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Pharmacodynamics of Drugs Used in Rheumatism in Young Children

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Abstract: Rheumatism or acute rheumatic fever according to the International Classification of Diseases (ICD) is a systemic inflammatory disease of connective tissue with the main localization of the process in the cardiovascular system, and in people prone to it develops in connection with acute streptococcal infection. mostly 7-15 years old. Although not a common disease, rheumatism is a serious problem in cardiorheumatology due to the frequent formation of heart defects and the development of temporary and permanent disability. According to ICD-10, acute rheumatic fever is classified as a disease of the circulatory system (class IX) under the following codes: Rheumatism was known in the 5th century BC. Hippocrates wrote in his "Four Books of Diseases": "With arthritis, fever occurs, sharp pains grip all the joints of the body, and these pains sometimes die. sharper, sometimes weaker, affecting the first or other joints." In ancient times, doctors believed that inflammation in the joints was caused by some toxic fluid circulating throughout the body. The name of the disease comes from here - "rheumatism" (Greek "rheum" - flow). Damage to the cardiovascular system was considered a complication of articular syndrome. Only after the publication of the wonderful works of the French doctor Buyot (1836) and the Russian doctor IG. Sokolsky (1838), rheumatism was defined as an independent disease associated with heart damage.

Key words: Etiology, Pathogenesis, Pharmacokinetics, Prevention.

For more than a century and a half, the study of this severe, often disabling disease, the relationship between its development and streptococcal infection was determined, a system of diagnosis, treatment and prevention was developed, and the current done. This contributed to a widespread decline in the incidence of rheumatism by the middle of the 20th century. However, in recent years, due to a number of negative socio-economic processes, the incidence of rheumatism has increased in all age groups and in children. This trend is also associated with the presence of secular rhythms characteristic of aggressive streptococcal infections and a decrease in the susceptibility of streptococci to penicillins. The study of the dynamics of the epidemic process shows that streptococcal infection has appeared and is growing in the last decade, which is similar to the previous period and contributes to the increase and exacerbation of rheumatism. Therefore, the problem of rheumatism will not lose its relevance in the future.

Etiology and pathogenesis

The development of rheumatism is closely related to a previous acute or chronic nasopharyngeal infection caused by group A beta-hemolytic streptococci. A special role is given to protein M, which is part of the streptococcal cell wall. Of the more than 80 known types of M protein, M-5, M-6, M-18, and M-24 are called rheumatogenic. In this case, a stable hyperimmune response to various streptococcal antigens is determined by the formation of antibodies - antistreptolysin O (ASL-O), antistreptohyaluronidase (ASH), antideoxyribonuclease, etc.

An important role is played by genetic factors, which is confirmed by the frequent occurrence of the disease in children in families with one of the parents suffering from rheumatism. The importance of genetic factors is confirmed to a certain extent by the results of the study of the association of

histological compatibility antigens, which revealed that Dr5-Dr7, Cw2-Cw3, and a number of other diseases are frequent in patients with various forms. rheumatism. The genetic marker of this disease, according to a number of researchers, is the B-lymphocyte alloantigen, which is detected with the help of D8/17 monoclonal antibodies at a high frequency both in patients with rheumatism and in their close relatives. It is associated with a hyperimmune response to streptococcal antigen.

In the pathogenesis of rheumatism, the direct or indirect harmful effect of streptococcal components and its toxins on the body with the development of immune inflammation is not insignificant. Anti-streptococcal antibodies (molecular mimics) interacting with heart tissue are responsible for selective damage to heart valves and myocardium with the development of immune aseptic inflammation.

Morphological changes reflect systemic disorganization of connective tissue, especially specific necrotic-proliferative reactions (Ashoff-Talalaev granulomas) and non-specific exudative manifestations of the cardiovascular system. The latter is more obvious in childhood, which determines the greater (compared to adults) severity and activity of the process, the severity of carditis and other manifestations of rheumatism.

Rheumatism in children is characterized by different clinical manifestations and variability of the course. As a rule, it occurs at school age, less often in preschool children, and almost never occurs in children under 3 years of age.

Usually, the initial symptoms of rheumatism are detected 2-3 weeks after tonsillitis, febrile pharyngitis, signs of intoxication, articular syndrome, carditis and other manifestations of the disease. In addition, the disease can begin asymptomatically with the appearance of fatigue, low-grade fever, if there are no significant disorders of the joints or the heart, this can be mistakenly considered as a residual effect of a previous infection.

Joint syndrome

One of the first signs of rheumatism is joint syndrome (arthritis or arthralgia), which is detected in 60-100% of affected children. Rheumatoid arthritis is characterized by acute onset, involvement of large or medium joints (usually knee, ankle, elbow) in the form of mono- or oligoarthritis, variability of the lesion and rapid reversal of the process. Articular syndrome develops separately at the beginning of the disease in relatively rare cases;

Heart damage

Symptoms of heart damage (carditis) in 70-85% of cases at the beginning of the disease and slightly more during subsequent attacks depend on the predominant localization of the process in the myocardium, endocardium and the degree of involvement; of the pericardium. The term "rheumatic carditis" is used in practice due to the difficulty in identifying the signs of damage to this or that mucous membrane of the heart.

