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Somatic Status and Clinical Laboratory Manifestations in Patients with Juvenile Idiopathic Arthritis

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Abstract The article presents clinical and laboratory features and prognostic criteria for juvenile rheumatoid arthritis. The clinical features of the disease, the results of laboratory analysis are important when choosing an effective method of treatment. Depending on the severity of the disease, the characteristics of the clinical course and the results of the functional laboratory analysis, drug and surgical treatment of joints is recommended.

Keywords Juvenile rheumatoid arthritis, Somatic status, Breastfeeding, Diagnosis, Prognosis

1. Relevance

Juvenile idiopathic arthritis (JIA) is the most common multifactorial rheumatic disease that develops in children under 16 years of age [1]. The International League of Rheumatological Associations distinguishes 7 variants of JIA: systemic, o Juvenile idiopathic arthritis (JIA) is the most common multifactorial rheumatic disease that develops in children under the age of 16 years [1]. According to multicentre studies, only one third (36%) of newborns in the world are exclusively breastfed during the first six months of life [11]. Breastfeeding frequency varies dramatically across regions and remains resistant to change. Poor nutrition is responsible for 40% of child deaths under the age of five in developing countries every year, and a lack of exclusive breastfeeding and breastfeeding immediately after birth results in an additional 1.5 million child deaths [12,13].

It is known that it is the first years of the disease that 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 still incompletely formed autoimmune mechanisms and the absence of pannus, the morphological basis of articular destruction [4,8]. 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. Numerous studies on the study of JRA have shown that erosive changes in the joints also occur at an early stage. Thus, X-ray examination of 90 patients with early JRA (<1 year) over the next 3 years showed that changes in the joints of the hands and feet occurred during this period in 70% of cases [19,11,21]. According to most recent studies, 25% of patients have erosive changes in the joints as early as the 1st year of the onset of clinical symptoms of JIA [10,12]. The dynamics of clinical and laboratory manifestations of juvenile idiopathic arthritis (JIA) is one of the widely debated difficulties in rheumatology, the relevance of which is clarified by two main factors - the subtleties of the course of the disease in children with different debut options and the effectiveness of various approaches to fundamental therapy. The results of retrospective studies of JIA reflect the scientific and practical statements of reviewers about the age-related evolution of the disease - the number of patients with the incessant development of the disease varies from 33% to 75%, some researchers believe that only 10 - 20% of patients have a serious disability and in most babies the disease acquires a favorable course (1 - 4). At the same time, the literature demonstrates the negative dynamics of the course of JRA, the functioning of a gross functional deficit in 30% of cases and disability - in 51.5% of patients with different ways of debut. Long-term follow-up of patients revealed that an important aspect that characterizes the severity of the condition, the severity of bone destruction and the development of the articular syndrome is the activity of the disease.

Among the drugs used taking into account the daily rhythm, corticosteroids attract the most attention. It was for the therapy with these hormones that a method of imitation 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 daily rhythm of their secretion. In the treatment of corticosteroids, the opposite direction of action in the body of cortisol and aldosterone is taken into account. In this regard, the activity of mineralocorticoids (pro-inflammatory hormones) can be suppressed by the introduction of an adequate dose of glucocorticoids (anti-inflammatory

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hormones) in the afternoon. Based on the data on the daily rhythm of pro-inflammatory and anti-inflammatory hormones in the body, it can be assumed that that NSAIDs have a more pronounced effect in the afternoon and evening. According to Yu.E. Veltishcheva et al. (1995), a single administration of ibuprofen to children with glomerulonephritis in the evening, one to two hours before the transamidinase acrophase, increases their effectiveness and significantly reduces side effects. The conducted analysis of the literature testifies to the aggressiveness and high probability of disability in children with JRA. Traditional therapy of the disease is far from always effective, which dictates the need to search for new effective methods of treating this disease. The method of chronotherapy allows to increase the effectiveness of treatment while reducing the doses of the drugs used, as a result of which their side effects are reduced and the cost of treatment is reduced. a single administration of ibuprofen to children with glomerulonephritis in the evening, one to two hours before the transamidinase acrophase, increases their effectiveness and significantly reduces side effects. The conducted analysis of the literature testifies to the aggressiveness and high probability of disability in children with JRA. Traditional therapy of the disease is far from always effective, which dictates the need to search for new effective methods of treating this disease. The method of chronotherapy allows to increase the effectiveness of treatment while reducing the doses of the drugs used, as a result of which their side effects are reduced and the cost of treatment is reduced. a single administration of ibuprofen to children with glomerulonephritis in the evening, one to two hours before the transamidinase acrophase, increases their effectiveness and significantly reduces side effects. The conducted analysis of the literature testifies to the aggressiveness and high probability of disability in children with JRA. Traditional therapy of the disease is far from always effective, which dictates the need to search for new effective methods of treating this disease. The method of chronotherapy allows to increase the effectiveness of treatment while reducing the doses of the drugs used, as a result of which their side effects are reduced and the cost of treatment is reduced.

