

## RESEARCH STUDIES

### Improvement of onychomycoses treatment using the agents which optimize the structure of nail plate and its growth

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#### Abstract

**Background:** Onychomycosis is one of the current medico-social challenges. The article deals with the advantages of combined comprehensive therapy rendered to patients with onychomycoses using systemic antimycotics and vitamin agent Wolvit over standard therapeutic regimen determined by a comparative study of two groups.

**Material and methods:** We observed 43 patients with onychomycosis of hands and feet: the main group (33 patients) received Wolvit 5 mg per day and systemic antimycotic in standard dosage, control group (10 persons) – systemic antimycotic. The course of treatment was 1.5 months for onychomycosis of the hands and 3 months for onychomycosis of the feet. All patients underwent a comprehensive clinical and laboratory examination. Mycological research was on the fourth, sixth, eighth, tenth, twelfth and sixteenth weeks of treatment.

**Results:** The administration of vitamin agent Wolvit together with systemic antimycotics allows to achieve a significant improvement of nail plate structure as it acquires even light pink translucent color, glossy surface, smooth and thick free edge, normotrophic structure. Participation of biotinum in the formation of keratine, necessary for the development of hair matrix and nail plate, results in acceleration of healthy nail growth in patients with onychomycoses. Biotinum is also a source of sulphur, which transports sulphur into the skin and its accessory organs, contributing to collagen formation and therefore eliminates signs of early hair depigmentation, normalizes sebaceous glands function and exerts a positive impact on the structure of skin and its accessory organs (hair, nails).

**Conclusions:** The obtained results show that the developed complex is effective, safe and allows to achieve both clinical and etiologic recovery.

**Key words:** Wolvit, vitamins, onychomycosis, systemic antimycotic, nail plate growth.

#### Introduction

The success in onychomycoses treatment that has been achieved for the last decades allows to provide significant improvement of the patients' life quality. However, the incidence of this disease, late presentation, heredity, long duration of contagious period in patients and an increase in the number of patients make the improvement of methods used for the treatment of onychomycoses one of the current medico-social challenges [4, 5].

Nail plate in a healthy person is considered to be essentially impervious to mycotic infection. Fungus penetration is usually preceded by nail injury, impairment of natural resistance of the body associated with immune deficiencies and disorders of vital functions resulting in neurotrophic alterations of the nail bed [8].

A healthy fingernail plate grows by 2-4.5 mm per month. Toenails grow half less slowly, growing on average by 1-2 mm per month. Entire fingernail plate grows over a period of 4-6 months and toenails require a period 12-18 months [9]. Various factors exert impact on the growth rate. Nails grow quicker in children than in adults and quicker in young men than in young women but with age this correlation changes. Nails in elder people demonstrate the slowest growth rate. Nails grow slightly quicker at daytime. In winter and in people who live in areas with colder climate nails grow less slowly. Injuries and whole nail plate removal stimulate its formation.

Hypo- or avitaminosis, general severe diseases, which result in matrix function deficiency, slow down nail growth rate. Nail plate formation is deteriorated when the patient is treated with cytostatics [6, 7, 12].

The choice of the best possible method of treatment for patients with onychomycosis depends on the character of nail plate impairment, type of pathogenic agent, the amount of affected nail plates, age of the patient and many other factors. But one correlation which remains unchanged in employment of local or systemic therapy is the dependence of treatment on the nail plate growth rate. Thus, the longer the affected nail plate renews, the higher the risk to develop adverse reactions and complications following a prolonged intake of systemic antimycotics or a prolonged local exposure to antifungal agents (contact dermatitis, eczematization).

In onychomycoses nail plate growth rate is significantly reduced due to thickening and deformation of plates, peripheral trophism impairment and insufficient supply of vitamins and microelements, which take an active part in the structure formation and nail plate growth. In atrophic onychomycoses nail plate growth practically ceases due to partial or complete destruction of free edge by mycelium.

