Turk J Med Sci
32 (2002) 35-38

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Nosocomial Fungal Infections in a Teaching Hospital in Turkey: Identification of the Pathogens and Their Antifungal Susceptibility Patterns

Received: April 03, 2001

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Abstract: From January 1999 through April 2000, 208 *Candida* strains were obtained from hospitalized patients with nosocomial infection. Most of the species were isolated from urine (77.8%) followed by oropharynx (8.2%), blood stream (6.1%), drain (6.1%), peritoneum (0.9%) and cerebrospinal fluid specimens (0.9%). The distribution of the species obtained was *Candida* albicans (75.4%), *C. glabrata* (8.2%), *C. tropicalis* (4.8%), *C. kefyr* (3.4%), *C. parapsilosis* (2.5%), *C. lusitaniae* (1.9%), *C. famata* (1.4%), *C. krusei* (1.4%), and *C. guilliermondii* (1%). The antifungal susceptibility of the isolates to 5-fluorocytosine (5FCU), amphotericin B (AMP), nystatin (NYS), econazole (ECO), miconazole (MIC) and ketoconazole (KET) was tested by means of the ATB fungus method ((bioMerieux sa Marcy-l'Etoile/France). All the isolates were susceptible to amphotericin B, though a small number of in vitro resistant isolates were observed against nystatin and 5-fluorocytosine (3.4%). The resistance to miconazole, econazole and ketoconazole was higher at 18.8%, 15.8% and 23.6% respectively.

Key Words: Nosocomial fungal infections, antifungal susceptibility, ATB fungus, *Candida*.

Introduction

It is apparent that nosocomial fungal infections are becoming more prominent. They are increasingly isolated from immunocompromised patients and patients receiving a broader range of antimicrobial agents. Consequently, infections due to previously obscure fungi are being seen more commonly in hospitalized patients. In addition, standards for susceptibility testing are currently being developed and should help in guiding clinicians and hospital epidemiologists in the management of nosocomial fungal infections. However, continued epidemiological and laboratory research is needed to better characterize these pathogens, allowing for improved diagnostic and therapeutic strategies in the future (1).

The majority of nosocomial fungal infections are reported to be caused by *Candida* spp. All *Candida* spp. may cause a similar spectrum of diseases, ranging from thrush to invasive diseases such as arthritis, endophthalmitis, meningitis or fungemia. However, there may be differences in severity and therapeutic options worth noting. *C. albicans* is by far the most common *Candida* spp. causing infection in humans (1-3).

The aim of this study was to determine the species distribution and the antifungal susceptibility profile of isolates causing nosocomial fungal infections.

Materials and methods

From January 1999 through April 2000, a total of 208 isolates of *Candida* spp. were obtained from hospitalized patients with nosocomial infection in the university hospital in Konya, Turkey. All patients were from the reanimation unit of the anesthesiology department. All patients had been at the hospital for a long time and all had risk factors which predispose patients to hospital infection. Infections developed after one or two weeks of hospitalization. For urine cultures, when accompanied by clinical symptoms and white cells in the urine, the presence of yeast in the urine of patients with indwelling urinary catheters defined as urinary infection was determined (4).

All isolates were identified using the commercial identification system API 20 C AUX (bioMerieux sa Marcy-l'Etoile/France). The antifungal susceptibility of the isolates against 5-fluorocytosine, amphotericin B,

nystatin, econazole and ketoconazole was tested by means of the commercial system ATB FUNGUS (bioMerieux sa Marcy-l'Etoile / France). ATB fungus was found a reliable and reproducible method with a repeatability of 96.6%, and a reproducibility of 95.4% and showed an excellent correlation of 91.7% with reference MICs (5).

Results

Antifungal susceptibilities of 208 isolates from the *Candida* species were evaluated. The isolates were obtained from 208 hospitalized patients. All of these *Candida* infections were nosocomial infections. Most of the species were isolated from the urinary tract (77.8%), followed by oropharynx (8.2%), blood stream (6.1%), drain (6.1%), peritoneum (0.9%) and cerebrospinal fluid specimens (0.9%). The isolates involved 157 *C. albicans*, 17 *C. glabrata*, 10 *C. tropicalis,* 7 *C. kefyr*, 5 *C. parapsilosis*, 4 *C. lusitaniae*, 3 *C. famata*, 3 *C. krusei*, and 2 *C. guilliermondii* (Table 1).

Antifungal susceptibility of these species against 5FCU, AMP, NYS, MIC, ECO and KET is summarized in Table 2.

Discussion

Candida albicans is an important opportunistic pathogen because of its ability to infect seriously ill hospitalized patients. *Candida* species account for 15% of all hospital-acquired infections and ≤80% of all nosocomial fungal infections (6). In our hospital, nosocomial fungal infections are about 10% of all hospital-acquired infections.