Complaints of a cardiac nature (pain in the heart, palpitations, shortness of breath) are mainly observed in children with severe heart diseases. Often, especially at the beginning of the disease, various asthenic manifestations (lethargy, restlessness, increased fatigue) are observed.

The first objective signs of rheumatic carditis: heart rate disturbances (tachycardia, less often - bradycardia); an increase in the size of the heart, mainly to the left; suffocation of heart sounds, appearance of systolic murmur.

The nature of the systolic murmur and its localization are determined by the degree of participation of the myocardium and endocardium in the process. With myocarditis, the murmur is usually weak or moderate and rarely goes outside the heart. In rheumatism (valvulitis) with endocarditis, which is the most characteristic lesion of the mitral valve, the systolic murmur is heard at the peak and at Botkin's point, which is maximally elongated, on the left side and during exercise, it increases outside the heart. . This is mitral valve valvulitis, which plays a key role in the formation of heart valve defects, the development of which can be determined 6 months before the onset of the

disease. The development of rheumatic carditis can be accompanied by circulatory failure, usually does not exceed the I stage.

With rheumatic carditis, ECG often shows rhythm disturbances (tachy- or bradyarrhythmia, pacemaker migration, sometimes extrasystole, atrial fibrillation), slowing of atrioventricular conduction, mainly I degree, ventricular electrolysis and prolongation.

The phonocardiogram (PCG) records a decrease in the amplitude of the first tone at the apex and an increase in the amplitude of the third and fourth sounds. In the case of myocarditis, FCG detects a systolic murmur that is not related to the first sound, is variable in different heart cycles and has a medium-amplitude, medium-frequency character. Mitral valve valvulitis is manifested by high-frequency pansystolic or protosystolic noise of different amplitudes.

Radiologically, along with the expansion of the heart, which is not always clear, signs of a decrease in the tonic and contractile function of the mitral (with mitral valve valvulitis) or aortic (with damage to the aortic valve) configuration of the heart are revealed.

During echocardiography, thickening of the leaflets of the affected valves, a "shaggy" echo, a decrease in their excursion, signs of impaired myocardial contraction function, and a number of other symptoms are detected. Children can also develop pericarditis with rheumatic carditis, its clinical appearance is less pronounced than instrumental signs on ECG and especially EchoCG.

Currently, with timely treatment, primary rheumatic carditis in most children ends with recovery. Often, with the development of mitral insufficiency, the formation of heart valve defects is detected in 15-18% of cases during the first attack, mainly in the severe, long-term or hidden course of the disease.

According to the recommendations of the American Heart Association (AHA), heart defects often appear in a combined form with repeated attacks, which are considered as a new episode of acute rheumatic fever, rather than a recurrence of the first one. and/or combined valvular lesions, reaching 100%. As a result of rheumatic carditis, the formation of mitral (less often aortic) valve prolapse, the development of myocardiosclerosis with rhythm and conduction disturbances (extrasystole, atrial fibrillation, complete atrioventricular block), as well as adhesive pericarditis are possible. . Severe rheumatic carditis, its recurrence, the presence of myocardiosclerosis and heart defects contribute to the development of permanent heart failure, which leads to disability and death in patients.

Small chorea is characteristic for rheumatism in childhood, it occurs in 12-17% of cases, mainly in early puberty and in girls. Classic symptoms of minor chorea: hyperkinesia, hyper- or hyporeflexia, muscle hypotonia, impaired coordination of movements, changes in psychological status and various autonomic disorders.

The disease begins acutely or often gradually. Children develop emotional lability, irritability, mood swings, tears, inattention, memory loss, and learning disabilities. In the objective examination, it is determined by involuntary twitching of the muscles of the face and limbs, smiling, swaying, awkward movements; slurred, slurred speech, changes in handwriting, difficulty walking, eating, dressing, and learning. Hyperkinesis often has a bilateral character, increases with excitement, weakens until it stops completely during sleep.

Often, small chorea precedes the development of rheumatic carditis or continues without obvious disturbances in cardiac activity and is characterized by a torpid course and a tendency to relapse.

Other symptoms

Less common symptoms of rheumatism include annular rash and rheumatic nodules.

Annular rash (erythema annulare) is a pale pink, pale rash that does not rise above the surface of the skin and disappears with pressure. It is found in 7-10% of children with rheumatism, mainly at the height of the disease, and is usually unstable.

Subcutaneous rheumatic nodules are round, dense, inactive, painless, one or more formations located in the area of large and medium joints, spines, tendons and spinal processes of the aponeurosis. Currently, they are rare, mainly in severe forms of rheumatism, lasting from a few days to 1-2 months.

Abdominal syndrome, damage to the lungs, kidneys, liver and other organs due to rheumatism in children is now very rare, mainly in severe cases.