The treatment of onychomycoses takes much time and requires thorough monitoring of functional status of the liver and bile ducts. Side effects, possible in case of prolonged administration of systemic antimycotics are as follows: dys-

peptic events (nausea, vomiting, abdominal fullness or pain in the abdomen, sometimes loss of appetite, loss or change of taste during treatment), allergic reactions (urticaria), headache and dizziness, photosensitivity, toxic effects such as hepatotoxicity, agranulocytosis, organ of vision impairment and some other [5]. To avoid all the above mentioned adverse effects comprehensive treatment of onychomycoses should include hepatoprotectors and agents which improve nail plate structure and contribute to a quicker nail plate growth and this results in the promotion of earlier mycologic negative reaction, providing a possibility to reduce the period of systemic antimycotics administration and to decrease the risk of adverse effects. Biothinum (vitamin H) belongs to the agents which exert a positive effect on skin structure and its accessory organs [6, 7].

Wolvit includes vitamin which belongs to water-soluble vitamin B complex (Biothinum or vitamin H). Biothinum has an impact on metabolic processes, takes part in carboxylation, decarboxylation, deamination of proteins and carbohydrates, assists in lipids metabolism and is considered to be an important component necessary for neurotrophic processes and cell differentiation [6, 10].

Biothinum takes part in the formation of keratin, necessary for hair matrix and nail plate development, contributes to the improvement of its structure and growth, brings off signs of early hair depigmentation. Biothinum is a source of sulphur which contributes to collagen formation exerting a positive impact on the structure of skin and its accessory organs (hair, nails) and normalizing sebaceous gland function. This Biothinum potential can be used for the reduction of aging processes intensity and for skin changes renewal [2, 10].

The aim of this research is to evaluate the efficacy of therapeutic complex which includes systemic antimycotic and vitamin agent Wolvit produced by Kusum Healthcare PVT LTD, India in the treatment of onychomycoses on fingers and toes.

### Material and methods

We observed 43 patients with onychomycosis of fingers and toes aged from 34 to 75. The diagnosis was confirmed by microscopic examination. The patients were divided into two groups: main and control groups. The treatment of all the patients was carried out at the department of dermatology, infectious and parasitic skin diseases at Institute of Dermatology and Venereology of National Academy of Medical Sciences of Ukraine.

Prior to treatment all the patients underwent comprehensive clinical laboratory investigation. All the patients before and after the treatment underwent examination to determine complete blood cell count (the level of hemoglobin, erythrocytes, leukocytes and blood sedimentation rate), urine analysis (to determine its specific gravity, pH, protein, sugar, leukocytes, erythrocytes, casts) and evaluation of liver function (determination of alanine aminotransferase, serum glutamic oxalacetic transaminase, glucose level, total bilirubin and total protein, an indicator of synthetic ability of the liver) [3, 11].

Mycologic examination of nail plates in patients of both

groups was rendered by the method of microscopic evaluation of unstained preparations with prior processing (clearing) of material under investigation. Pathologic material was collected and microscopically examined before the onset of treatment and on the fourth, sixth, eighth, tenth, twelfth and sixteenth weeks of treatment [1].

Every other week before, after and during treatment each patient underwent evaluation of subjective signs of the disease (itching, soreness), objective examination data (measurement of nail plate length from nail fold to distal end, oozing lesions, hyperemia, exfoliation, dryness of skin, cracks, microscopic examination of nail plates). Recording of objective signs indicating nail plate disorders was carried out before and after the treatment according to the following characteristics: distal impairment, lateral impairment, and total impairment with the involvement of growth plate, total impairment without the involvement of growth plate, subungual hyperkeratosis, onycholysis, alteration of healthy nail plate growth. Sign manifestation rate was evaluated by the following scale:

- 0 – Absence of sign;
- 1 – Slight manifestation rate;
- 2 – Moderate manifestation rate;
- 3 – Significant manifestation rate.

The main group comprised 33 persons: 15 men and 18 women, who received comprehensive treatment, which included systemic antimycotic drug and agent Wolvit. The disease duration in patients who took part in the investigation constituted from 2 months to 10 years.

Systemic antimycotic was used according to the schedule in compliance with the instructions. Wolvit was administered in the dosage of 5 mg once a day before meals during the whole course of treatment with systemic antimycotic. The course of treatment with systemic antimycotic comprised 1.5 months in onychomycosis of fingers and 3 months in onychomycosis of toes.

