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THE IMPORTANCE OF SECONDARY PREVENTION IN SYSTEMIC SCLERODERMA

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Abstract:

Aim of the study: Systemic scleroderma is a multisystemic disease involving skin and internal organs (gastrointestinal tract, lungs, heart, kidneys, and peripheral nervous system). The pathogenesis of the disease includes dysfunction of the endothelium, epithelium, fibroblasts, as well as activation of the immune system and inflammatory mediators. In addition, the disease is characterized by impaired angiogenesis. Vasculopathy is the basis of pulmonary arterial hypertension, renal pathology, and digital ulcers. This article is devoted to a review of the diagnosis of systemic scleroderma, consideration of its secondary preventive criteria and approaches to treatment from the point of view of evidence-based medicine. This article provides an overview of the results of scientific research on the problem of systemic scleroderma over the past 10-15 years.

Keywords: systemic scleroderma, secondary prevention

Despite the rapid development of practical medicine and the availability of various methods of treatment and prevention of SSD, this disease causes several difficulties in the practice of doctors. [14]. Of course, today there is a huge arsenal of drugs, which have justified their place in experience for many years. It is known that it is very important to pay attention to the secondary prevention of diseases. Because through secondary prevention, it is possible to prevent the exacerbation and complications of the disease, and improve the patient's quality of life. This can be done by relying on the pathogenesis of SSD and by solving the problems that arise in patients [13, 22]. Currently, secondary prevention of SSD focuses on the treatment of the observed vascular pathology and prevention of its exacerbation (especially Raynaud's phenomenon), slowing of the exacerbation of fibrosis, correction of immune changes and immune inflammation, and treatment of internal organ injuries. [13].

Vasodilators and antiaggregants have been recommended by scientists in recent years to correct Raynaud's phenomenon, which has a negative effect on tissue reperfusion and microcirculation deficiency observed in SSD. In this regard, calcium channel blockers are chosen first, and dihydropyridine products are mainly used in them. According to randomized studies [19], the use of nifedepine, a representative of this group, in SSD results in a dramatic reduction in the frequency and, in some cases, the duration of Raynaud's phenomenon. According to the data, taking it under the tongue accelerates the blood flow in the veins of the muscles under the skin layer of the fingers and shoulders. Although the positive effect of nifedepine in Raynaud's phenomenon has been proven, the observation of many side effects in its long-term reception limits its recommendation by doctors in practice. The introduction of retarded forms of dihydropyridine products into medicine led to a decrease in the side effects of the drugs. Compared with placebo-controlled studies [14], the use of amlodipine, a representative of this group, in patients with SSD leads to a decrease in vasospastic attacks and positive changes in the blood flow of the fingers. But according to these data, in addition to this, under the influence of the drug, 50% of patients cause swelling of the paws. According to the data in the literature [1,3, 5], another representative of this group, isradipine, is used in SSD to improve skin perfusion, but due to the high cost of these drugs, there are limitations in prescribing it by doctors. According to the latest literature, scientists are interested in the positive effect of angiotensin II receptor blocking drugs on SSD. Because in primary Raynaud's phenomenon, the use of losartan, a representative of this group, leads to a decrease in ischemic attacks [11,17]. However, according to the results of the study covered in other literature [13], there was no significant difference between the results obtained during the treatment of SSD patients treated with losartan and nifedepine. According to scientific studies of foreign scientists [10], analogues of prostacyclin iloprost also lead to a decrease in episodes of Raynaud's phenomenon. Also, the positive dynamics of serotonin 5-NT2 receptor blockers is being proven in studies aimed at improving Raynaud's phenomenon. According to this evidence [11], it is characterized by antispastic and disaggregation effects. Alternatively, there is vasoprastan, which contains prostaglandin E1, which is clearly effective in severe vascular syndrome. According to data [14], the

