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In vitro susceptibility of pharyngeal isolates of Candida albicans to some antifungal drugs

Under predisposing conditions, microorganisms of natural microflora, including yeast-like fungi belonging to *Candida* sp., mainly C. *albicans*, may cause endogenous infections. Candidiases of the airways are usually preceded by colonization of mucous membrane of the upper respiratory tract by *Candida* sp. (1, 2).

Increasing consumption of antifungal drugs may result in the possibility of selection and spread of drug-resistant strains and, in consequence, may lead to therapeutic failure. Therefore, it was necessary to monitor susceptibility of fungal strains isolated from clinical specimens to generally applied antifungal drugs (3, 5, 6).

In this paper we assessed the susceptibility of pharyngeal *C. albicans* strains, potential agents of endogenous candidiases, for some antifungal drugs used in superficial mycoses and in deep mycoses: polienic antibiotics – amphotericin B and nystatine, pirymidyn derivative: flucytosine, imidazole derivatives: clotrimazole, miconazole, econazole and ketoconazole and triazole derivatives: fluconazole and itraconazole.

MATERIAL AND METHODS

A total collection of 100 pharyngeal isolates of *C. albicans*, isolated from healthy people, was used in the present assay. Sensitivity of the isolated strains to nystatine, clotrimazole, miconazole, econazole and ketoconazole was assayed using disc-diffusion method onto Casitone Agar (Bio-Rad). Besides, minimal inhibitory concentration (MIC) was determined for flucytosine, amphotericin B, fluconazole and itraconazole by microtest ATB FUNGUS 2 (bioMerieux).

RESULTS

Disc-diffusion method revealed that all the studied pharyngeal *C. albicans* isolates were sensitive to nystatine and ketoconazole. Some of these strains showed decreased susceptibility to: miconazole (17% isolates), econazole (1% isolates) and clotrimazole (6% isolates) (Fig. 1).

According to MIC determinations, all the studied *C. albicans* strains were sensitive to amphotericin B (range MIC = 0.25 – 1 mg/l, $MIC_{50} = MIC_{90} = 0.5$ mg/l) and flucytosine (MIC = $MIC_{50} = MIC_{90} =$ 0.5 mg/l). Some of these strains showed decreased susceptibility to triazole derivatives: fluconazole

– 1% isolates (MIC = 32 mg/l) and itraconazole – 5% isolates (MIC = 0.25 – 0.5 mg/l). Moreover, 3% strains (MIC = 128 mg/l) and 5% strains (MIC = 2 – 4 mg/l) were resistant to fluconazole and itraconazole, respectively. Besides, a big difference in MIC values for fluconazole and itraconazole was found (Table 1 and Table 2).

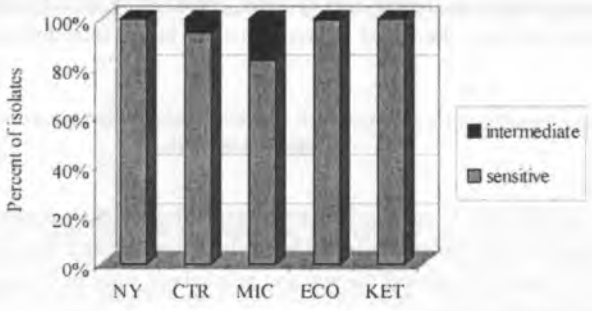

Fig. 1. *In vitro* susceptibility of pharyngeal isolates of *C. albicans* to nystatine and some azole derivatives assessed by disc-diffusion method (n = 100); NY – nystatine, CTR – clotrimazole, MIC – miconazole, ECO – econazole, KET – ketoconazole

Table 1. *In vitro* susceptibility to amphotericin B, flucytosine, fluconazole and itraconazole of pharyngeal isolates of *C. albicans*

Antifungal drugs	Range MIC (mg/l)	MIC_{50} (mg/l)	MIC_{90} (mg/l)
Amphotericin B	0.25–1	0.5	0.5
Flucytosine	0.5	0.5	0.5
Fluconazole	0.25–128	0.5	4
Itraconazole	0.125–4	0.25	0.25

Table 2. Differences in MIC values for fluconazole and itraconazole of pharyngeal isolates of *C. albicans*

MIC (mg/l)	Fluconazole	Itraconazole
	percent of isolates (n =100)	
0.125	-	90
0.25	35	1
0.5	45	4
1	6	-
2	4	1
4	2	4
8	4	-
32	1	-
128	3	-