The control group included 10 persons: 2 men (20%) and 8 women (80%). The patients of this group were treated with systemic antimycotic. The course of treatment with this drug agent comprised 1.5 months in onychomycosis of fingernails and 3 months in onychomycosis of toenails.

### Results and discussion

Potency assignment of the complex under investigation was carried out on the ground of results, obtained in clinical and mycologic investigations. Clinical judgment of the method included evaluation of complaints and dynamics of objective disease manifestations. Mycologic efficiency consisted in fungi elimination.

The patients of both groups demonstrated positive dynamics of skin process in the course of treatment: itching and soreness were found to decrease significantly, as well as hyperemia, exfoliation and maceration. Five patients with mycosis of feet and onychomycosis were found to have active epithelialization of cracks and patients with dyshidrotic type of disorder were found to reduce the appearance of new

vesicular elements, the previously developed vesicles became dry and started to flake off.

Of 24 patients who belonged to the main group with complaints of soreness, 14 patients (46.6%) were found to have regression of soreness on the 4<sup>th</sup> week, 5 patients (16.6%) on the 6<sup>th</sup> week and five patients (16.6%) on the 8<sup>th</sup> week of treatment.

Itching was completely absent in 9 patients of the main group (4 men and 5 women). Of 21 patients who belonged to the main group with complaints of itching of the feet prior to treatment and in 10 patients (33/3%) it disappeared on the 4<sup>th</sup> week of treatment and in the same number of patients on the 6<sup>th</sup> week. In one patient (3.3%) itching persisted till the 8<sup>th</sup> week of treatment.

Subjective signs regression in the control group was observed later. Absence of subjective signs constituting itching and soreness was noted in 1 patient of the control group (10.0%).

Of 9 patients who complained of soreness, 1 patient (10%) was found to have a regression on the 2<sup>nd</sup> week of treatment, two patients (20%) on the 4<sup>th</sup> week and in three patients (30%) on the 6<sup>th</sup> week of treatment. In two patients (20%) of the control group soreness disappeared on the 8<sup>th</sup> week and persisted till 12 weeks of treatment in one patient (10%).

Of 5 patients with complaints of foot itching, two patients (20%) were found to overcome it on the 4<sup>th</sup> week of treatment and three patients on the 6<sup>th</sup> week (30%).

The structure of impaired nail plates in all the patients started to improve during the course of treatment: it acquired light pink color, its surface became glossy and smooth, free edge of nail plates became flatter and thicker. Nails started to acquire normotrophic structure.

Data are represented in table 1.

Studying the data provided in table 1 it is possible to note that soreness regressed 1.1-fold quicker on the 4-8<sup>th</sup> weeks of

Table 1

The dynamics of subjective signs in patients of the main and control group during the course of treatment

Subjective signs	Main group (n-33)					Control group (n-10)				
	4 wk	6 wk	8 wk	10 wk	12 wk	4 wk	6 wk	8 wk	10 wk	12 wk
Soreness	14	5	5	-	-	2	3	2	-	1
%	42.4%	15.1%	15.1%	-	-	20%	30%	20%	-	10%
Itching	10	10	1	-	-	2	3	-	-	-
%	30.3%	30.3%	3.03%	-	-	20%	30%	-	-	-

treatment in patients of the main group than in the control group. Full regression of soreness was observed in patients of the main group on average on the 8<sup>th</sup> week and in patients of the control group on the 12<sup>th</sup> week. Regression of itching was noted to be 1.3-fold quicker on the 4<sup>th</sup> and 6<sup>th</sup> week of treatment in patients of the main group than in patients of the control group. Full regression of itching was observed in all the patients of the main group on the 8<sup>th</sup> week and in the patients of the control group it was seen on the 6<sup>th</sup> week of treatment.

Nail plate length from nail fold to distal edge was measured prior to the study and the second, fourth, sixth, eighth, twelfth and sixteenth weeks of treatment in order to assess the dynamics of nail plate regrowth in patients of both groups. Student-Fischer test was applied for independent samples in order to compare the indices of the main and control groups. Data are represented in table 2.

