ISSN NO: 2770-0003
November 2024

Characteristics Of Genetic Predisposition To The Development Of Juvenile Idiopathic Arthritis In Children.

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Summary
The article presents clinical laboratory features and prognostic criteria of juvenile rheumatoid arthritis. The clinical characteristics of the disease and the results of laboratory analysis are important in choosing an effective treatment method. Medicinal and surgical treatment of joints is recommended, depending on the severity of the disease, the characteristics of the clinical flow and the results of the functional laboratory analysis.
Keywords: juvenile rheumatoid arthritis, diagnostics, prognosis.

Relevance.

Juvenile rheumatoid arthritis (JRA) is a destructive inflammatory disease of joints with unknown etiology, complex immunogenic pathogenesis, characterized by symmetric chronic arthritis, systemic lesions of internal organs, which leads to the disability of sick children. Improving the effectiveness of treatment for this disease is therefore a highly topical issue in terms of both scientific and practical pediatrics. There are many factors that trigger the disease. The most frequent are viral or mixed bacterial-viral infection, joint injury, excessive or supercooling insolation, prophylactic inoculations carried out against the background or immediately after the acute respiratory infection of a viral or bacterial nature [3,11].

It is known that it is the early years of the disease that are decisive in the development and progression of the pathological process. In the earliest period of the JRA, when the process is in the primary, exudative, phase, the reversibility of the disease is significantly higher due to the still-inconclusive autoimmune mechanisms and the absence of a pannus, the morphological basis of the joint destruction [4,8,9,12,14]. It has been shown that within 2-4 months of the onset of the disease, there are morphological signs of chronic synovitis in the joints. Numerous studies of the JRA have shown that erosion changes in joints also occur at an early stage. For example, an X-ray examination of 90 patients with early (<1 year) Over the next three years, it was found that changes in the joints of the brushes and the stop occurred in 70% of cases [3,7,23,24,27]. According to most recent studies, 25% of patients have erosive joint changes already in the first year of the onset of clinical symptoms of the JRA [10, 12]. Clinical dynamics - laboratory manifestations of juvenile rheumatoid arthritis (JRA) - one of the widely debated difficulties of JRA rheumatology, The relevance of which is explained by two main factors - the subtleties of the disease in babies with different debut variants and the effectiveness of all possible approaches of basic therapy. The results of the retrospective studies of the ADP reflect the scientific and practical statements of reviewers on the evolution of the disease - the number of patients with continuous development of the disease ranges from 33% to 75%, some researchers estimate that only 10 - 20% of patients have the most severe disability, and most infants have a favorable illness (1-4). At the same time, the literature also shows the negative dynamics of the JRA - the functioning of gross functional deficiency of 30% of cases and disability - in 51.5% of patients with different debuts. Prolonged follow-up has revealed that an important aspect of the severity of the condition, the severity of bone decay and the development of articular syndrome is disease activity.

Corticosteroids attract the most attention among daily rhythms. It was for these hormones that a simulation method was developed, as it was found that minimal changes in adrenal corticosteroid function are observed when assigned corticosteroids only in accordance with the natural daily rhythm of their secretion. The treatment of corticosteroids takes into account the opposite direction of action in cortisol and aldosterone. Therefore, the activity of mineralocorticoids (pro-inflammatory hormones) can be suppressed by the introduction in the afternoon of an adequate dose of glucocorticoids (anti-inflammatory hormones). Based on information on the daily rhythm of inflammatory and anti-inflammatory hormones in the body, it can be assumed that Nsaids have a more pronounced effect in the afternoons and evenings. According to Y.E.

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Veltisheva and co-op. (1995) The one-time appointment of ibuprofen to children with glomerulonephritis in the evening, one to two hours before the acrophase of Transamidinase, increases their efficiency and significantly reduces side effects. An analysis of the literature shows the aggressiveness and high probability of disability of children with JRA. Traditional disease therapy is far from being effective, necessitating the search for new and effective treatments for the disease. The chronotherapy method makes it possible to increase the effectiveness of the treatment while simultaneously reducing the doses of the drugs used, thereby reducing their side effects and making the treatment cheaper.

Purpose of the study. Study clinical and laboratory manifestations of juvenile rheumatoid arthritis and determine predictive outcome criteria.

Material and methods.

Eighty-four children between the ages of 3 and 16 (average age 11) with rheumatoid arthritis were monitored, of whom 74 (per cent) were articular and 10 (per cent) were systemic. Of the cases examined, 47 (56 per cent) were boys and 37 (44 per cent) were girls. The patients were divided into two groups depending on the treatment provided: 54 patients constituted the main group that received chronotherapy by nimesulide and 30 patients with traditional therapy Nsaids formed a comparison group. The control group consisted of 20 practically healthy children.

