Compared sensitivity of *C. albicans* isolated from different pathological produces to antimycotic drugs

Monica JUNIE, Carmen COSTACHE

Catedra de Microbiologie UMF “Iuliu Hațieganu” Cluj-Napoca, România

**ABSTRACT.** Antimycotic activity of Clotrimazole, Miconazole, Fluconazole, Nystatin, Griseofulvin, Flucytosine, Terbinafine, Natamycin, Ketoconazole, Bifonazole and Econazole on collection *C. albicans* and on different strains isolated from patients with mycosis was studied, by performing disk diffusion antimycotic susceptibility test. The majority of tested strains were S to Nystatin, Ketoconazole, Clotrimazole, Fluconazole and Miconazole. There are high proportions of IS strains to Terbinafine and Natamycin and the majority of tested strains are R to Bifonazole, Flucytosine and Griseofulvin. Our data recommend the usage of Clotrimazole, Fluconazole, Nystatin and Ketoconazole in vaginitis, but also of Natamycin and Terbinafine, which seem to be more efficient against vaginal strains of *C. albicans* than against strains isolated from other locations. Terbinafine, Bifonazole, Flucytosine, and Natamycin are not indicated in pulmonary and urinary candidiasis therapy because of high proportion of R strains. Our results establish the antimycotic spectrum of different antimycotic drugs and can be used as an orientation guide in antimycotic therapy.

**Key words:** disk diffusion antimycotic sensitivity test, Candida albicans.

**Material and methods**

The antimycotic activity of Clotrimazole, Miconazole, Fluconazole, Ketoconazole, Bifonazole, Nystatin, Griseofulvin, Flucytosine, Terbinafine, and Natamycin, on collection strain of *C. albicans* and on 105 different strains isolated from patients with mycosis was studied, by performing disk diffusion antimycotic sensitivity test. The method consists of depositing disks impregnated with various antifungal agents, some of them at different concentrations, onto the surface of a Sabouraud medium. The results are read by measurement of inhibition diameters and associate them with the appropriate kind of sensitivity from tables: sensitive (S), intermediately sensitive (IS) and resistant (R).

**Results**

*C. albicans* collection strains are most sensitive (S) to Ketoconazole, followed in descending order of sensitivity by Terbinafine, Clotrimazole, Nystatin and Econazole and are intermediately sensitive (IS) to Miconazole, Fluconazole, Natamycin and Griseofulvin.

From all isolated strains, 100% are S to Nystatin, 93.8% to Ketoconazole, 87.5% to Clotrimazole and 81.3% to Fluconazole. The rest of strains are either IS (3.1% for Ketoconazole, 6.2% for Clotrimazole and 3.1% for Fluconazole) or resistant (R): 3.1% for Ketoconazole, 6.3% for Clotrimazole and 15.6% for Fluconazole.

The majority of strains (84.4%) are IS for Natamycin and only 12.5% of the tested strains were S. Only 6.5% of tested strains are S to Terbinafine, 29% were IS strains and 64.5% of strains were R. There were 4.8% S strains to Flucytosine, 11.3% IS strains and 83.9% were R strains. These results are illustrated in graphic 1.

There is a difference of sensitivity of *C. albicans* strains according with the location of the candidiases.
Sensitivity pattern of *Candida albicans* strains isolated from pharyngeal exudates

According with our results, 100% of *C. albicans* strains isolated from oral candidiases are S to Nystatin, 92.9% to Ketoconazole, 85.7% to Clotrimazole, 71.4% to Fluconazole and 50% to Miconazole. The sensitivity to Natamycine is 14.3%, to Terbinafine is 7% and to Flucytosine is 6.3%. All strains were R to Bifonazole (graphic 2).

**Graphic 1**

**Graphic 2**
**Sensitivity pattern of Candida albicans strains isolated from sputum**

C. albicans strains isolated from sputum of patients with pulmonary candidiases are 100% S to Clotrimazole and Nystatin, 75% S to Fluconazole, Miconazole, Ketoconazole and only 25% S to Natamycine. They are 100% R to Terbinafine and Bifonazole and 90.9% R to Flucytosine (graphic 3).

**Sensitivity pattern of Candida albicans strains isolated from urine**

All Candida albicans strains isolated from urine are 100% sensitive to Nystatin, Ketoconazol, 80% are sensitive to Fluconazole, 60% to Clotrimazole, and a smaller proportion are sensitive to Miconazole (40%), Terbinafine (20%), Natamycine (20%). Strains isolated from this location are in great proportion resistant to Bifonazole, Terbinafine and Flucytosine.