Laboratory indicators

In patients with rheumatism, laboratory parameters reflect the symptoms of streptococcal infection, the presence of inflammatory reactions, and the immunopathological process. In the active phase, the following are determined: leukocytosis with a shift to the left, increased ESR and often anemia; increased reaction of seromucoid, diphenylamine; dysproteinemia with hypergammaglobulinemia; An increase in ASH, ASLO titers, an increase in class A, M and G immunoglobulins; C-reactive protein (CRP), circulating immune complexes, anticardiac antibodies.

Diagnostics

It is known that there are no special tests for the diagnosis of rheumatism. In practice, they use the syndromic method to assess the patient's condition, the principle of which was proposed by the local pediatrician AAKisel in 1940. The author identified syndromes such as migratory polyarthritis, carditis, chorea, annular erythema and rheumatic nodules, which are pathognomonic for rheumatism as the main diagnostic criteria. Later, AI Nesterov made additions to the criteria, and for a long time doctors used the Kisel-Jones-Nesterov criteria to diagnose rheumatism. Later, this scheme was repeatedly changed, and currently, in accordance with WHO recommendations, the Jones diagnostic criteria revised by AKA in 1992 are used as the international criteria for acute rheumatic fever.

The detection of two major or one major and two minor criteria in a patient, together with information documenting a previous infection with group A streptococci, indicates a high probability of acute rheumatic fever. However, nosological diagnosis causes certain difficulties in the case of vague and non-specific symptoms in the early stages.

The final diagnosis is often determined after dynamic monitoring of the patient with a full differential diagnosis and evaluation of the results of therapy.

Differential diagnosis

Differential diagnosis of rheumatism is carried out with a large group of diseases and diseases that occur with joint syndrome (reactive arthritis, juvenile rheumatoid arthritis, Lyme disease, leukemia, neoplastic processes); with a number of inflammatory diseases of the heart (non-rheumatic carditis, infectious endocarditis); congenital and acquired disorders of the heart structure (mitral valve prolapse, congenital mitral valve insufficiency or abnormality of its development); autonomic dystonia syndrome. The diagnosis of minor chorea primarily requires the exclusion of chorea in children with thycoid hyperkinesis, Tourette's syndrome, and systemic lupus erythematosus.

Determination of the level of activity of the process (I, II, III) is carried out taking into account the severity of clinical and laboratory manifestations. The acute course reflects the rapid development of rheumatism, polysyndromic nature and bright clinical and laboratory manifestations (duration - 2-3 months). The subacute course (in the beginning) can be similar to the acute one or is characterized by a slower onset of the disease, less specific clinical and laboratory manifestations (duration - up to 6 months). Prolonged course is characterized by symptoms of moderate activity, torpidity of therapy (duration - more than 6 months). With a reversible course, polysyndromic nature, severity of clinical manifestations and relapses are noted. The latent course is characterized by the development of heart diseases without signs of process activity.

Treatment

Treatment of rheumatism in children is based on the early application of complex therapy aimed at suppressing streptococcal infection and the activity of the inflammatory process, preventing the development or progression of heart diseases. The implementation of these programs is carried out according to the principle of stages: 1st stage - inpatient treatment, 2nd stage - further treatment in the local cardio-rheumatological sanatorium, 3rd stage - dispensary observation in the clinic.

Stage 1

In the hospital, at the 1st stage, the patient is prescribed drug treatment (antibacterial, antirheumatic and symptomatic), nutritional correction and physical therapy, which are determined individually, taking into account the characteristics of the disease and, first of all, the severity of carditis. Due to the streptococcal nature of rheumatism, etiotropic therapy is carried out with penicillin. Antirheumatic therapy includes non-steroidal anti-inflammatory drugs (NSAIDs), which are prescribed alone or in combination with glucocorticosteroid hormones (GCS), depending on the indications (Table 3).

Antibacterial therapy with penicillin is carried out for 10-14 days. In the case of chronic tonsillitis, frequent exacerbations of focal infection, the duration of treatment with penicillin is increased or other antibiotics are additionally used - amoxicillin, macrolides (azithromycin, roxithromycin, clarithromycin), cefuroxime axetil and other cephalosporins. special dosage.

NSAIDs are used for at least 1-1.5 months until the symptoms of process activity disappear. Prednisolone is prescribed at the initial dose for 10-14 days until the clinical effect is obtained, then the daily dose is reduced by 2.5 mg every 5-7 days under the control of clinical and laboratory indicators, and then the drug is stopped.

The duration of treatment with quinoline drugs for rheumatism lasts from several months to 1-2 years or more, depending on the course of the disease.

Chronic infection foci are also rehabilitated in hospital conditions, in particular, tonsillectomy is performed 2-2.5 months after the onset of the disease if there are no signs of process activity.

Stage 2

The main task in the second stage is to achieve complete remission and restore the functional capabilities of the cardiovascular system of children with rheumatism. In the sanatorium, the therapy started in the hospital is continued, the foci of chronic infection are neutralized, and the appropriate treatment and rehabilitation regime is implemented with differentiated physical activity, physiotherapy, and exercise procedures.

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