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**Frequency of the paradoxical effect of the 3 echinocandins against *Candida* spp. studied using EUCAST**

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**Background:** Echinocandins are the drugs of choice for the treatment of invasive candidiasis. The paradoxical effect is an in vitro phenomenon shown by echinocandins and is defined as attenuation of activity against *Candida* spp. at high concentrations. However, data regarding the frequency of invasive *Candida* spp. isolates showing the paradoxical effect are limited. We report data on the frequency of the paradoxical effect of the 3 echinocandins against clinically relevant *Candida* spp. using spectrophotometric reading of microtiter plates according to the EUCAST procedure.

**Material/methods:** We studied 665 *Candida* spp. isolates from patients with candidemia (n=652) admitted to Gregorio Marañón Hospital, Madrid, Spain between January 2007 and March 2015. Isolates were identified after amplification and sequencing of the ITS1-5.8S-ITS2 region and further tested for *in vitro* susceptibility to micafungin, anidulafungin, and caspofungin according to the EUCAST EDef 7.2 procedure. Plates were incubated for 24 hours. The MIC was defined as a  $\geq 50\%$  reduction compared with the growth control; the paradoxical effect was defined as an increase in the optical density of 0.02 compared with the growth control in wells containing a candin concentration that was at least 4-fold greater than the MIC. The percentage of isolates showing a paradoxical effect against the 3 echinocandins was studied.

**Results:** Overall, 16.8% of the isolates showed the paradoxical effect with at least 1 echinocandin. However, differences between species were found with *Candida tropicalis* as the species with the highest percentage of isolates showing the paradoxical effect, followed by *Candida albicans*, *Candida parapsilosis*, and *Candida glabrata* ( $P < 0.001$ ). Caspofungin was the drug in which the paradoxical effect was most frequently observed, followed by anidulafungin and micafungin ( $P < 0.001$ ).

**Conclusions:** Up to 17% of *Candida* isolates showed a paradoxical effect to 1 or more echinocandins, with caspofungin being the drug that most commonly presented this phenomenon. The paradoxical effect was a species-specific phenomenon, and *C. tropicalis* was the species with the highest percentage of isolates showing the effect.

**Table:**

Species	No.	No. of isolates showing the paradoxical effect (%)			
		Caspofungin	Anidulafungin	Micafungin	Any drug
<i>C. albicans</i>	315	34 (10.8)	36 (11.4)	4 (1.2)	52 (16.5)

<i>C. parapsilosis</i>	189	13 (6.8)	2 (1.1)	1 (0.6)	15 (7.9)
<i>C. glabrata</i>	70	0 (0)	2 (2.9)	1 (1.4)	3 (4.2)
<i>C. tropicalis</i>	53	33 (62.3)	25 (49.1)	21 (39.6)	33 (62.3)
Other <i>Candida</i> spp.	26	7 (26.9)	4 (15.4)	4 (15.3)	9 (34.6)
Overall	665	87 (13.1)	69 (10.3)	31 (4.6)	112 (16.8)