The development of the disease may be preceded by trauma, bacterial and viral infection, including ARI, preventive vaccination, insolation, psychological trauma. The distribution of the factors causing the development of the JRA among the patients we observe is shown in Table 1.

Table 1.
Triggering factors of the JRA

Factors	Age			
	up to 7 years		over 7 years of age	
	abs.	%	abs.	%
Hypothermia	**9**	**10.7**	**36**	**42.8**
Infectious diseases	5	6.0	12	14.3
Trauma	-	-	1	1.2
Allergy	4	4.8	6	7.2
Unknown	2	2.4	8	9.5
In total:	**20**	**23.8**	**64**	**76.2**

As can be seen from the table, hypothermia has been observed as a provocative factor for most patients of both pre-school and school age. Of the infectious diseases, 11 had severe ARI, 3 had anamnesis from pneumonia in the last 3 months, 2 had acute intestinal infection and 1 had follicular angina. In third place, allergies are the trigger factor: allergic to 4, allergy to 3, allergy to 2, and polynosis to 1. One child suffered a knee injury as a contributing factor. Ten children failed to identify the causative factor of the disease. It should be noted that in the polyarticular variant of the articular shape and the joint-visceral shape, the stimulating moment was the infection, and in the oligo-monoarthritic variants of the articular shape, hypothermia was the provocative factor.

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

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

Table 2.
Frequency of JRA clinical criteria

№	Clinical signs	abs.	%

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1	Arthritis lasting 3 months. and more	84	100
2	Arthritis of the second joint, 3 months later. And	73	86.9
3	Symmetrical joint failure	60	71.4
4	Joint contracts	40	47.6
5	Tendosinovite or bruvit	43	51.2
6	Muscular atrophy (more commonly regional)	15	17.8
7	Morningness	68	81.0
8	Rheumatoid eye disease	7	8.3
9	Rheumatoid knots	19	22.6
10	Elbow in the joint	55	65.4

As can be seen from the table, the vast majority of the patients we examined had 3-month arthritis. And more, the morning shudder, the arthritis of the second joint, which appeared after three months. and later, symmetrical small joint lesions, effed into the joint cavity. The joint suffered pain, swelling, deformation and restriction of movement, and increased skin temperature. More frequent were the large and middle joints - knee, ankle, radius, ulna, hip. In 10 (11.9%) patients suffered a lesion of the cervical spine.

Clinical manifestations of the JRA in the patients we examined were characterized by significant polymorphism of symptoms. Anamnesis analysis showed that the first clinical signs of the disease appeared within 6 months-2 before the diagnosis of the disease.

In the debut of the disease, the absolute majority (86.9%) of the patients we examined showed a worsening of the general condition: weakness, morning curiosity, arthralgia, loss of weight, subfebrile fever. All of these symptoms usually preceded a clinically pronounced joint injury. In addition, 58.3 per cent of patients with active articular syndrome had extraarticular manifestations: development of atrophy of muscles located proximal joints involved in the pathological process, general dystrophy, stunting.

Result and discussion

The polyarticular variant of the JRA was observed in 35 patients examined, of which 6 were seropositive for the rheumatoid factor. In the seropositive subtype, the start with symmetric polyarthritis was noted. The wrist and foot joints were usually affected. Structural changes in the joints developed during the first six months of the disease. By the end of the first year, diseases in the joints of the wrist formed ankylosis in two patients. One patient developed destructive arthritis. According to literature, this form of JRA is the early debut of adult rheumatoid arthritis.

The seronegative subtype had a sub-prime, with symmetric polyarthritis. The arthritis flow was relatively benign.

Some features of articular syndrome have been identified, depending on the type of disease, the nature of the JRA, sex and age of the patients. Thus, the joint form of the disease with a posterior onset was accompanied by the development of arthritis with a higher incidence of knee and ankle joints (68 and 28 per cent respectively). Later, radial and ulnar joints were the most common. The process was moderately progressive and productive changes prevailed. Radiologically, the Steinbrocker II degree was determined. At the acute onset of this variant, the diseases were most often involved in the process of radiated-carpal, metacarpal-phalanx and interphalanx joints of the brush.

The joint-visceral form was observed in 10 of the patients we examined and was characterized by a high temperature reaction, which was intermittent and did not decrease when treated with antibiotics. The fever was accompanied by a polymorphic rash of bright pink. All groups of peripheral lymph nodes have increased. Several joints were involved - knee, ankle, elbow, neck. All the joints were painful and swollen. There was an increase in liver and spleen size.