2. Purpose of the Study

To study the clinical and laboratory manifestations of juvenile rheumatoid arthritis and determine the prognostic criteria for the outcome of the disease.

3. Material and Methods

Under observation were 164 children aged 3 to 16 years (mean age 11) with juvenile rheumatoid arthritis, of which 154 (%) patients with the articular form, 10 (%) with a systemic variant of the disease. Of the examined patients, 47 (56%) were boys, 37 (44%) were girls. The patients were divided into 2 groups depending on the therapy: 154 patients made up the main group who received chronotherapy with nimesulide and 30 patients on traditional NSAID therapy made up the comparison group. The control group consisted of 20 practically healthy children.

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

Table 1. Factors provoking 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, the majority of patients of both preschool and school age had hypothermia as a provoking factor. Of the infectious diseases, 11 children had a severe course of acute respiratory viral infections, 3 patients had a history of pneumonia in the last 3 months, 2 had an acute intestinal infection, and 1 had follicular tonsillitis. In third place as a provoking factor is allergy: 4 - allergic dermatitis, 3 - food allergy, 2 - drug allergy and 1 - polynosis. In one child, a knee joint injury was noted as a provoking factor. In 10 children, it was not possible to identify the provoking factor of the disease. It should be noted that whenIn the polyarticular variant of the articular form and the articular-visceral form, the provoking moment was infection, and in the oligo-monoarthritic variants of the articular form, hypothermia was the provoking factor.

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

When making a diagnosis of JRA, we were guided by the diagnostic criteria for JRA adopted in Russia. The frequency of occurrence of diagnostic clinical criteria for JRA among the patients examined by us are presented in Table 2.

As can be seen from the table, for the absolute majority of the patients examined by us, such criteria as arthritis lasting 3 months were characteristic. and more, morning stiffness, arthritis of the second joint, which arose after 3 months. and later, symmetrical damage to small joints, effusion into the joint cavity. In the affected joint, pain, swelling, deformity and limitation of movement, and an increase in skin temperature were noted. Large and medium joints were more often affected - knee, ankle, wrist, elbow, hip. In 10 (11.9%) patients, lesions of the cervical spine were noted.

Table 2. Frequency of occurrence of JRA clinical criteria

No.	Clinical signs	abs.	%
1	Arthritis lasting 3 months. and more	164	100
2	Arthritis of the second joint, which arose after 3 months. and later	73	86.9
3	Symmetric lesion of small joints	60	71.4
4	Joint contractures	40	47.6
5	Tenosynovitis or brucite	43	51.2
6	Muscular atrophy (often regional)	15	17.8
7	morning stiffness	68	81.0
8	Rheumatoid eye disease	7	8.3
9	Rheumatoid nodules	19	22.6
10	Effusion in the joint cavity	55	65.4

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

At the onset of the disease, the absolute majority (86.9%) of the patients examined by us showed a deterioration in the general condition: weakness, morning stiffness, arthralgia, weight loss, low-grade fever. All these symptoms, as a rule, preceded the clinically pronounced damage to the joints. In addition, 58.3% of patients with active articular syndrome had extra-articular manifestations: the development of atrophy of the muscles located in the proximal joint involved in the pathological process, general dystrophy, growth retardation.

4. Result and Discussion

The polyarticular variant of JRA was noted in 35 examined patients, of which 6 were seropositive for rheumatoid factor. In the seropositive subtype, a subacute onset with symmetrical polyarthritis was noted. 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 developed in the wrist joints in 2 patients. One patient developed destructive arthritis. According to the literature, this form of JRA is an early onset of adult rheumatoid arthritis.

The seronegative subtype had a subacute onset, with symmetrical polyarthritis also noted. The course of arthritis was relatively benign.

Some features of the articular syndrome have been established depending on the form of the disease, the nature of the course of JRA, the sex and age of the 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). In the future, the wrist and elbow joints joined more often than others. At the same time, the process progressed moderately and productive changes prevailed. X-ray was determined mainly II degree according to Steinbrokker. In the acute onset of this variant of the disease, the wrist, metacarpophalangeal and interphalangeal joints of the hand were more often involved in the process.

The articular-visceral form was noted in 10 patients examined by us and was clinically characterized by a high temperature reaction, which was intermittent in nature and did not decrease during antibiotic treatment. Against the background of fever, patients developed a polymorphic rash of a bright pink color. Characteristic was the increase in all groups of peripheral lymph nodes. Several joints were involved in the process - knee, ankle, elbow, neck. All joints were painful and swollen. There was an increase in the size of the liver and spleen.

