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Mycoses – prophylaxis and treatment

A permanent increase in the mycotic infections has been observed in recent decades. It is the effect of the development of industry, large migrations, usage of the public swimming pools, intensive diaphoresis, wearing impervious clothes and shoes. Systemic diseases: diabetes, obesity, hormonal disorders, immune and food deficiency, AIDS, systemic disorders, neoplasms and prescription drugs: antibiotics, corticosteroids and immunosuppressants cause mycoses. Therefore, permanent increase in mycotic infections requires health promotion and drug therapy to restrict primary infection and prevent reinfection (2).

There are many forms of mycosis. Tinea pedis and onychomycosis are the most common infections. The predisposing factors are the use of public showers and swimming pools, practicing sports and wearing synthetic shoes in warm, damp rooms. That is why sanitary rules are so important in everyday life. Thus, wearing shoes made from natural materials is highly recommended. When rubber boots or synthetic boots are worn, regular washing and drying of the feet should routinely follow. While using public showers, balneotherapy centers or swimming-pools, wearing one`s own shoes is recommended (4,8).

Prevention of recurrence of the illnesses is a very important component of therapeutic procedure. Shoes, socks and tights ought to be changed after a therapeutic session or disinfected with an antimycotic disinfectant. Socks must be washed in fungicidal solutions, and aerosols are helpful in disinfection of shoes. A broad dish filled with a 10% solution of formalin placed together with the shoes and socks in a hermetic plastic bag is a good way of carrying out disinfection. After 12–18 hours the shoes ought to be aired and the socks washed. Fungicidal action of formalin vapour is used. Another method of disinfection is the use of 0.1–1% chinoxysole solution. Cotton wool or gauze soaked in the chemical ought to be placed inside the shoes and socks, which should soak in it for 24 hours. Next, the shoes should be aired and the socks washed. The same procedure is recommended to disinfect underwear in case of dermatomycosis. Ironing the clothes is an additional method of overcoming infection (14).

Heat and moisture encourage epidermis maceration and create excellent conditions for mycoses development. Natural pH of the skin is changed by hyperhidrosis, which results in the impairment of defense mechanisms responsible for overcoming infections (14). Interdigital spaces of the feet, axillary and inguinal fossas, women's submammary regions and epidermic folds ought to be well taken care of. The above rules of prophylaxis must be conscientiously followed by diabetics, patients with compromised immunity or treated with a broad spectrum of antibiotics as well as by premenopausal women and sportsmen. High temperature and moisture increase the growth of fungi, therefore the use of other people's towels, sponges and underwear is absolutely forbidden (2, 8).

Such measures help prevent infections with dermatophytes and yeast-like fungi which show a tendency to affect skin folds, mucous membranes, nails and internal organs. There are some occupations especially predisposing to such infections, e.g. cleaners, laundresses, workers employed in sugar-produce industry or fruit- processing industry. They should properly look after the skin of their hands and see the doctor immediately if they notice alarming lesions (erythema and maceration of the epidermis, especially in case of the interdigital spaces and the walls of the nails inflammation). Elderly people and pregnant women are often affected by mucous membrane candidiasis, which is often the first symptom of diabetes (8). Proper diet and right quantities of vitamins, especially of B group, are recommended for elderly patients. The excess of carbohydrates, lipids and hypovitaminosis, as well as deficits of minerals contribute to mycosis (1). Yeast infections may accompany other systemic diseases. There is some information about frequent occurrence of chronic mucous-skin or nail candidiasis among patients with Cushing syndrome and Raynaud disease (7). Candidiasis is more likely to develop in patients with cancer of the oral cavity and undergoing radiological treatment (13).

