

Case Report

Use of Antifungal Creams in the Combined Treatment of Obliterating Diseases of Lower Extremities Arteries

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Abstract

To perform clinical analysis of the effectiveness of the complex treatment of occlusive vascular diseases and fungal lesions of feet with addition of local antifungal medicines.

Materials and Methods. The results of examination and treatment of five patients with obliterating diseases of the lower limb vessels and diabetes mellitus with dermatomycosis and onychomycosis of the feet were analyzed. Onychomycosis or mycosis of feet were treated with the help of the combination of the following antifungal creams was used in the treatment: miconazole, clotrimazole, tioconazole in a ratio of 1:1:6.5 contained in the combined preparation cream "XaTonic".

Results and discussion. The use of an antifungal mixture of creams after 7 days has led to the disappearance of the clinical manifestations of dermatomycosis of the feet in three patients, and in two patients with onychomycosis after 14 days there was the reduction of clinical symptoms.

Conclusions. The combination of three local antifungal components: miconazole, clotrimazole, thioconazole is effective in treatment of dermatomycosis of the feet. In the treatment of fungal lesions of the feet by dermatologists in patients aged after fifty years, an angiologist/vascular surgeon's consultation is required.

Keywords

diabetes mellitus; obliterating atherosclerosis of the lower extremities; dermatomycosis; onychomycosis

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Problem statement and analysis of the latest research

Fungal lesions of the feet and nails are a concomitant disorder of peripheral arterial diseases of the lower extremities. Fungal lesions of the feet happen nine times more likely in patients with obliterating diseases of arteries of the lower extremities and 175 times more likely in patients with diabetic angiopathy of the lower extremities compared to healthy people [1, 2]. It was found that onychomycosis is an early manifestation of the vascular lesion, and the reduction of the ankle-brachial index statistically correlates with onychomycosis [2]. The presence

of onychomycosis significantly increases the risk of development of diabetic ulcers in patients with diabetes mellitus [3]. Dermatomycosis and onychomycosis are difficult to treat in patients with the obliterating diseases of peripheral vessels of the feet [4]. In combination of diabetes mellitus, obesity, hypertension with the damage of peripheral vessels of the lower limbs there are the major risk factors for development of fungal infections of the feet and nails. That is why it is recommended to treat onychomycosis with the help of oral antifungal medicines [5]. These drugs have a high level of hepatotoxicity, and quite often may lead to gas-

trointestinal disorders and other complications [5]. The fungal skin lesions and onychomycosis may create the source for pathogenic microflora, which delays healing of postoperative wounds, ulcers, and necrotic process also may progress in diabetic foot syndrome [3].

Objective. To perform a clinical analysis of the effectiveness of the combination of the local antifungal treatment for dermatomycosis and onychomycosis of the feet in patients with occlusal vascular diseases.

1. Materials and Methods

There were five patients with fungal lesions of the feet and nails under our supervision. There were three patients with obliterating arterial atherosclerosis of IIa degree (according to the classification of Fontaine) and two patients with obliterating arterial atherosclerosis of IIb degree and type II diabetes mellitus. The characteristics of patients is shown in Table 1.

The patient M. had had diabetes mellitus for 8 years. The level of glycosylated hemoglobin (HbA1) was 7.5% at the moment of examination. According to the classification of the compensation degree of carbohydrate metabolism in the patient M., there was decompensated form of diabetes mellitus and moderate (II degree) of the severity of diabetes mellitus. The femoral and popliteal arteries were stenosed from 20 to 50%. The anterior and posterior tibial arteries were stenosed at 50-75%.

The patient Ya. had had diabetes for 15 years. The level of glycosylated hemoglobin (HbA1) was 8.1% at the moment of study. According to the classification of the degree of compensation of carbohydrate metabolism in the patient Ya., there was a decompensated form of diabetes mellitus and moderate (II degree) severity of diabetes mellitus. The femoral artery was stenosed from 20 to 50%. The popliteal, anterior and posterior tibial arteries were stenosed at 50-75%.

In all patients (patients B., S., V.) without diabetes mellitus, stenosis of the femoral and popliteal arteries was from 20 to 50%. The anterior and posterior tibial arteries in all patients were stenosed

within 50-75%.

The ankle-brachial index (ABI) was measured in the supine position using a portable vascular doppler "Sonoline" with a frequency of 8 MHz. We applied a blood pressure cuff on the shoulder and air was inflated until the blood flow in the shoulder artery disappeared, then air was slowly released and the pressure was noted when the blood flow appeared again. Thereafter, the procedure was repeated on the calf, which was symptomatic during walking. The lowest measurement of blood pressure was detected on the posterior tibial artery and dorsalis pedis artery. Then, the ratio between the systolic blood pressure on the lower extremities to the systolic blood pressure on the upper extremities was calculated. Because of the fact that in patients with diabetes mellitus the ABI was successfully determined with the use of this method, we haven't measured the toe-brachial index.

