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CLINICAL AND LABORATORY MANIFESTATIONS OF JUVENILE RHEUMATOID ARTHRITIS

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Abstract
The article describes the clinical and laboratory features of juvenile rheumatoid arthritis and the consequences of the disease after treatment with chronotherapy. Clinical features of the disease, laboratory analysis results are important when choosing an effective treatment method. An effective treatment method is characterized by a faster onset of remission, prolongation of its duration and reduction of side effects of drug treatment.

Keywords: Juvenile rheumatoid arthritis, prognosis, chronotherapy

Introduction

Juvenile rheumatoid arthritis (JRA) is a destructive inflammatory disease of the joints with unknown etiology, complex immunoaggressive pathogenesis, characterized by symmetrical chronic arthritis, systemic damage to internal organs, leading to disability of sick children.

There are many factors that trigger the development of the disease. The most common are viral or mixed bacterial-viral infection, joint trauma, excessive insolation or hypothermia, preventive vaccinations given against the background of or immediately after an acute respiratory infection (ARI) of viral or bacterial origin [3,11].

It is known that the first years of the disease are decisive in the development and progression of the pathological process. In the earliest period of JRA, when the process is in the primary, exudative phase, the reversibility of the disease is significantly higher due to the autoimmune mechanisms that have not yet fully developed and the absence of pannus - the morphological basis of joint destruction [4,7]. It has been shown that morphological signs of chronic synovitis are observed in the joints already 2-4 months after the onset of the disease.

The results of retrospective studies of JRA reflect the controversial opinions of the authors about the age-related evolution of the disease - the number of patients with continuous progression of the disease varies from 33% to 75%, some researchers believe that only 10-20% of patients have serious disabilities and in most children the disease has a favorable course (1-4). At the same time, the literature also presents negative dynamics of the course of JRA - the development of gross functional deficit in 30% of cases and disability - in 51.5% of patients with various options for debut.

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Research by E.Yu. Yemelyanchik and co-authors (2011) established that the activity of JRA largely determines the nature of the course of the disease: with the first degree of activity, clinical and laboratory remission was noted in 5% of cases and the remaining 95% had a favorable course of the disease; with the second degree, arthritis spread was detected in 43% and eye damage was detected in 12.8%, which required the use of combined basic therapy in 49% of cases and urgent remission induction therapy in 18% of children [4,6].

The development and progression of JRA is determined by a complex combination of genetically determined and acquired defects in regulatory mechanisms that limit pathological activation of the immune system in response to potentially pathogenic, and often physiological, stimuli.

Among the drugs used taking into account the circadian rhythm, corticosteroids attract the most attention. It was for therapy with these hormones that the imitation method was developed, since it was found that minimal changes in the function of the adrenal cortex are noted when corticosteroids are prescribed only in accordance with the natural circadian rhythm of their secretion. When treating with corticosteroids, the opposite direction of action of cortisol and aldosterone in the body is taken into account. In this regard, the activity of mineralocorticoids (pro-inflammatory hormones) can be suppressed by introducing an adequate dose of glucocorticoids (anti-inflammatory hormones) in the second half of the day. Based on information about the circadian rhythm of pro-inflammatory and anti-inflammatory hormones in the body, it can be assumed that NSAIDs have a more pronounced effect in the second half of the day and evening. The chronotherapy method allows increasing the effectiveness of treatment while simultaneously reducing the doses of the drugs used, as a result of which their side effects are reduced and the treatment becomes cheaper.

The aim of the study was to study the clinical and laboratory manifestations of juvenile rheumatoid arthritis and determine prognostic criteria for the outcome of the disease.

Material and methods.

The study involved 364 children aged 3 to 16 years (mean age 11) with juvenile rheumatoid arthritis, including 354 (%) with the articular form and 10 (%) with the systemic variant of the disease. Of the examined patients, 196 (54%) were boys and 168 (46%) were girls. The patients were divided into 2 groups depending on the therapy: the main group consisted of 54 patients who received chronotherapy with nimesulide and the comparison group consisted of 30 patients who received traditional NSAID therapy. The control group consisted of 20 practically healthy children.

The development of the disease may be preceded by trauma, bacterial, viral infection, including acute respiratory viral infection, preventive vaccination, insolation, psychological trauma. The distribution of factors provoking the development of JRA among the patients we observed is presented in Table 1.