DISCUSSION

Data presented in this paper indicate that pharyngeal *C. albicans* isolates were the highest sensitive to flucytosine and polienic antibiotics (amphotericin B and nystatine), showing decreased sensitivity to imidazole (clotrimazole, miconazole, econazole and ketoconazole) or triazole derivatives (fluconazole or itraconazole). The obtained data are in agreement with those described by other authors, who found that polienic antibiotics as well as flucytosine had high effectiveness

towards *C. albicans* strains isolated from blood (4), throat and nasal specimens (1, 2, 3, 5, 7). Besides, also other authors indicate that some pharyngeal *C. albicans* isolates showed decreased sensitivity to azole derivatives (1, 2, 3, 5, 6, 7).

It is worth mentioning that the increased insensitivity of *C. albicans* to azole derivatives observed in recent years is an increasingly disturbing problem (1, 2, 3, 5), especially that these drugs (e.g. fluconazole) are very often used in prophylaxis of fungal infections in immunocompromised patients (7).

CONCLUSIONS

Our data confirm that *C. albicans* strains isolated from healthy people may reflect sensitivity to antifungal agents of the isolates obtained from clinical specimens. Such information may also be useful in order to modify empirical therapy and prophylaxis rules in *Candida* sp. infections, which are usually endogenous in origin.

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SUMMARY

Candidiases of the airways are usually preceded by colonization of mucous membrane of the upper respiratory tract by *Candida* sp. Increasing consumption of antifungal drugs, may result in the possibility of selection and spread of drug-resistant strains to generally applied antifungal drugs and therapeutic failure. In this paper we assayed susceptibility of pharyngeal *C. albicans* strains, isolated from healthy people, to various drugs: polienic antibiotics – amphotericin B and nystatine, pirymidyn derivative – flucytosine, imidazole derivatives – clotrimazole, miconazole, econazole and ketoconazole and triazole derivatives – fluconazole and itraconazole. A total collection of 100 pharyngeal isolates of *C. albicans* was used in the present assay. Sensitivity of isolated strains was assayed using disc-diffusion method and by microtest ATB FUNGUS 2. Among pharyngeal strains

of *C. albicans* the isolates sensitive to flucytosine and polienic antibiotics dominated showing simultaneously decreased sensitivity to imidazole (1–17% strains) and triazole derivatives (4–10% strains). Our data confirm that *C. albicans* strains isolated from healthy people may reflect sensitivity to antifungal agents of the isolates obtained from clinical specimens. Such information may also be useful in order to modify empirical therapy in *Candida* sp. infections, which are usually endogenous in origin.

Wrażliwość *in vitro* szczepów *Candida albicans*, izolowanych z błon śluzowych gardła, na wybrane antymikotyki

Kandydozy układu oddechowego są poprzedzone kolonizacją błon śluzowych górnych dróg oddechowych przez *Candida sp.* Wzrost zużycia antymikotyków stwarza możliwość selekcji i rozprzestrzeniania się szczepów grzybów opornych na powszechnie stosowane leki, a tym samym niepowodzeń terapeutycznych. W pracy określiliśmy wrażliwość szczepów *C. albicans*, izolowanych z błon śluzowych gardła zdrowych ludzi, na różne leki: antybiotyki polienowe – amfoterycynę B i nystatynę, pochodną pirymidyny – flucytozynę, pochodne imidazolu – klotrimazol, mikonazol, ekonazol i ketokonazol oraz pochodne triazolu – flukonazol i itrakonazol. Materiał badany stanowiło 100 izolatów *C. albicans*. Wrażliwość na leki przeciwgrzybicze określano przy pomocy metody krążkowo-dyfuzyjnej i mikrotestu ATB FUNGUS 2. Wśród wyosobnionych szczepów *C. albicans*, dominowały izolaty wrażliwe na flucytozynę oraz antybiotyki polienowe, wykazujące też obniżoną wrażliwość na pochodne imidazolu (1–17% szczepów) oraz triazolu (4–10% szczepów). Nasze dane potwierdzają, że szczepy *C. albicans* izolowane od zdrowych ludzi odzwierciedlają wrażliwość na leki przeciwgrzybicze szczepów uzyskiwanych z materiałów klinicznych. Takie informacje mogą być także użyteczne w modyfikacji terapii empirycznej infekcji wywoływanych przez *Candida sp.*, będących zazwyczaj pochodzenia endogennego.