Prevention of fungal infections ought to be carried on in physiological conditions, such as pregnancy and the perinatal period. It is of great importance because of the child's direct contact with the mother's genital tract which, when infected, may cause intrauterine and perinatal candidiasis infections. It is diagnosed as oral candidiasis, diapper dermatitis, pustular rash and vesicular eruption, or as generalized multiorgan infections (7). In children with low birth weight (less than 1000 g) the presence of an intrauterine device or uterine colli suture predispose newborn to congenital cutaneus candidiasis. The most common course of cutaneus candidiasis in such cases is generalized exfoliative dermatitis, a state similar to scalded skin. In case of diagnostic troubles, the most recommended diagnostic methods are micro- and macroscopic examination of the placenta or umbilical cord (3). The use of certain therapeutic drugs, such as broad spectrum antibiotics, immunosuppressive drugs and glycocorticosteroids leads to dangerous local or general fungal infections. Physicians treating patients with these drugs should draw the patients' attention to certain symptoms that are indicative of a fungal infection. In order to begin treatment as quickly as possible, physicians should prescribe a medication which contains lactic acid bacillus. This bacterium is part of the physiological flora in the human digestive system. It is very important to remember about prevention in a long-term treatment with immunosuppressive drugs in transplantology. In case of multifocal dermatomycosis following immunosuppressive therapy, it is necessary to diagnose each focus separately. This is in connection with the presence of different species in the cutaneous eruptions (10).

Children are more susceptible to mycotic infections because of thin and soft horny layer of the epidermis. Superficial mycosis of the scalp, especially microsporia, is most common in children (8). In this case the source of infections, apart from people, are animals (e.g. cats, dogs, hamsters, guinea pigs). Children are infected while playing with their pets. Here, prophylaxis is realized by isolation and treatment of the ill animal. The sources of infection, in large cities, are also homeless cats and dogs, which should be isolated. Prevention of the spread of mycosis in domestic animals, like pigs, cows and horses is realized by good veterinary care in rural areas. Microsporiasis is very infectious and that is why epidemics in kindergartens, schools and boarding- schools are very common. Standard procedures for treating children with mycosis of the scalp depend on the kind of dermatophytes. If a child is infected by anthropophilic fungus, it is recommended that he should stay at home for one week at least (14). Susceptibility to mycotic infection of the scalp caused by zoophilic dermatophytes is probably caused by low sebum secretion. According to many reports, fatty acids with medium length of the chains, which inhibit microsporia growth, are on a low level in small children and the elderly (7).

Mycoses belong to chronic diseases and are very diffcult to treat. With regard to the frequency of mycotic infections in human population, an intensive research is conducted on introduction of new and more effective preparations.

Currently used antimycotic drugs are divided into five pharmacological groups. These are: 1. Polyens (nystatin, natamycin, amphotericin B). 2. Azoles where two subgroups are distinguished: imidazols (myconazol, clotrimiazol, econazol, izoconazol, chlormidazol, bifonazol, ketoconazol); triazols (itraconazol, fluconazol). 3. Alliloamines (terbinafine). 4. Morpholines (amorpholine). 5. A diversified group of compounds (grizeophulvine and cyclopyrox) – 2,5.

Among these drugs there are preparations for local and systemic use. The mechanism of action of antimycotic drugs is different. They are divided into: 1) acting on synthesis of nucleic acids and mitosae fungus cellule for example grizeophulvine, 2) acting on fungus cell membrane: a) disturbing a cell membrane integrality – polyens, b) blocking ergosterol synthesis through: suppression of skvalene epoxydase (alliloamine and benzyloamine), inhibition 14 α-desmutase depending on P-450 cytochrom (azoles), blocking Δ14 reductase or Δ8 - Δ7 isomerase (morpholine), c) storage of substances indispensable to cell membrane synthesis is disturbed (cyclopyrox) suppressing fungus cell membrane synthesis by which the process of assimilation takes place (5, 8).

Antimicotic drugs may be used oraly or locally. Oral treatment has many advantages and is indicated: in onychomycosis and tinea capitis; when the changes cover large surface of the skin; in immunological disorders; when the penetration of local drugs into infection focus is weak; when there are persistent infection foci. It is necessary, in some kinds of mycotic infections, to conduct systemic therapy, because external drugs do not penetrate into foci (for example in tinea capitis, mycotic cells penetrate into hair follicle deeply). Moreover, in onychomycosis, when mycotic cells grow mainly into internal side of the nail, the nail plate is practically impermeable for drugs. Sometimes surgical removal of nail plates under anaesthetic and suitable protection of the nail bed is recommended. Daily antiseptic bath (chinoxysole) and regular curettage of the nail bed is applied (1,5).

