# MANAGEMENT OF MUCOCUTANEOUS CANDIDIASIS

# **GEORGETA OLTEAN**

PhD candidate, University of Medicine and Pharmacy, Tg. Mureş

Abstract: Candidiasis is a mycotic infection caused by members of the genus Candida. The clinical manifestations may be acute, subacute or chronic and may be localized on skin, nails or mucosa (mouth, gastrointestinal tract, genital, lungs) and represents 25% from all mycotic infections. The first step in the management of candidiasis should be to correct the underlying conditions. Topical therapy is sufficient in most patients; oral therapy is indicated in severe cases or in immunosuppressed patients.

Keywords: Candidiasis, treatment

**Rezumat:** Candidozele sunt infecții micotice acute, subacute, mai rar cronice provocate de specii din genul Candida, cu localizare pe piele, unghii sau mucoase (gură, tub digestiv, genital, plămâni) și reprezintă aproximativ 25% din totalul infecțiilor micotice. Tratamentul candidozelor cutaneo-mucoase este în principal local, tratamentul antimicotic sistemic este indicat în formele severe, recidivante sau la imunodeprimati. Se asociază, de asemenea, igiena locală și tratamentul afecțiunilor favorizante.

Cuvinte cheie: Candidoza, tratament

### INTRODUCTION

The fungal infection is a process that consists of all interactions between the fungus and the receptive macroorganism. Essential aspects for accurate approach of the fungal infection are not always taken into consideration: the underlying conditions and the systemic consequences of candidiasis. Therefore, the administration of antifungal agents alone, in the absence of hygienic-dietetic measures and immunostimulant therapy, is not sufficient.

Etiological treatment implies the administration of antifungal drugs with strict efficiency on fungi and minimal adverse effects on the patient. A correct diagnosis, confirmed through the isolation of the fungus and evaluation of its susceptibility to available therapeutic agents, should precede the treatment recommendation.

#### Main classes of antifungal agents

## 1. Inorganic:

- chemical elements: iodine, sulphur;
- acids: boric acid, hydrochloric acid;
- salts: potassium iodide, potassium permanganate, copper sulphate, sodium thiosulphate;

- 2. Organic:
- natural: active principles in plants, propolis
- synthetic and semisynthetic:
  - organic acids (benzoic, caprylic, propionic, salicylic);
    - allylamines (Naftifine, Terbinafine);
  - polyenes (Nystatin);
  - pyrimidine derivatives (5-Flucytosine);
  - derivatives of hidroxipiridona
  - imidazoles (Ketoconazole, Miconazole);
  - triazoles (Fluconazole, Itraconazole, Voriconazole);
  - echinocandins (Caspofungin).(1,8)

## Topical antifungal agents

Topical antifungal drugs are used in the treatment of mucocutaneous mycosis and are not absorbed systemically following topical application. Candidiasis is mainly a benign infection and requires only topical therapy. Some antifungal agents are not absorbed intestinally and therefore the oral administration is not efficient for candidiasis of the skin, mucosa or nails.

Dyes: 1% Gentian violet represents the classical treatment of oral candidiasis and is used in applications on mouth mucosa. The alcalinisation of the region will be obtained with 5% borax glycerine or 5% sodium bicarbonate solution. Methyl blue and methyl green are active on anal and genital mucosa and in skin folds.

For skin, Streptomicosan preparation or Castellani solution are used.

Iodine is used under the form of alcohol iodine, tincture of iodine (Sabouraud), Lugol's solution, with 1-2% halogen concentration.

Sulphur has antiparasitic, antifungal, keratolytic, antiseboreic effects. Today, it is rarely used because of its bad smell and irritating reactions.

Propolis is a natural product, obtained through the activity of honey bee families, which implies collecting and processing exudations of buds from various plants. The composition of propolis is complex and various, depending on the collection time and place. The compositional diversity of propolis explains its varied use in therapy. Propolis has antifungal properties, especially on Candida species and dermatofitys, as well as antibacterial, antiviral, cytotoxic, immunomodulating and anaesthetic properties. Propolis enhances the effects of

AMT, v. II, no. 2, 2009, p. 161

antifungal drugs, acting in synergy. 5-10% propolis extracts in propyleneglycol have a sure antimycotic effect (1).

Nystatin, a polyenic antibiotic is not absorbed systemically, and it is used in superficial mucosal candidiasis, cutaneous candidiasis or otomycosis. After prolonged glucocorticoid or immunosuppressive therapy, Nystatin can be administrated concomitantly with widespectrum antibiotics in the prophylaxis of digestive and mucocutaneous candidiasis.

Miconazole, broad-spectrum antifungal drug, persists for over 4 days in stratum corneum.

Econazole, Bifonazole, Fenticonazol nitrate (Lomexin), Butoconazole, imidazole derivatives, broad-spectrum fungicide antifungal drugs.