The most common pathogens of dermatomycosis and onychomycosis are *Trichophyton rubrum* and *Candida parapsilosis*, accounting for about 85-90% of all possible causes [9, 10]. These pathogens are sensitive to the topical local antifungal drugs such as miconazole, clotrimazole, and tioconazole, which were used in this study. In this regard, we've treated patients empirically and did not identify specific agents of mycotic infection.

the patients were performed an ultrasound duplex scanning of the lower extremities' arteries with the determination of their stenosis by identifying the peak systolic blood flow velocity (PSV, cm/sec). We considered that stenosis of arteries ranged from 20 to 50% if the PSV ranging from 150 to 200 cm/sec. At PSV from 200 to 300 cm/sec the stenosis of arteries ranged from 50 to 75%.

Onychomycosis or mycosis of feet was treated locally with the help of a combination of the topical anti-fungal creams of wide spectrum of action: miconazole (2% cream, manufacturer of PJSC "Pharmaceutical firm "Darnytsa", Ukraine), clotrimazole (1% cream, manufacturer PJSC "FITOFARM", Ukraine), tioconazole (1% cream, manufacturer PFIZER, USA) in a ratio of 1:1:6.5. This combination was used because of the reporting of the effectivity of the medicine "XaTonic" for onychomy-

Table 1. Characteristics of patients before admission to the hospital

	Sex	Age, years	Type 2 diabetes, yes / no	Ankle-brachial index	Blood pressure, mmHg	Type of fungal lesion	Stage according to Fontaine classification
Patient B.,	male	67	no	0.62	160/95	Bilateral feet mycosis	IIa
Patient S.,	male	65	no	0.73	140/90	Bilateral feet mycosis	IIa
Patient V.,	male	61	no	0.75	130/85	Bilateral feet mycosis	IIa
Patient Ya.,	male	63	yes	0.58	150/90	Bilateral onychomycosis and feet mycosis	IIb
Patient M.,	male	66	yes	0.69	165/90	Bilateral onychomycosis and feet mycosis	IIb

cosis (manufacturer PUNCH Skin Care, USA) [6], which is not registered in Ukraine.

The patients were explained how to prepare a leg before application of a mixture of antifungal creams (washing of the feet with warm water and soap, safe removal of part of the affected nail, cleaning of the outer surface of the nail plate and nail bed, clearing the gaps between the fingers). Creams were applied to the feet, nail beds and plates twice a day, and carefully rubbed into the folds of the skin.

in the process of the complex treatment, there were appointed consultations of other specialists (cardiologist, endocrinologist) and administered appropriate therapy for diabetes mellitus, hypertension and coronary heart disease, as well as anti-aggregate therapy (cilostazol) as one of the main directions of the obliterating atherosclerosis treatment of the vessels of the lower extremities.

Treatment results were evaluated by ad oculus, as well as by the presence or absence of symptoms of dermatomycosis.

2. Results and Discussion

After 7 days of complex treatment with the use of the mixture of creams in two patients (patients B. and S.), there was the complete disappearance of clinical manifestations of dermatomycosis on the feet (Fig. 1), and in one patient there was a significant improvement on the skin and the absence of any symptoms of the irritation (patient B.).



Figure 1. The appearance of the affected by dermatomycosis foot in patient B., before (on the left side) and after (seven days of treatment on the right side) with the mixture of creams twice a day.



Figure 2. The appearance of the affected by dermatomycosis and onychomycosis foot in patient Ya., before (on the left side) and after 14 days of treatment (on the right side) with the mixture of creams twice a day.

However, in patients Ya., and M., with onychomycosis after 14 days of treatment, there was improvement only on the affected skin, while the nails were still affected (Fig. 2). Irritation symptoms have decreased significantly.

All patients have a warm feeling and pleasant slight tingling in the area of feet during the use of the combination of creams. The number of symptoms of irritation (itching, burning sensation, etc.) decreased in all patients. Side effects were absent in all patients. Unfortunately, after the discharge from the hospital, the connection with all patients was lost.

3. Prospects of Further Researches

The weak effect of the complex treatment with antifungal drugs in patients with onychomycosis may be explained by poor penetration of active substances under the nail bed and into the area of nail plate growth. Also, the growth rate of the nail on the lower extremity is 1.67 mm per month in healthy people [7]. That is why it can be concluded that the complete renewal of the nail on the lower limb is on average six months. By the way, the epidermis of the skin is completely renewed in about 1.5 months [8]. This means that by increasing the du-

ration of treatment at least 4-fold (minimum, up to 28 days) may reveal the effectiveness of treatment with topical antifungal drugs in patients with onychomycosis.

4. Conclusions

The combination of three topical antifungal drugs for seven days (miconazole, clotrimazole, tioconazole) was effective for treatment of the skin dermatomycosis on the feet in three patients with the occlusal diseases of the arteries of the II degree.

The combination of three local antifungal components for 14 days (miconazole, clotrimazole, tioconazole) was not so effective for the treatment of onychomycosis in two patients with the occlusal diseases of the arteries of the II degree and type 2 diabetes mellitus.

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