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drug improves microcirculation due to coordination of vasodilation and blood rheology properties. The entry of D-penicillamine into medicine for antifibrosis treatment was a great news for practicing doctors according to many literature sources, and it was distinguished by its clear positive clinical indications. According to the data in the literature [2,10], under the influence of D-penicillinamine, there is a decrease in the amino-terminal propeptide of type III collagen in blood serum. This amount of propeptide, in turn, can be said to be a marker of the intensity of fibrillogenesis. According to research by Steen and co-authors, the prevalence of skin tightening was reduced in patients who received this drug compared to those who did not, and skin softening and elasticity were improved. But these scientists say that side effects observed in high doses of the drug lead to limiting its prescribing to patients. In later years, the long-term use of these drugs [1,3,6] in small doses led to a radical change. Because in this regard, the observation of side effects in patients decreased, positive changes in skin syndrome and especially the absence of kidney damage caused D-penicillamine to become one of the basic remedies. Further literature reports that its positive effects on other visceral injuries have been proven. According to these studies [10], long-term use of the drug in patients with SSD increased lung diffusivity from 76% to 87%, and radiographic pulmonary fibrosis was not observed. In addition [15], it is also noted in the literature that the exacerbation of the decrease in the diffusive properties of the lungs is mainly observed in patients who did not receive D-penicillamine. However, there are differences of opinion among scientists regarding the dosage of D-penicillamine [12, 14]. According to the sources, there was no significant difference between low and high doses of D-penicillamine in double-blind controlled studies [15]. According to the research of other scientists [12,14,18,20], clinical efficacy is higher in patients who receive this drug in higher doses. However, according to other literature [25], long-term administration of even a small dose of the drug leads to an increase in the number of patients with a 5-year survival rate. In addition, the effects of D-penicillamine on the immune system have also been studied. According to these works [19, 21], it leads to attenuation of the selective properties of T-helpers. According to literature sources, the total amount of CD26+, CD24+ and T-lymphocytes decreases on the basis of this drug. In addition, there are side effects of D-penicillinamine on internal organs [6, 10], such as cases typical of autoimmune reactions in patients receiving it: nephrotic syndrome, myasthenia, and the like, as well as hemolytic changes, kidney and lung damage are expressed in literature sources . However, taking into account the main antifibrosis effect of D-penicillamine in SSD, i.e., it has antiproliferative power on fibroblasts and prevention of fibrosis, it continues to be widely used by doctors in practice. At the same time, literature sources [7, 20,25] state that side effects disappear as soon as patients stop taking this drug. Currently, there are new drugs belonging to this group of drugs: bianodin and artamin, and their effectiveness indicators are in the research period. The use of aminoquinoline group of antifibrosis drugs in SSD is described in many literature sources [23, 24], they are used as basic treatment in almost all clinical manifestations of this disease. According to the results of studies published in the literature [15], exacerbation of SSD during long-term use of aminoquinoline drugs leads to reduction of clinical symptoms. In addition, their positive effects on the immune system have also been shown in evidence [23]. But at the same time, the side effects of these drugs, especially negative changes in the eye and peripheral blood, have been proven [17, 18]. Nevertheless, these drugs are used as the main base drugs of SSD.

It is known that today glucocorticosteroids are widely used in practice. According to the available literature [9], glucocorticosteroids dramatically reduce immune inflammation in tissues by reducing the amount of increased immune complexes. The use of glucocorticosteroids in SSD has two purposes [2, 11, 16]. Usually, hormones can be used as a basic drug in the period of high activity of SSD and the sharp development of clinical signs of the disease (myositis, alveolitis, serositis, refractory arthritis, tenosynovitis), as well as in situations of immune activity. In other situations, according to the literature [9], the basis is not used as a treatment, for example, glucocorticosteroids do not have a mitigating effect on the progression of fibrosis. At the same time, it may increase the risk of normotensive renal failure [20]

