patients. For the assessment of the left ICA, the data were as follows: TCIM - <0.9 mm at 26.7%, 0.9-1.3 mm -4.6.7%,> 1.3 mm in 26.7% of the subjects. After the treatment, which lasted for 3 months, the following parameters were obtained: TCIM - <0,9 mm on right VAA in 43,5%, 0,9-1,3 mm in 30,4%,> 1,3 mm in 26,1 . The left CCA study was 56.5%, 26.1% and 17.3% respectively, indicating a positive effect of treatment and indicating an increase in the number of patients with normal CI (<0.9 mm) and a significant decrease in CIM thickening.

Therefore, the use of anti-atherosclerotic therapy at the stage of subclinical atherosclerosis, which is diagnosed with a color duplex scan with the evaluation of TCIM, makes it possible to reduce the level of coronary and cerebral pathology, and the use of hypolipidemic therapy significantly reduces the signs of atherosclerosis.

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## DRUG–INDUCED SCLERODERMA-LIKE SYNDROMES

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Systemic sclerosis (SSc) or scleroderma is a group of autoimmune connective tissue disorders which features include fibrosis of the skin, obliterative vasculopathy, changes in muscles, and internal organs. To differentiate SSc with scleroderma-like syndromes provoked by drugs is important in clinical practice.

Our aim was to analyse, according to the modern literature data, the peculiarities, pathogenic mechanism of development and occurrence of drug-induced variants of scleroderma.

A variety of medications have been associated with the development of scleroderma-like conditions. Drugs can also induce sclerotic skin changes along with Raynaud phenomenon, scleroderma-like conditions, including morphea, linear scleroderma and diffuse scleroderma with pulmonary fibrosis and other internal organ involvement.Sometimes local scleroderma or morphea may occur at the site of the injected drugs.Causative medications include a wide spectrum of chemotherapeutic agents, analgesics, neurological drugs, appetite suppressants, vitamins and many other agents. Localized scleroderma-like changes can be provoked by antimitotic drugs (Bleomycin, Taxanes, Pemetrexed, Gemcitabine, Doxorubicin), Ergot alkaloids (Ergotamine, Methysergide, Opioids, Pentazocine, Methadone). Morphea like-syndrome is caused by Vitamin K1, Beta-blockers (Metoprolol, Atenolol, Bisoprolol), Anticonvulsants (Ethosuximide, Penicillamine). Diffuse scleroderma-like syndrome may occur due to the use of: drug of abuse (Cocaine), food supplement (L-tryptophan), cytokines (Interferon α, Interleukin-2), checkpoint inhibitors (Pembrolizumab, Nivolumab), miscellaneous (Hydroxyurea, Letrozole, Balicatib). Antineoplastic drugs (Bleomycin), disease-modifying antirheumatic drugs (Methotrexate, Leflunomide, TNF inhibitors) and Amiodarone can cause pulmonary fibrosis, which against the background of connective tissue disorders such as rheumatoid arthritis often becomes difficult to ascertain the causality (Sahoo RR et al., 2020). Takumi Toya et al., 2019 report a case of severe Dasatinib-induced pulmonary arterial hypertension complicated with scleroderma that was successfully treated with Dasatinib discontinuation and using of pulmonary vasodilators.

The real mechanisms are still unknown since the reported cases of drug induced fibrosis are unclear and few. However, one commonly suggested hypothesis concerns ischemia. Since drugs like ergot derivatives cause vasoconstriction and β-blockers lead to decreased cardiac output, ischemia was initially postulated to lead to fibrosis (Ahmed Sakir et al.,2019). Other mechanisms such as endothelial mesenchymal transition, inflammation activation, M2 macrophage polarization, and NETosis may also play a certain role similar to systemic sclerosis. This finally culminates in the activation of fibroblasts and deposition of extracellular matrix including collagen (Gupta L et al., 2017). Chronic injection of analgesic Pentazocine can leads to disorders in microcirculation and ischemia. Similarly, cocaine and appetite suppressants have sympathomimetic activity and cause contraction of blood vessels. Cocaine may also cause diffuse scleroderma-like alterations in the skin. Appetite suppressant drugs are responsible for Raynaud's symptom, hand edema, sclerodactyly and dysphagia.

Thus, the clinician should be aware of the drugs that have strong associations with fibrosis, consideringthe difficulty of making the differential diagnosis. Awareness of drug-induced forms of scleroderma is important because some of them can be reversed by withdrawal of the drug indicated early.

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## THE USE OF ROSUVASTATIN AND EZETIMIBE COMBINATION FOR CORRECTION OF DYSLIPIDEMIA IN PATIENTS WITH HIGH CARDIOVASCULAR RISK (ISCHEMIC HEART DISEASE AND TYPE 2 DIABETES MELLITUS)

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Approximately 80% of cardiovascular disease-related deaths are associated with patients suffering from coronary atherosclerotic heart disease. Atherosclerosis is a complicated chronic inflammatory process which primary essence includes an excessive inflammatory response and lipid accumulation. Patients with type 2 diabetes have a significantly increased risk of developing cardiovascular disease. Atherosclerosis kills more diabetic patients than all other causes combined. Statin treatment markedly reduces the incidence of acute coronary events in patients with coronary atherosclerosis. Special features of pharmakinetics, mechanism of action of statins (rosuvastatin) and ezetimibe and their effect on the correction of dyslipidemia have been introduced. A good combination of statins with ezetimibe has been proven, which is that statins reduce the synthesis of cholesterol in the liver, and ezitimibe, localized in the brush border of the small intestine, prevents cholesterol absorption. These lead to a decrease in the intake of cholesterol from the intestine into the liver, lowering cholesterol in the liver and, accordingly, increase its excretion from the blood. In addition, ezetimibe in combination with statins reduces the levels of total cholesterol, low-density (LDL) cholesterol, triglycerides (TG) and increases high-density lipoprotein (HDL) cholesterol in patients with hypercholesterolemia significantly more effectively than monotherapy.

The aim of the study was to compare the effect of rosuvastatin with combination therapy of rosuvastatin and ezetimibe. The study group comprised 36 patients (20 women and 16 men) with chronic ischemic heart disease and type 2 diabetes mellitus. The blood lipid profile of the patients was determined before the beginning of the study and after 4 and 12 weeks of rosuvastatin use and its combination with ezetimibe. The patients were divided into 2 groups. Patients of the first group received rosuvastatin alone in the dose of 20 mg and patients of the second group received combination of rosuvastatin and ezetimibe (10 mg + 10 mg). Within 4 weeks of observation, group 1 showed insufficient reduction in LDL levels (9,6%), while in the second group there was a decrease of 12,6%.

The use of combination therapy for 4 weeks made it possible to achieve the target level of LDL and reduced it by 54,4% compared with 25,3% of rosuvastatin monotherapy. The initial dose of rosuvastatin (20 mg) was effective in achieving cholesterol targets in 71,2% of patients after 12 weeks and in achieving LDV targets in 71,3%. In patients of the 2nd group this parameter was 21% higher. The combination of ezetimibe and rosuvastatin decreased total cholesterol, low-density lipoprotein cholesterol, triglycerides and increased high-density lipoprotein. And compared with rosuvastatin alone group, the primary endpoint decreased more effectively in combination group.

Ezetimibe combined with low- or intermediate-intensity statin therapy possesses lipid-lowering efficacy comparable to or better than that of high-intensity rosuvastatin monotherapy. The results of the present study indicate that the combination treatment with ezetimibe is beneficial in that it permits dose reduction of rosuvastatin without compromising the lipid-lowering efficacy of rosuvastatin.