The same considerations must be noticed in the interpretation of the sensitivity test, a great proportion of intermediary sensitive and resistant strains at low concentrations of antymycotic become sensitive or intermediary sensitive at higher, standard concentration of antymycotic drug (graphic 4).

**Graphic 3**

| Antimycotic sensitivity of C. albicans strains isolated from sputum |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Nystatin | Clotrimazole | Ketoconazole | Fluconazole | Miconazole | Natamycine | Terbinafine | Flucytosine | Griseofulvin | Bifonazol |
| S | 100 | 100 | 75 | 75 | 75 | 25 | 0 | 9.1 | 0 | 0 |
| IS | 0 | 0 | 0 | 0 | 25 | 75 | 0 | 0 | 0 | 0 |
| R | 0 | 0 | 25 | 25 | 0 | 0 | 100 | 90.9 | 100 | 100 |
Sensitivity pattern of Candida albicans strains isolated from vaginal discharge

The small number of strains isolated from women with vaginitis does not allow us formulate a competent conclusion, demanding for further, more extensive studies. However, according to our results, all strains were sensitive to Clotrimazole (100%), Fluconazole (100%), and Nystatin (100%), Ketoconazol (100%) and a large proportion of them were intermediary sensitive to Terbinafine (66.7%), Miconazole (100%), Natamycine (100%) and a smaller proportion to Flucytosine in small concentration (16.7%). This last percentage may be higher for optimal dosage of antimycotic. Our data recommend the usage of Clotrimazole, Fluconazole, Nystatin and Ketoconazol in vaginitis, but also of Natamycine and Terbinafine, which seem to be more efficient on vaginal strains of Candida than on strains isolated from other locations (graphic 5).
Results obtained by performing the antimycotic sensitivity test with lower concentrations of antimycotic, after applying the correction factor according to previous studies, show that the most efficient antimycotic drug on vaginal strains is Nystatin, to which all the strains were sensitive. Nystatin is followed by Ketoconazole (83.3% sensitive strains), Clotrimazole (66.7% sensitive strains), Miconazole (50% sensitive strains), Fluconazole (50% sensitive strains), Terbinafine (50% intermediary sensitive strains), Natamycine (33.3% intermediary sensitive strains) and Flucytosine (16.7% intermediary sensitive strains).

**Discussions**

Methods to appreciate fungal susceptibility to antimycotic drugs are still of interest in laboratory research due to a variety of reasons (1,4).

The NCCLS gold standard to appreciate fungal susceptibility (M-27A) is a broth dilution method, both too complex and labor-intensive for routine testing. E-test is expensive and not yet standardized for fungi so that disk diffusion methods seem to be the correct alternative for clinical laboratories (2).

There are several antifungal disks used for diffusion method on the market, that’s why the diameter of inhibition zone obtained with a given disk must be interpreted according with the medium used for cultivation and with the concentration of antifungal agent used for impregnation and correlated with the standard method. Our study was performed on Sabouraud media containing Chloramphenicol with disks containing different concentrations of antifungal agents in such a manner to afford appreciation of dose-dependent resistance (3, 5).

We are aware that further comparative studies are needed in order to obtain a method to be routinely used in clinical laboratories and in order to obtain clinical reliable data. Actually we are working to a comparative study for testing...
antimycotic susceptibility of different fungal strains.

**Conclusions**

1. The best antimycotic drugs in candidiases are Ketoconazole, Clotrimazol, Fluconazole and Nystatin, to which the majority of the tested strains were sensitive. Miconazole, Natamycine and Terbinafine are less efficient, because of the high proportion of intermediary sensitive strains. Bifonazole, Flucytosine and Griseofulvin are not indicated in candidiases therapy due to the resistance of tested strains to these antimycotic drugs.

2. Nystatin has an extensive spectrum of action so that it can be used in the treatment of all studied mycosis. All other antimycotic drugs are efficient on some fungi, less efficient on others and some fungi acquired resistance to these drugs.

3. We recommend the usage of Clotrimazole, Fluconazole, Nystatin and Ketoconazole in vaginitis, but also of Natamycine and Terbinafine, which seem to be more efficient against vaginal strains of C.albicans than against strains isolated from other locations.

4. Terbinafine, Bifonazole, Flucytosine, Griseofulvin and Natamycine are not indicated in pulmonary and urinary candidiases therapy because of high proportion of R strains.

Our results establish the antimycotic spectrum of different antimycotic drugs and can be used as an orientation guide in antimycotic therapy. On the other hand the changing in sensitivity pattern of the strains isolated from patients with a diversity of mycotic disease in relation with standard strains, impose the performing of antimycotic sensitivity test for each isolated strains and the establishment of therapy according with sensitivity.

**References**