In 4 patients, the disease proceeded with kidney damage, in 3 patients with heart damage, in 1 with lung damage, in 2 - combined lesions of internal organs were noted. In 1 girl of preschool age, the disease proceeded according to the type of Still's syndrome, and in 1 boy, according to the type of Wissler-Fanconi syndrome. In systemic forms, the articular syndrome also had its own distinctive features. So, in one patient with an allergic-septic variant, the disease began with persistent arthralgia in large (knee, hip) and medium (ankle, wrist and elbow) joints without visible changes in them. The duration of the period of arthralgia without distinct signs of arthritis was 1.5 months in this patient. Then joined exudative and productive changes in the joints with the rapid development of usuration and erosion. The articular syndrome in Still's disease was presented most fully. One sick girl with this form of the disease at the earliest stages developed a generalized articular syndrome involving the joints of the hand, foot, cervical spine, maxillotemporal, as well as larger joints. The initial exudative phase rather quickly, over 2-3 months, was replaced by productive processes, erosion and cartilage destruction, which led to early ankylosis in the wrist joints.

In the laboratory diagnosis of JRA, we relied on a clinical blood test, the definition of rheumatoid factor. The degree of JRA activity according to laboratory criteria proposed by Nasonova V.A., (1997) was assessed as follows: 0-ESR up to 12 mm/hour, CRP not detected, I- ESR 13-20 mm/hour, CRP weakly positive (+), II - ESR 21-39 mm/h, CRP positive (++), III- ESR 40 mm/h or more, CRP strongly positive (+++, ++++).

Table 3. The frequency of occurrence of JRA radiological criteria

stages	signs	abs.	%
1	Epiphyseal osteoporosis	53	63.1
2	Narrowing of the joint space, single erosion	27	32.1
3	Destruction of cartilage and bone	3	3.6
4	Fibrous and bone ankylosis	1	1.2

Of the instrumental methods of research, we conducted an X-ray examination, which allows us to judge the degree of damage to the joints and determine the stage of anatomical changes in accordance with the criteriaSteinbrocker. In the first months of the disease, the main radiographic indicator is

epiphyseal osteoporosis, small cystic restructuring of the bone structure of the epiphysis. Then erosion appears. The frequency of occurrence of JRA radiological criteria according to the Steinbrokker criteria is presented in Table 3.

As can be seen from the table, half of the patients examined by us had the first stage of anatomical changes according to Steinbrokker, i.e. - epiphyseal osteoporosis, in 1/3 of the patients we noted narrowing of the joint space and the presence of single erosions. Cartilage and bone destruction occurred in three patients with a disease period of more than 3 years. Ankylosis was formed in one sick girl with Still's syndrome.

Therapy of various forms of JRA, especially severe, progressive ones, is not an easy task, requiring the joint efforts of a doctor, a sick child, his parents and the family as a whole. Effective therapy leads to the achievement of remission of the disease and an improvement in the quality of life of the patient. The emergence in recent years of new biological agents (infliximab, etanercept, rituximab, adalimumab, etc.), which significantly affect the course of the disease, and the first experience of using some of them gives hope for improving the outcome of the disease.

We have developed algorithms for predicting the state of health of schoolchildren. In the table 3 above, compiled on the basis of Wald's sequential analysis, each of the features has its own numerical value with a (+) or (-) sign. The numerical threshold for making a certain conclusion (with 95% probability) is equal to±13. It is obtained by algebraically adding the prognostic coefficients of each feature proposed in the table. When forecasting, it is assumed as the main condition that the student will be in some standard conditions of existence, receive currently generally accepted drugs for the treatment of diseases, etc. and for the better.

In the presented algorithms, approximately 5% forecast error is planned. The discrepancy between the forecast and reality is due to two reasons. First, at the time of making the forecast, all influencing factors are not taken into account; secondly, the child's health is influenced by factors that joined later, are not acting and therefore are not taken into account at the time of making the forecast. It is quite clear that if the doctor can take into account these factors from the first stage of the examination and anticipate their appearance, the accuracy of the forecast increases.

A poor prognosis in JRA also means radiographic progression of joint destruction, the formation of an irreversible decrease in the function of the musculoskeletal system, an increase in the risk of the need for surgical operations on the joints and a decrease in the life expectancy of patients. Predicting an unfavorable outcome is not fatally inevitable, it should mobilize all the forces and means of modern medicine to prevent such an outcome.

5. Conclusions

1. On the basis of a complex of clinical-laboratory-instrumental and functional research methods, the clinical variant of the disease, its degree of activity, and course features were specified. All this is the basis for the development of a complex 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 the progression of the disease and choose the most optimal variant of therapeutic tactics.
3. The nature of feeding and care in infancy due to changes in the immune system, metabolism and related morbidity leads to a regression in the health status of children who did not receive the proper amount of mother's milk, which is expressed in the predominance of mixed and especially artificial feeding of children in groups II and III group of dispensary observation, and by the age of 14 in the group of children with artificial feeding there are also patients belonging to group IV - children with chronic diseases in the stage of subcompensation. All this emphasizes the role of breastfeeding and modern methods of care in the period up to 1 year of age in the prevention of morbidity in older children.

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