Comparative *in vitro* activities of eight antifungal drugs against a national collection of clinical *Candida parapsilosis* complex

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Candida parapsilosis complex is composed of three distinct species, namely *C. parapsilosis* sensu stricto, *C. orthopsilosis*, and *C. metapsilosis*. This species complex is a significant cause of bloodstream infections in otherwise healthy individuals. Although *C. parapsilosis* complex is usually susceptible to most antifungal agents, recent studies have reported decreased susceptibility to azoles and echinocandins, as well as frequent relapses and failures. The current study aimed to determine the in vitro activities of echinocandins (i.e., anidulafungin and micafungin) and five comparator drugs against a large national collection of clinical *C. parapsilosis* complex obtained from different geographical regions of Iran, where *C. parapsilosis* is one of the common non-albicans Candida species.

The collection consisted of 87 clinical strains of *C. parapsilosis* complex isolates obtained from a variety of specimens, including nail (n=63), skin lesions (n=12), groin (n=6), ear swabs (n=2) blood (n=2), vaginal discharge (n=1), and sputum (n=1). All isolates were initially identified to species level by DNA sequencing of ITS rDNA region. They were also reconfirmed using the matrix-assisted laser desorption ionization–time of flight mass spectrometry. *In vitro* antifungal susceptibility testing was adjusted according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

In vitro susceptibilities of antifungal drugs against clinical isolates of *C. parapsilosis* complex.

Strains and antifungal drugs	Range	MIC50/MIC90	GM	%≤ ECV*	MICs (µg/ml)												
					0.008	0.016	0.031	0.063	0.125	0.25	0.5	1	2	4	8	16	>32
All *C. parapsilosis* isolates (n=87)																	
AMB	0.016-2	0.016/0.15	0.0314	100		**58**	7	11	3	2		2	4				
FLU	0.25-8	1 / 2	1.0573	93.1						1	18	**49**	13	4	2		
ITC	0.031-2	0.25/1	0.211	88.5			2	21	20	11	**23**	6	4				
VRC	0.016-0.125	0.016/0.031	0.0176	100		**76**	10		1								
POS	0.016-0.125	0.016/0.016	0.0101	100		**81**	2	3	1								
AFG	0.008-1	0.25/0.5	0.2081	100	2	1	1	7	18	**36**	18	4					
MFG	0.008-1	0.125/0.31	0.1268	100	3		10	15	19	**32**	7	1					
***C. parapsilosis* sensu stricto (n=75)**																	
AMB	0.016-2	0.016/0.125	0.0308	100		**53**	5	7	3	1		2	4				
FLU	0.25-8	1 / 2	0.9726	93.3						1	18	**46**	5	3	2		
ITC	0.031-2	0.125/0.5	0.1821	92			2	**21**	19	8	19	4	2				
VRC	0.016-0.125	0.016/0.016	0.0171	100		**69**	5		1								
POS	0.016-0.031	0.016/0.016	0.0110	100		**71**	3	1									
AFG	0.008-1	0.25/0.5	0.2137	100	2	1	1	5	15	**30**	17	4					
MFG	0.008-1	0.25/0.5	0.1461	100	3		4	11	18	**31**	7	1					
***C. orthopsilosis* (n=12)**																	
AMB	0.016-0.25	0.031/0.125	0.0352	100		**5**	2	4		1							
FLU	1-4	2/4	1.7817	91.6								3	**8**	1			
ITC	0.125-2	0.5/2	0.5297	66.6					1	3	**4**	2	2				
VRC	0.016-0.031	0.016/0.031	0.0210	100		**7**	5										
POS	0.016-0.016	0.016/0.016	0.0170	100		**10**	2										
AFG	0.062-0.5	0.25/0.5	0.1765	100				2	3	**6**	1						
MFG	0.031-0.25	0.031/0.125	0.0522	100			**6**	4	1	1							

All strains had low MICs for posaconazole, voriconazole, itraconazole, followed by anidulafungin and micafungin. Fluconazole was found to be the less active drugs. The GM MIC values of posaconazole and voriconazole against all C. parapsilosis complex isolates were > 6-fold and > 5-dilution steps lower than those of fluconazole, respectively. 56% and 8% of *C. parapsilosis* sensu stricto isolates were susceptible and resistant to itraconazole, respectively. 27 (36%) isolates were susceptible-dose dependent, one of which was also susceptible-dose dependent to fluconazole. On the contrary, 1 (8.34%), 7 (58.33%), and 4 (33.33%) isolates of *C. orthopsilosis* were susceptible, susceptible-dose dependent, and resistant to itraconazole, respectively. However, no statistically significant difference was observed among the *C. parapsilosis* sensu stricto and *C. orthopsilosis* isolates in terms of the MIC values for posaconazole, voriconazole and anidulafungin (P > 0.05).

Distribution of *C. parapsilosis* complex species within different age groups, gender and sites of isolation

		C. parapsilosis sensu stricto (n=75)	C. orthopsilosis (n=12)	Total (n=87)
Gender	**Male**	27 (36%)	3 (25%)	30(34.5%)
	Female	48 (64%)	9 (75%)	57 (65.5%)
Age (years)	**0–15**	6 (8%)	0	6 (6.9%)
	16–29	15 (20%)	3 (25%)	18(20.68%)
	30–49	30 (40%)	3 (25%)	33(37.94%)
	≥50	24 (32%)	6 (50%)	30(34.48%)
Site of isolation	**Groin**	5 (6.6%)	1 (8.3%)	6 (6.9%)
	Nail	53 (70.6%)	10 (83.3%)	63(72.41%)
	Skin	11 (14.6%)	1 (8.3%)	12 (13.7%)
	Sputum	1 (1.3%)	0	1 (1.15%)
	Ear	2 (2.6%)	0	2 (2.3%)
	Vaginitis	1 (1.3%)	0	1 (1.15%)
	Blood	2 (2.6%)	0	2 (2.3%)