint radiography. The effectiveness of maltofer was studied in 57 patients with JRA. A comparative analysis of the effectiveness

chronotherapy maltofer, in addition to basic therapy for JRA, in the active period of the disease in 57 patients and the dynamics of clinical and laboratory parameters in 26 patients with an active form of the disease receiving only basic therapy for JRA. Evaluation of the effectiveness of therapy was carried out on the basis of a clinical examination, the presence of positive dynamics in the general condition of the patient, the nature of the articular syndrome and the DAS index 4. The functional activity of patients was evaluated according to the Steinbrokker criteria.

Results and discussion. The incidence of anemia in 502 analyzed medical histories was 81.3%. Of the examined 129 patients with JRA, 99 (76.7%) were diagnosed with anemia. When determining the severity of anemia, we were guided by WHO criteria (2015); most patients were diagnosed with stage I anemia. The distribution of examined JRA patients with and without anemia by age and gender is presented in Table 1.

Table 1.

Distribution of examined JRA patients with and without anemia by age and gender

Age	With anemia				Without anemia			
	boys		girls		boys		girls	
	abs.	%	abs.	%	abs.	%	abs.	%
3-7 years	14	14.1	13	13.1	2	6.7	1	3.3
7-18 years	33	33.3	39	39.4	15	50.0	12	40.0
Total:	47	47.5	52	52.5	17	56.7	13	43.3

Anemia was more often observed in girls of school age - 39.4 % The indicators of hemoglobin and

erythrocytes, depending on gender and age, are presented in Table 2.

Table 2.

Hemoglobin and erythrocyte parameters depending on gender and age in JRA patients with anemia

Gender / Age		Hb, g/l	Erythrocytes, 10 ¹² /l
Gender	Girls (n = 52)	100.2 (80.0-114.0)	3.64 (3.0 -4.44)
	Boys (n=47)	96.8 (71.0-114.0)	3.58 (2.6-4.49)
Age	3-7 years old (n = 27)	99.1(79.0- 114.0)	3.75(3.18-4.33)
	8-16 years old (n = 72)	98.3(71.0-114.0)	3.57 (2.6 -4.49)

Analysis of the material shows that, despite a slight prevalence in the number of girls with anemia, more

severe variants of anemia were more often observed in boys.

Currently, as a rule, the treatment of iron deficiency anemia is

recommended to be carried out at home after discharge from the hospital, in the stage of clinical remission. The difference of the proposed method, in addition to the chronopharmacological approach, is that we proposed and proved a great efficiency in the treatment of IDA in the active phase of JRA. The basis for the use of IDA chronotherapy was the recommendations of Russian scientists [1,11]. We recommended Maltofer to

JRA patients with IDA at 19 pm once a day for 1 month.

The effectiveness of Maltofer therapy in patients with JRA was assessed based on clinical and laboratory data after 4 and 8 weeks. Comparative characteristics of the effectiveness of including chronotherapy with iron supplements and traditional therapy in patients with JRA are presented in Table 3.

Table 3

Comparative characteristics of the effectiveness of the inclusion of chronotherapy maltofer in the complex of treatment and traditional therapy of JRA.

Index	Traditional JRA therapy + chronotherapy maltofer		Traditional JRA therapy	
	Before treatment	After treatment	Before treatment	After treatment
Hb, g/l	94.7±9.3	119.4±7.6**	95.6±4.1	101.3±5.2
Erythrocytes, 10 ¹² /l	3.5±0.6	4.1±0.2*	3.7±0.5	3.9±0.2
Number of painful joints	8.4±1.02	2.5±0.4**	8.1±1.1	4.5±0.6
Morning stiffness, min.	60 (30 - 120)	20 (0 - 40)	60 (30 - 150)	40 (0 -90)
Ritchie index	15.1±2.0	9.6±0.8*	15.9±1.8	12.3±1.08
DAS index 4	4.1±0.3	2.6±0.7*	4.3±0.2	3.1±0.3