During the study period, we obtained 208 yeast isolates from different body sites of the hospitalized patients. The urinary tract (77.8%) being the most involved body site among the nosocomial fungal infections, Chen et al. (3), indicated that bloodstream and urinary tract infections were the most frequently seen nosocomial fungal infections.

In this study *C. albicans* was the most frequently isolated species in patients with nosocomial fungal infection (75.4%). It was followed by *C. glabrata* (8.2%), *C. tropicalis* (4.8%), *C. kefyr* (3.4%), *C. parapsilosis* (2.5%), *C. lusitaniae* (1.9%), *C. famata* (1.4%), *C. krusei* (1.4%) and *C. guilliermondii* (1%) (Table 1). The distribution of species reported by Rodero et al. (7) was *C. albicans* 50.6%, *C. tropicalis* 22.5%, *C. parapsilosis* 20.2%, and *C. krusei* and *C. glabrata* 2.2%.

Table 2 summarizes the in vitro susceptibilities of 208 yeast isolates to 5-FCU, AMP, NYS, MIC, ECO and KET. All the isolates were susceptible to AMP, while a small number of in vitro resistant isolates were observed against NYS and 5-FCU (3.4%). The resistance to MIC, ECO and KET was higher at 18.8%, 15.8% and 23.6% respectively.

In the study of Quindos et al. (8), the antifungal susceptibilities of 443 clinical isolates from both

Table 1. Body sites and the species isolated.

Isolate	Urine (n:162)	Oropharynx (n:16)	Blood stream (n:13)	Drain (n:13)	Peritoneum (n:2)	CSF* (n:2)	TOTAL
C. albicans	123	12	9	10	1	2	157(75.4)
C. glabrata	14	2	1	-	-	-	17(8.2)
C. tropicalis	7	1	-	1	1	-	10(4.8)
C. kefyr	7	-	-	-	-	-	7(3.4)
C. parapsilosis	-	1	2	2	-	-	5(2.5)
C. lusitaniae	4	-	-	-	-	-	4(1.9)
C. famata	3	-	-	-	-	-	3(1.4)
C. krusei	3	-	-	-	-	-	3(1.4)
C. guilliermondii	1	-	1	-	-	-	2(1)
TOTAL n(%)	162 (77.8%)	16 (7.7%)	13 (6.1%)	13 (6.1%)	2 (0.9%)	2 (0.9%)	208

*CSF: Cerebrospinal fluid

Table 2. Antifungal susceptibility of the isolates.

N:208	5FCU		AMP		NYS			MIC			ECO			KET		
	S	R	S	R	S	I	R	S	I	R	S	I	R	S	I	R
C. albicans	154	3	157		150	1	6	96	31	30	79	55	23	82	35	39
C. glabrata	17		17		17			14	1	2	14	1	2	13	1	3
C. tropicalis	10		10		10			4	3	3	4	3	3	4	3	3
C. kefyr	7		7		7			7			6	1		6	1	
C. parapsilosis	5		5		5			5			4		1	4		1
C. lusitaniae	1	3	4		4			4			4			4		
C. famata	3		3		2		1			3			3	1		2
C. krusei	2	1	3		3			2		1	1	1	1	2		1
C. guilliermondii	2		2		2			2			2			2		
Total number of isolates n(%)	201 (96.6)	7 (3.4)	208 (100)	0 (0)	200 (96.1)	1 (0.5)	7 (3.4)	134 (64.4)	35 (16.8)	39 (18.8)	114 (54.8)	61 (29.4)	33 (15.8)	118 (56.7)	41 (19.7)	49 (23.6)

S: Sensitive I: Intermediate R: Resistant

serotypes of *C. albicans* to 5FCU, AMP, NYS, ECO, MIC and KET were tested by means of the ATB Fungus method. All these isolates were susceptible to amphotericin and nystatin. A small number of isolates were observed to be resistant to azole compounds.

Araj et al. (9) studied the antifungal susceptibility patterns of 70 clinical *Candida* isolates (each from one patient) representing 48 *C. albicans*, 12 *C. tropicalis*, 6 *C. parapsilosis*, 2 *C. krusei* and 2 *Torulopsis glabrata* against AMP, 5-FCU, KET, fluconazole and itraconazole using an E test, despite the uniform susceptibility to AMP and 5-FCU, resistance to azoles existed in a range of 4 to 17%. Eighty-three *Candida* spp. isolated from clinical specimens were tested in vitro by Morance et al. (10) for their susceptibilities to 5FCU, AMP, KET, itraconazole, fluconazole and MIC. AMP and 5FCU were active against the majority of the yeasts, while azole derivatives showed species-specific activity.

The epidemiology of nosocomial yeast infections is complex. The mechanism by which our patients acquired yeast infection remains unproven but the indirect contact route is the most likely. Fungal pathogens are important in nosocomial infections and there has been increasing resistance to antifungal agents. Therefore, it is important to conduct epidemiological studies and to establish in vitro antifungal susceptibility testing to enhance efforts to control nosocomial fungal infection and to minimize the risk for the emergence of antifungal resistance.

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