Е.П. Аммосова, Е.Н. Сивцева

Introduction

The localized scleroderma (LS) is characterized by involvement in sclerodermical process of a skin, a hypodermic cellulose, muscles and sometimes an osteal tissue [1,3]. Prevalence of the localized scleroderma among adults is 2,7 cases per 100000 population, about 34%-40% of which are children[1,9]. In children more common are forms of linear scleroderma, which is characterized by an aggressive course with the involvement of soft tissues up to the destruction and deformation of bones [1,3,9]. These serious forms include “en coup de sabre”, linear scleroderma which mainly localized on the extremities. Until now, clinicians consider LS as a dermal disease and extensively use local therapy, which usually does not prevent the progression of the disease [1,3]. In recent years there were many researches on studying of a pathogenesis of LS and many similar with system scleroderma pathogenetic units was found [2]. Thus views on the disease treatment have changed in favor of the necessity of using "disease-modifying" agents, for the treatment of LS.

Till now there is no standard scheme of therapy of a scleroderma. At present in domestic (Russian) medicine one of the most widely used preparations is D-penicillamin (DP). The precondition for using DP is its multilateral influence on a collagen metabolism and first of all its antifibrous effect [5,7,10]. Recently the increasing importance in treatment of a system scleroderma is got by cytostatic immunosuppressants, in particularly a methotrexate (MTX). In spite of wide use of MTX by foreign rheumatologists, there are only five researches, devoted to an evaluation of methotrexate's efficiency in LS therapy [4,6,8,9,11]. It is necessary to notice that the evaluation of efficiency of therapy was spent on small number of patients from 9 to 34 with a maximum period of observation of 2 years.

Aim of the research - to develop the differentiated approach to the basic therapy at the localized scleroderma among children.

Materials and Methods of the research. The efficiency analysis of four treatment schemes of 97 children with LS is carried out: D-penicillamin in doses from 7 to 10 mg/kg/day, MTX in a dose of 10 mg per square meter per week, MTX and DP in combination with glucocorticoids (GC) in a medical dose of 0,5 mg/kg/days for 3 months with gradual reduction to a maintenance dose of 0,1 mg/kg/day. The analysis of efficiency of therapy was estimated clinically with the help of specially developed technique, for separating of pathological process was identified four parameters of dermal process: local activity (LA), fibrosis index (FI), dermal

score (DS) and depth of sclerodermical process. Local activity determined by evaluation of brightness and prevalence of a peripheral crown on 4 point scale. Fibrous process characterized visually and by palpation, for this was made such parameter as index of fibrosis, which was estimated on 4 ball scale. Considering that the fibrosis index not fully reflects depth of a lesion of soft tissues and bone deformation by the moment of observation, that is an important point to characterizing a severity level and aggressiveness of the process, we have developed additional parameter characterizing depth of diffusion of pathological process. It should be noted that the given parameter is dynamically stable as shows already formed process. The depth of sclerodermical process was evaluated visually and by palpation on 3 point scale. For the aggregate analysis of selected 4 signs of the disease and allocation of treatment's efficiency groups used a mathematical method of "recognition of images» (Nejmark J.I., Batalova Z.S., Vasin J.G., Brejdo M. D «Recognition of images and medical diagnostics», M: the Science, 1972). By efficiency of treatment patients were divided into three groups: "good", "moderate" and «no effect» and these patients were estimated every 3, 6, 12, 24 months. The statistical importance of differences and correlation of surveyed signs was determined by nonparametric statistical criteria (Wilcoxon, Kruskal-Wallis). As authentic was considered the significance level of $p < 0,05$.

Clinical characteristic of patients: at the beginning of basic therapy the total duration of disease averaged 21,68 ± 2,6 months. 22 (22,7 %) boys and 75 (77,33 %) girls, the ratio 1:3,5 that corresponds to the literary data. The patients' ages at the beginning of observation ranged from 4-16 years (M ± m - 10,0 ± 3,37). The majority of patients had a linear form of scleroderma 50 (51.54%). "En coup de sabre" was in 15 (30%) patients and 6 (40%) of them at the beginning of treatment had a cosmetic defect of face with various degrees of deformation of the skull bones. Plaque form of scleroderma had 23 (23.7%) patients. Common form had 24 (24.7%) patients.

It should be noted that at the beginning of prescribe of basic therapy search, in 32 (32,9%) of 97 was already formed a rough cosmetic defect or functional insufficiency, associated with the defeat of the musculoskeletal system with the development of a thinning, shortening and formation of periarticular contractures.

Results of the research and discussion. Observation period of the patients varied from 6 to 24 months and on average was 15.8 a16 2,2 months.

The dynamics of the local activity: In all groups significant decrease in the average values of the local activity have been observed at 3 months of treatment, except for the group of patients treated with D-penicillamine monotherapy, significant decrease in the average values of the local

activity was only observed at 6 months of treatment (Fig. 1). Thus, methotrexate has a more pronounced anti-inflammatory effect as compared with D-penicillamine. In the application of combination therapy of methotrexate and D-penicillamine with glucocorticoids in most patients by 3 months of therapy and disappeared reduce the appearance of local activity, in spite of pronounced signs of local activity by the beginning of therapy, reflecting the powerful anti-inflammatory effect of the combination of basic drugs with glucocorticoids.

Dynamics of fibro-sclerotic process: the average value of the index of fibrosis statistically decreased by 6 months of treatment in all groups except for patients with methotrexate monotherapy, which reduced the average values of the index of fibrosis was observed only for 12 months of treatment (Fig. 2). Thus, D-penicillamine as a single agent has a more pronounced effect of antifibrotic compared with methotrexate. Also note that the use of basic drugs with antifibrotic effect is enhanced by glucocorticoids, which reflects the significant decrease in the average values of the index of fibrosis at 6 months of treatment, despite an initially high average value of the index to the top of fibrosis therapy.

The effectiveness of various schemes of basic therapy in a linear form of scleroderma: the proportion of patients with good effect predominates in patients receiving combined therapy with corticosteroids compared with patients treated with a basic compound (Table 1). When comparing the effectiveness of methotrexate with methotrexate in combination with glucocorticoids, and D-penicillamine with D-penicillamine in combination with glucocorticoids received with that combination therapy is effective in monotherapy was statistically confirmed by a Kraskela-Wallis test.

Thus, in the treatment of the linear form of the operating system is more efficient combination of a basic drug with glucocorticoids.

Conclusion:

1. Methotrexate monotherapy has therapeutic effect in patients with localized scleroderma, as evidenced by the cessation of progression of the pathological process, a statistically significant reduction of local activity to 3 and the index of fibrosis at 12 months of therapy. Compared with D-penicillamine has more potent anti-inflammatory effect.
2. Monotherapy with D-penicillamine has a therapeutic effect in patients with localized scleroderma, as evidenced by the cessation of progression pathology process, a statistically significant reduction of local activity, an index of fibrosis at 6 months of therapy. Compared with methotrexate has a large antifibrotic effect.

3. The combination of methotrexate with corticosteroids effective in the treatment of scleroderma Limited linear form involving the deep soft tissues (subcutaneous fat, muscle, fascia, tendons) compared with monotherapy with methotrexate.
4. The combination of D-penicillamine with glucocorticoids effective in patients with the linear form of scleroderma involving the deep soft tissues (subcutaneous fat, muscle, fascia, tendons) compared with monotherapy D-penicillamine.