Most antifungal drugs, in sufficient concentration, cause the fungistatic effect, which means that they reach the peak stage of effectiveness, i.e. they inhibit growth of fungi. Only a few have the fungicidal effect, which means they kill microorganisms. This is very important in patients with immunological system insufficiencies. Fungicidal drugs are recommended among the patients with immune system deficiencies. Application of these drugs leads to elimination of fungal cells and spores. This is the main reason why they reduce both the amount of recurrences and length of therapy. Trichophyton rubrum inhibits local cellular immunity due to mannan – a component of its cell wall, which is of the most importance, because this species is responsible for approximately 80–90% of infections. Fungicidal agents should be applied until complete recovery is achieved. Due to the fact that spores cause reinfection, therapy should be continued for 3–4 weeks despite the absence of clinical manifestations. The choice of therapy depends on the type of dermatomycosis. Before appropriate drugs are selected, it is necessary to consider: clinical picture, age of patient, pregnancy, breast-feeding, renal and liver function, other concomitant diseases, especially hematological and immunological disorders, applied therapeutic agents (8, 9).

The therapy is more likely to be effective under the following conditions: mycological diagnosis before beginning of treatment; elimination of factors which play a role in developing an infection; appropriate choice of drug and familiarity with therapy; cooperation with the patient; regular check-ups including physical and mycological examination (12,14).

Partial removal of the nails is possible by using ointment with 40% urea with potassium iodide. After a 3–4 week dressing with ointment treatment, it is easy to remove a pathologically changed nail plate. After cleaning, local antimycotic treatment is necessary. Local therapy is to be continued as long as complete growth of the nail plate is accomplished. Because of hyperkeratosis of the epidermis of the hands and feet, local antimycotic treatment does not penetrate deep enough and it is easier to heal by the use of oral drugs. Despite the developed methods, the treatment of mycosis is still difficult and the methods insufficient. The reasons are: improper diagnosis, inappropriate action of the drug, lack of cooperation between patient and doctor, too short therapy (9,14). Inefficiency of antimycotic treatment is caused by improper

diagnosis. Psoriasis, eczema and bacterial infections are a problem in differential diagnosis (8). Recurrence of infection is often a problem because of incorrect cooperation between patient and doctor and breaking the rules of disinfection of footwear and clothes. Another reason for inefficiency of treatment is resistance to antimycotic treatment. In patients with chronic mucocutaneous candidiasis and AIDS azolic drugs are ineffective. Reduction of side effects and improvement of efficiency of the treatment are still the main aims in the treatment of mycoses. Drugs should be administered once daily and the time of therapy should be shortened. Still, some points in inhibition of ergosterole synthesis, such as oxidoskvalene enzymes and Δ 24-methyl-transferase, are not applied (9,11). A new aim of ideal therapy is the cellular wall, composed of chitin, glucan and mannan. The peptidonucleotide antibiotics such as nikkomycine, polimyxine are the inhibitors of synthesis of chitine. The synthesis of glucane is blocked by lipopeptide antibiotics: achinocandine, cilofungine, aculeacine, pneumocandine and pneumocandine B-glycolipide antibiotic. The inhibition of synthesis of fungal proteins may be used in the treatment of mycoses. To make the fungal growth impossible, you should block the topoisomerase-enzyme indispensable to transcription and replication of DNA. Covalent linkages between enzyme and DNA are stabilized by topoisomerase inhibitors and therefore the process of DNA threads junction is suppressed. Immunomodulators and monoclonal antibodies against fungal proteins may also be applied in the future. The ideal fungicide ought to have a broad spectrum of action, high effectiveness at minimal concentration of the drug, fungicidal activity and keratophilic and lipophilic properties. The prolonged therapeutic concentration of the fungicide in corneal layer after therapy, high percentage of mycological and clinical recoveries, low percentage of recurrent events, lack of side-effects and low price are very important issues (6, 9).