Currently, there is a debate on whether immunosuppressive-cytostatic therapy should be used in SSD, as opposed to other diffuse connective tissue diseases [18]. For example, in the absence of disease progression, cytostatic treatment has been reported [12] to be important, whereas other placebo-controlled studies [16] showed no change in visceral parameters in SSD patients receiving methotrexate, and thus In addition, some of these patients showed kidney failure and lung fibrosis due to kidney failure. However, data from another double-blind placebo-controlled study [13] reported no clear benefit in SSD patients receiving cytostatic therapy. On the other hand, among the representatives of this group, in SSD based on cyclophosphamide, coordination of lung function and reduction of skin hardening are observed [17], but at the same time, it leads to arterial hypertension, renal crises, and vasospastic syndromes [12]. Therefore, the use of cytostatics in SSD remains an open question. As

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for the prevention and treatment of internal organ damage observed in SSD, there is currently no disease modification therapy program, and there are many advances in the treatment of inflammation of certain organs. Widespread use of ACE inhibitors in patients with SSD has led to a reduction in the incidence of sclerodermatic kidney and chronic renal failure [1, 14]. At the same time, great progress has been made in the treatment of pulmonary hypertension, according to the literature [11, 16], in this regard, epoprostenol, a representative of type A and V endothelin blockers - vosentan is effective in reducing the exacerbation of pulmonary insufficiency and increasing exercise tolerance. proven effectiveness. In the treatment with proton pump inhibitors, in turn, the reflux-esophagitis, which is observed on the basis of sclerodermatous inflammation of the esophagus, has noticeable positive results. Thus, despite the fact that there are different types of fog treatments available, and based on the above data, there are certain challenges in the treatment of SSD. Therefore, the treatment of patients should be early, pathogenetic, based on medicine, complex and differentiated, and in addition, the clinical form and course of the disease, periods of activity should be taken into account. But in the secondary prevention of the disease, it is desirable to fully approach the pathogenesis of the disease. Including, in women with SSD, sex hormones play an important role in the pathogenesis of the disease. For example, according to recent literature [3, 8, 14], there is a decrease in estrogen and especially progesterone. According to literature [15, 20, 22], there is a physiological relationship between progesterone and T-cell immunity. In turn, deficiency of T-cell immunity observed in SSD is recognized as an autoimmune process [20] and exacerbation of this condition determines the degree of clinical course of the disease [12]. Elimination of T-lymphocyte deficiency is one of the main goals in autoimmune diseases [22]. However, it is desirable to coordinate progesterone deficiency in women with SSD, which is based on an autoimmune process. This problem is not widely covered in the current literature, but some scientists [12] have observed improvement of pulmonary hypertension syndrome in women with SSD who received progesterone. However, this does not fully explain the solution to the problem. According to data [19, 200], progesterone prevents degenerative changes in the skin by enabling normal collagen synthesis. At the same time, it increases the excretion of sodium and water, and has a positive effect on osteoporosis due to the possibility of osteoblast proliferation in bones [11]. According to scientific studies [9, 17], progesterone acts on fibroblasts through the RP receptor. In addition, progesterone has been shown to have a positive effect on mood through GABA receptors [12, 14]. As shown above, the appropriate immune response is ensured by a certain state of hormonal homeostasis, that is, when there is any change in female sex hormones, dynamics in the immunological process are observed. In fact, according to literature sources [13, 15, 16], positive clinical dynamics are observed with the use of progesterone in menopause in some autoimmune diseases. In addition, progesterone administration in pregnant women with progesterone deficiency leads to an increase in T-cell immunity, especially T-helper [17]. However, taking into account the decrease in estradiol in SSD, its correction should also be considered. However, according to the information provided in some literature [10, 15], proliferative effect of estradiol used in patients with SSD was noted on the endothelium of bronchial and wrist vessels. According to the US Women's Study Initiative Group [22], the rates of cardiovascular disease, myocardial infarction, and stroke among patients taking estrogen were significantly higher than those who did not take the drug. Because of this, estrogen affects the blood coagulation system, increases coagulation and causes proliferation of the vascular inner layers [16]. For example, observation of vascular pathology, microcirculation disorders in SSD limits the use of estrogen in this condition. In turn, the choice of progesterone drugs is also important. In this regard, according to available literature [19, 23], dydrogesterone is devoid of systemic, androgenic, thermogenic properties and side effects observed in other drugs. Therefore, according to the data, it is widely used in practice.

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