Four patients suffered from kidney damage, three suffered from heart damage, one suffered from lung damage and two suffered from a combination of internal injuries. One preschool girl had Still syndrome, and one boy had Wissler-Fancony syndrome. In systemic forms, articular syndrome also had its own distinctive features. For example, in one patient with an allergy-septic variant, the disease began with persistent arthralgia in large (knee, hip) and medium (ankle, radius and ulna) joints without any visible changes. The length of the period of

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arthralgia without clear signs of arthritis was 1.5 months for the patient. Then came the exudative and productive changes in joints with the rapid development of the usures and erosion. The most comprehensive presentation was of articular syndrome under Still's disease. One sick girl developed generalized articular syndrome at the earliest stages, involving the joints of the hand, foot, cervical spine, jaw-temporal, and larger joints. The initial exudative phase was quickly replaced by two to three months of production, erosion, and destruction of cartilage, which led to early ankylosis in the radial joints.

In the laboratory diagnostics of the JRA, we were based on a clinical blood test, a determination of the rheumatoid factor. The level of activity of the JRA according to the laboratory criteria proposed by Nasonova V.A., (1997) was estimated as follows: 0-OCE up to 12 mm/h, DRR not determined, I-OCE 13-20mm/h, DRR slightly positive (+), II-OCE 21-39 mm/h, DRR positive (++), III-OCE 40 mm/h and above, BDS is strongly positive (++, ++++).

We have conducted an X-ray examination of the instrumentation methods, which makes it possible to determine the degree of joint damage and to determine the stage of anatomical changes according to the Steinbrocker criteria. In the first months of the disease, the main radiological indicator is epiphyseal osteoporosis, a fine-cystic reconstruction of bone structure of epiphysis. Then you get erosion. The frequency of occurrence of the JRA x-ray criteria according to the Steinbrocker criteria is given in Table 3.3.2.

Table 4.
Frequency of JRA x-ray criteria

Stages	Signs	abs.	%
1	Epiphyseal osteoporosis	53	63.1
2	Joint cleft constriction, single erosion	27	32.1
3	Destruction of cartilage and bone	3	3.6
4	Fibrous and bone ankylosis	1	1.2

As can be seen from the table, half of the patients we examined had the first stage of anatomical changes for Steinbrocker, i.e. epiphyseal osteoporosis, and in 1/3 patients we found that the joint slit was constricted and that there was single erosion. Destruction of cartilage and bone occurred in three patients with a disease lasting more than three years. Ankylosis formed in a sick girl with Still syndrome.

The treatment of various forms of ADR, particularly severe and progressive, is a complex task requiring the joint efforts of the doctor, the sick child, his parents and the family as a whole. Effective therapy leads to the achievement of remission of the disease and improvement of the patient's quality of life. The emergence in recent years of new biological agents (infilksimab, ethanercept, rituksimab, adalimumab, etc.) that have a significant impact on the course of the disease, and the first experience with some of them offers hope for improving the outcome of the disease.

We have developed algorithms for predicting the health of schoolchildren. In Table 5 of Wald's successive analysis, each topic has a numerical value with a (+) or (-)sign. The numerical threshold for accepting a certain conclusion (with 95% probability) is 13. It is obtained by the algebraic addition of the predictive coefficients of each proposed topic in the table. In forecasting, it is assumed as a basic condition that the student will be in some standard living conditions, receive the drugs currently accepted for the treatment of diseases, etc., is excluded and, more precisely, partially relates to the error of the forecast, deviations, for better or worse.±

In the presented algorithms, about 5% of the prediction error is planned. The difference between the forecast and the reality is due to two reasons. First, all factors are not taken into account at the time of projection; Second, the health of the child is affected by factors that have subsequently joined, are not in force and therefore are not taken into account at the time of projection. It is understandable that if a physician can take these factors into account and foresee their occurrence from the first stage of the examination, the accuracy of the forecast increases.

Presence of prognostically unfavourable features: active disease (large number of painful and swollen joints), presence of erosion at an early stage, The increase in the Russian Federation, the increase in the EPR and/or the DRR gives reason to predict the progression of the disease and the high risk of the patient's

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disability. Poor prognosis in the JRA also means x-ray progression of joint decay, formation of irreversible reduction of the function of the supporting motor apparatus, increased risk of joint surgery and reduced patient life expectancy.

Predicting an adverse outcome is not fatal; it must mobilize all the forces and means of modern medicine to prevent such an outcome.

Conclusions.

1. On the basis of the complex of clinical-laboratory and instrumental and functional methods of investigation, the clinical variant of the disease, the level of its activity and the features of the current have been clarified. This is the basis for the development of a range of treatment measures.
2. Applying a predictive approach to determining the threat of adverse outcome of the ADP is a modern and effective way of preventing disease progression and choosing the most appropriate therapeutic tactic option.

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