Comparison of the indices shown in table 2 show that nail plate regrowth index in the control group comprised  $0.42 \pm 0.03$  whereas in the main group it was  $0.98 \pm 0.03$ , which implies that the amount of time necessary for nail plate regrowth reduced by 2.3-fold in patients of the main group.

Full clinical remission and elimination of fungi from the affected nail plates in the course of treatment with therapeutic complex including systemic antimycotic and "Wolvit" in patients of the main group were observed on the 8<sup>th</sup> week in one patient with onychomycosis of fingernails which comprised (3.03%), on the 12<sup>th</sup> week in the majority of patients of

the main group, namely 21 patients, which comprised 57.6% and on the 10<sup>th</sup> week in 10 patients (27.3%). And only in one patient (3.03%) negative reaction of mycologic microscopic examination occurred on the 16<sup>th</sup> week of the treatment.

Table 2

The assessment of nail plate growth rate in patients of the main and control groups

Subjective sign	Nail plate length from nail fold to distal edge*		
	Prior to treatment (cm)	Following treatment (cm)	Amount of growth
Main group (n-33)	$0.40 \pm 0.05$	$1.38 \pm 0.06$	$0.98 \pm 0.03$
Control group (n-10)	$0.71 \pm 0.08$	$1.13 \pm 0.08$	$0.42 \pm 0.03$

\* we refer to the site of the nail plate without clinical signs of onychomycosis (changes of structure, color and so on)

Full clinical remission and elimination of fungi from nail plates in patients of the control group who received only systemic antimycotic occurred at the same extent on the 12<sup>th</sup> and 16<sup>th</sup> weeks of treatment and there were five patients (by 50%) in each one. Negative reaction in the pathologic material of the patients still did not occur on the 10<sup>th</sup> week. Data are represented in table 3.

**Table 3**  
**The terms of negative reaction of the mycologic examination results**

Mycologic negative reaction	Main group (n-33)		Control group (n-10)	
	Number of patients	%	Number of patients	%
6 weeks	-	-	-	-
8 weeks	1	3.03	-	-
10 weeks	10	27.3	-	-
12 weeks	21	57.6	5	50.0
16 weeks	1	3.03	5	50.0

The comparison of indices, given in table 3 shows the acceleration of mycologic negative reaction in the patients of the main group.

The assessment of agent acceptability was carried out on the basis of subjective symptoms and sensations, reported by the patients and objective evidence, obtained in the course of treatment, based on laboratory indices dynamics as well as on the rate of occurrence and character of adverse reactions. The patients tolerated the treatment well, only one patient from the main group developed nausea on the 4<sup>th</sup> day of therapeutic complex administration but it did not require cancellation of agent intake. Patients of the both groups did not seem to develop any adverse allergic reactions.

The assessment of liver function following the termination of the course of treatment determined the absence of any significant changes in biochemical factors of blood in all the patients of the both groups. Clinical blood analysis and clinical urine analysis showed that fluctuations of indices in patients after the course of treatment did not exceed the normal rate.

Summing up the above mentioned, it is possible to suggest that the complex comprising systemic antimycotic and "Wolvit" shows good tolerability, does not cause any adverse or allergic reactions and is easy to use (it is sufficient to take it once a day). The administration of vitamin agent "Wolvit" together with systemic antimycotics allows to achieve a significant improvement of nail plate structure as it acquires even light pink translucent color, glossy surface, smooth and thick free edge, normotrophic structure. Participation of biotin in the formation of keratine, necessary for the development of hair matrix and nail plate, results in acceleration of healthy nail growth in patients with onychomycoses. Biotin is also a source of sulphur, which transports sulphur into the skin and its accessory organs, contributing

to collagen formation and therefore eliminates signs of early hair depigmentation, normalizes sebaceous glands function and exerts a positive impact on the structure of skin and its accessory organs (hair, nails).

### Conclusions

The developed complex with the employment of systemic antimycotic and agent "Wolvit" can be recommended for use in the treatment of dermatologic diseases as a current complex method for effective treatment of onychomycoses of fingernails and toenails, which gives a possibility:

- To achieve clinical remission as well as elimination of the causal organism and improvement of nail plate structure within a shorter period of time;
- To reduce the amount of time necessary for nail plate regrowth.

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