ESR, mm/h	31.5±2.1	17.6±0.5**	29.8±2.7	18.7±0.8
CRP level, mg%	18.1±3.1	6.8±1.3**	17.8±3.4	8.7±1.4

Note: Significance of differences compared to initial indicators: * - at $p < 0.05$,

** - at $p < 0.01$

In patients who received chronotherapy with Maltofer, a significant increase in hemoglobin, erythrocytes was noted, in all patients with mild and in the majority with moderate forms of anemia, the indicators returned to normal. The relief of anemia also led to an improvement in the articular syndrome in the form of a decrease in the number of painful joints, a reduction in the duration of morning stiffness. Positive dynamics was also noted in the value of the Ritchie and DAS 4 indices. All this led to an improvement in the general well-being of patients, an increase in activity, an improvement in appetite, a decrease and normalization of laboratory activity indicators of the underlying disease. In the group of patients who received only basic JRA therapy, there was a relatively

smaller positive trend in the relief of both articular and laboratory manifestations. We did not observe any side effects during therapy with Maltofer.

Conclusions. The results of the studies give grounds to recommend the inclusion of Maltofer by the method of chronotherapy in the complex therapy of the active period of JRA. The proposed method of treating anemia is applicable not only to patients with JRA, but also to IDA alone or against the background of other diseases.

LIST OF REFERENENS:

1. Barkova Z.N. Pathophysiological substantiation of chronodiagnostics and chronotherapy of iron deficiency. //Pathogenesis and pharmacocorrection of extreme and terminal conditions. Omsk, 1995. - p. 11-14.
2. Eshmurzaeva A.A., Sibirkin M.V. Anemia in patients with rheumatoid arthritis: incidence, age-sex and clinical

- features (according to a retrospective analysis)./ Bulletin TMA , 2017, No. 1. pp.135-138 .
3. Grinshtein Yu.I., Shabalin V.V., Kusaev V.V. Anemic syndrome in rheumatoid arthritis: approaches to diagnosis and possibilities of therapy. // Therapeutic archive No. 5, 2016. –p. 107-112.
 4. Juvenile idiopathic systemic arthritis / D. Baksiene , J. Kasparaviciene , M. Zebiene, B. Puteliene // Medicina (Kaunas). - 2003. - No. 39 (8). - P. 751-755.
 5. Ilkhamova Kh. A. Chronotherapy in the treatment of children with juvenile rheumatoid arthritis: scientific publication / Kh. A. Ilkhamova // Bulletin of the Association of Physicians of Uzbekistan. - Tashkent , 2017 . - N3 . - C. 49-53. - Bibliography : 6 titles.
 6. Koryakova Nina Vitalievna Anemia of various origins in patients with rheumatoid arthritis diss . Candidate of Medical Sciences Sciences, Petrozavodsk -2010, 133s.
 7. Mallaev Sh.Sh. Comparative effectiveness of traditional therapy and chronotherapy in the treatment of juvenile rheumatoid arthritis. / Alimov A.V.// New day in medicine, 2020, No. 1(29) P. 258-262
 8. Neudakhin E.V. Rationale for the chronobiological approach to prescribing medications for various diseases in children. / Practice of a pediatrician, 2012, pp. 15-19
 9. Neudakhin E.V. Chronotherapy in pediatrics is the basis for increasing the effectiveness of treating diseases in children. / Russian Bulletin of Perinatology and Pediatrics 2018; Volume 63, No. 6, P 7-14 . DOI : 10.21508/1027-4065-2018-63-5-7-14
 10. Oligoarticular juvenile idiopathic arthritis among Saudi children / MM Moued , HMAI- Saggaf , HS Habib, MA Muzaffer // Ann Saudi Med. - 2013. - No. 33 (6). - P. 529-532.
 11. Rozhina I.L. Biorhythms of erythropoiesis and iron metabolism in adolescents./ / Actual problems of pathophysiology. - St. Petersburg, 1998. - p. 56-57.