Izoconazol (Travogene), wide-spectrum azole derivatives, also active against some Gram positive bacteria.

Naftifine (Exoderil), allylamine derivative, also has anti inflammatory activity.

Ciclopiroxolamine (Batrafen) is a hydroxoproline that acts selectively on cellular membranes, interfering with the accumulation of products which are necessary for the cell wall synthesis; on the opposite antifungal drugs from the allylamines and azoles classes interfere with the fatty acids synthesis.

Amorolfine (Loceryl) acts by altering the fungal cell wall.

Natamicine (Pimafucin), macrolide antibiotic with fungicide action.

Fusafungine (Bioparox), topical cyclohexapeptide.(5,8)

#### Systemic antifungal agents

There are five classes of systemic antifungal drugs.

Polyenes (Amphotericin B) bind irreversibly to ergosterol and other specific fungal cell wall sterols and act as ionophores, causing leakage of vital cytoplasmic components, and the death of the organism.

Fluoropyrimidines (5-Flucytosine) block the fungal DNA synthesis and the nuclear division. In the fungal cells, it is converted to 5-fluorouracil by the enzyme cytosine deaminase, resulting in the disruption of the protein synthesis.

Allylamines (Terbinafine) affect the early stages of fungal sterol biosynthesis through the inhibition of squalene epoxidase, leading to ergosterol deficiency and fungal cell membrane disruption.

Azoles (imidazoles: Ketoconazole, triazoles: Fluconazole, Itraconazole, Voriconazole) owe their antifungal activity to the inhibition of cytochrome P-450dependent 14a-sterol demethylase, resulting in the formation of a plasma membrane with altered structure and function.

Echinocandins (Caspofungin, Anidulafungi) act as specific non-competitive inhibitors of b1-3D-glucan synthetase, a major structural fungal cell wall polymer.(2,8)

Main antifungal agents used in dermatology:

Terbinafine (250mg tablets) binds to plasma proteins followed by the rapid diffusion in dermis and the concentration of the drug in stratum corneum. After oral administration, it is concentrated in skin and nails, where it achieves fungicide levels. High concentrations are obtained in sebum, hair follicles and sebum rich skin.

Usual doses: Cutaneous candidiasis: 250mg/day, Onychomycosis: 250mg/day for 6 to12 weeks. Ketoconazole (200mg tablets) is indicated when the topical treatment cannot be administrated or when drug-

resistance occurs, in chronic, recurrent candidiasis, in the prophylactic therapy in the immunosuppressed patients.

Usual doses: children 15-30 kg: 100mg/day, adults: 200-400mg/day, prophylactic treatment: 400mg/day – adults, 4-8mg/kg – children.

The duration of the treatment depends on the evolution of the symptomathology and the patient's reactivity. It is recommended to continue the therapy one week after the symptomathology has disappeared and the cultures have become negative: vaginal candidiasis 5 days, cutaneous and oral candidiasis 2-3 weeks, onychomycosis 6-12 months.

Itraconazole (100mg tablets) is indicated in the treatment of vulvovaginal, oral candidiasis, dermatomycosis, onychomycosis. It is active against C. Albicans and less active against the non-albicans species of Candida. The accumulation of the drug in keratinized tissues is four times bigger than in serum. Plasmatic levels of the drug become not detectable seven days after treatment interruption, but the effect of the drug on the skin is maintained at therapeutic levels for 2-4 weeks after the end of the therapy.

Usual doses: Oral, vulvovaginal candidiasis: 100-200 mg for 7-15 days, Onychomycosis: 2x200 mg 7 days, repeated 2-3 times with a three week pause in between, or 200mg/day for a three months period.

Fluconazole (50, 100, 150mg tablets, 50mg/ml oral suspension, 2mg/ml iv solution) is active on Candida species and less on C. Glabrata, C. Krusei.

Usual doses: Cutaneous, genital candidiasis: 150 mg single dose or 50mg/day for 7-14 days. Oropharyngeal candidiasis: 50-100mg/day 7-14 days, Onychomycosis: 150mg/week 3-12 months, 3mg/kg – child.

Voriconazole (50mg, 200mg – tablets, 200mg iv solution) is used as first intention treatment in invasive candidiasis on immunosuppressed patients.(4,6)

### CONCLUSIONS

The accurate management of dermatomycoses is essential in healing the infection, but mainly in relapses prevention. It is indicated to:

- begin specific treatment after accomplishing the mycological exams to identify Candida species;
- maintain antifungal therapy for prolonged periods of time, during which the fungal parasites could be eliminated through exfoliation of the superficial epidermic layers;
- correct predisposing factors in relapse prevention.

- If the antifungigram is not available, the therapy will be guided by the known susceptibility of the Candida species to specific antifungal drugs: C. Albicans, C. Tropicalis to Fluconazole, C. Glabrata, C. Krusei to Caspofungin, C. Parapsilosis to Caspofungine, Voriconazol.

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