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Table 1. Factors that provoke the development of JRA

Factors	Age			
	up to 7 years		over 7 years old	
	abs .	%	abs .	%
Hypothermia	**9**	**10.7**	**36**	**42.8**
Infectious diseases	5	6.0	12	14.3
Injury	-	-	1	1,2
Allergy	4	4.8	6	7.2
Unknown	2	2.4	8	9.5
Total:	**20**	**23.8**	**64**	**76.2**

As can be seen from the table, hypothermia was noted as a provoking factor in most patients of both preschool and school age. Of the infectious diseases, 11 children had severe acute respiratory viral infections, 3 patients had a history of pneumonia in the last 3 months, 2 had acute intestinal infection, and 1 had follicular tonsillitis. Allergy is in third place as a provoking factor: 4 had allergic dermatitis, 3 had food allergy, 2 had drug allergy, and 1 had pollinosis. One child had a knee injury as a provoking factor. It was not possible to identify a provoking factor for 10 children.

It should be noted that in the polyarticular variant of the articular form and the articular-visceral form, the provoking factor was infection, and in the oligo-monoarthritic variants of the articular form, hypothermia was the provoking factor.

Thus, it has been established that the provoking factors in the development of JRA in all age categories in the absolute majority of cases are hypothermia and infection. Prevention and effective treatment of infectious diseases in children is one of the methods of preventing JRA.

When diagnosing JRA, we were guided by the diagnostic criteria of JRA adopted in Russia. The frequency of occurrence of diagnostic clinical criteria of JRA among the patients examined by us is presented in Table 2.

Table 2. Frequency of clinical criteria for JRA

No.	Clinical signs	abs .	%
1	Arthritis lasting 3 months or more	364	100
2	Arthritis of the second joint, which developed after 3 months and later	2 73	86.9
3	Symmetrical lesions of small joints	1 60	71.4
4	Joint contractures	1 40	47.6
5	Tenosynovitis or brucitis	43	51.2
6	Muscle atrophy (usually regional)	15	17.8
7	Morning stiffness	1 68	81.0
8	Rheumatoid eye disease	7	8.3
9	Rheumatoid nodules	19	22.6
10	Joint effusion	55	65.4

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As can be seen from the table, the absolute majority of patients examined by us were characterized by such criteria as arthritis lasting 3 months or more, morning stiffness, arthritis of the second joint occurring 3 months or later, symmetrical damage to small joints, effusion into the joint cavity. Pain, swelling, deformation and limitation of movement, and increased skin temperature were observed in the affected joint. Large and medium joints were most often affected - knee, ankle, wrist, elbow, hip. In 10 (11.9%) patients, damage to the cervical spine was noted.

Clinical manifestations of JRA in the patients we examined were characterized by significant polymorphism of symptoms. Analysis of the anamnesis showed that the first clinical signs of the disease appeared 6 months to 2 years before the diagnosis of the disease.

Result and discussion

The Polyarticular variant of JRA was observed in 35 examined patients, of whom 6 were seropositive for rheumatoid factor. In seropositive subtype was characterized by a subacute onset with symmetrical polyarthritis. As a rule, the joints of the hand and feet were affected. Structural changes in the joints developed in the first 6 months of the disease. By the end of the first year of the disease, ankylosis had formed in the wrist joints of 2 patients. Destructive arthritis developed in 1 patient. According to the literature, this form of JRA is an early debut of rheumatoid arthritis in adults.

Seronegative The subtype had a subacute onset and was also associated with symmetrical polyarthritis. The course of arthritis was relatively benign.

Some features of the articular syndrome were established depending on the form of the disease, the nature of the course of JRA, sex and age of patients. Thus, the articular form of the disease with a subacute onset was accompanied by the development of arthritis with a predominant lesion of the knee and ankle joints (68 and 28%, respectively). Later, the wrist and elbow joints were most often added. In this case, the process progressed moderately and productive changes prevailed. Radiologically, grade II according to Steinbrocker was mainly determined. With an acute onset of this variant of the disease , the wrist, metacarpophalangeal and interphalangeal joints of the hand were most often involved in the process.

Conclusions

1. Based on a set of clinical, laboratory, instrumental and functional research methods, the clinical variant of the disease, its degree of activity, and the characteristics of its course have been clarified. All this is the basis for developing a set of therapeutic measures.
2. The use of a prognostic approach to determine the threat of an unfavorable outcome of JRA is a modern and effective way to prevent disease progression and select the most optimal therapeutic option.

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