Mycoses are prolonged, difficult to treat and recurrent diseases therefore proper prophylaxis, early diagnosis and effective treatment are necessary to overcome them.

REFERENCES

1. Brennan B., Leyden J.: Overview of topical therapy for common superficial fungal infections and the role of new topical agents. J.Am. Acad. Dermatol., 36, 3, 1997.
2. Broniarczyk-Dyła G., Joss-Wichman E.: Zakażenia grzybicze skóry i paznokci oraz metody ich leczenia. Mikol. Lek.,5, 2, 15, 1998.
3. Darmstadt G. et al.: Congenital cutaneus candidiasis: clinical presentation, pathogenesis, and manegement guidelines. Pediatrics,105, 2, 438, 2000.
4. Dzierżanowska D.: Zakażenia grzybicze, patogeneza, klinika i leczenie. Terapia, 10, 3, 1998.
5. Elewski B.: Mechanisms of action of systemic antifungal agents. J.Am.Acad. Dermatol., 28,28,1993.
6. Hay R.: Antifungal drugs on the horizon. J. Am. Acad. Dermatol., 31, 82, 1994.
7. Hejniak B. et al.: Etiopatogeneza i klinika zakażeń grzybiczych skóry i jej przydatków. Dermatologia, 6, 11, 1151.
8. Jabłońska S., Chorzelski T.: Choroby skóry dla studentów medycyny i lekarzy. PZWL, Warszawa 1994.
9. Langner W., Stąpór W.: Współczesne leczenie wybranych chorób skóry. Polfa, Warszawa 1998.
10. Kołodziej T.: Przypadek wieloogniskowej grzybicy skóry wywołanej różnymi patogenami Mikol. Lek., 9,163, 2002.
11. Nowicki R.: Współczesne leki przeciwgrzybicze w dermatologii. Mikol. Lek., 2, 111, 1995.
12. Richardson M., Warnock D.: Grzybice. Rozpoznanie i leczenie. Springer PWN, Warszawa 1995.

13. Stryjski A.: Zagrożenie zakażeniami grzybami drożdżopodobnymi u chorych leczonych radioterapią z powodu nowotworow głowy i szyi. Mikol. Lek., 9, 3, 125, 2002.
14. Szepietowski J.: Grzybice skóry i paznokci. Medycyna Praktyczna, Kraków 2001.

SUMMARY

An increase in the mycotic infections has been observed in recent decades. It is the effect of the development of industry, large migrations, living in huge aglomerations, usage of the public swimming-pools, wearing impervious clothes and shoes. Systemic diseases: diabetes, obesity, hormonal disorders, immune and food deficiency, AIDS, neoplasms and prescription drugs: antibiotics, corticosteroids and immunosuppressants, cause mycoses. Mycoses belong to chronic diseases, they are difficult to treat and very often reccurred. A lot of antimycotic drugs are known, but the most effective are azoles and alliloamines. An intensive research is conducted on introduction of new and more effective and cheaper preparations.

Profilaktyka i leczenie grzybic

W ostatnich dziesięcioleciach obserwuje się ciągły wzrost występowania zakażeń grzybiczych. Związane jest to z rozwojem gospodarki, rosnącą migracją ludności, mieszkaniem w dużych aglomeracjach, częstym korzystaniem z łaźni i basenów publicznych, noszeniem odzieży i butów z nieprzewiewnych materiałów. Grzybicom sprzyjają również zaburzenia ogólnoustrojowe, jak: cukrzyca, otyłość, zaburzenia hormonalne, niedobory odporności, żywieniowe, AIDS, choroby układowe oraz stosowanie leków, m. in. antybiotyków, kortykosteroidów i środków immunosupresyjnych. Grzybice należą do schorzeń przewlekłych i bardzo trudnych w terapii. Często nawracają. Znanych jest obecnie wiele leków przeciwgrzybiczych, wśród których dużą skutecznością odznaczają się pochodne azolowe oraz alliloaminy. Prowadzone są także badania nad wprowadzeniem nowych, bardziej skutecznych oraz tańszych metod leczenia.