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Candida spp. clinical isolates causing candidaemia show differences in the kinetic parameters

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INTRODUCTION

- We studied the potential differences in the growth kinetics among clinically relevant *Candida* species isolates causing candidaemia. Furthermore, we assessed the potential impact of *FKS2* mutations in the kinetic parameters of *C. glabrata*.

METHODS

705 fluconazole and echinocandin-susceptible isolates from patients with candidemia admitted to Gregorio Marañón Hospital (Madrid, Spain) between 2007-2017.

+

31 echinocandin-resistant *C. glabrata* isolates obtained in previous studies were tested.

+

10 fluconazole-resistant *C. glabrata* isolates from patients with candidemia admitted to Gregorio Marañón Hospital and from the CANDIPOP project.

All 746 isolates were identified by amplification and sequencing of the ITS1-5.8S-ITS2 regions.

The same adjusted inocula prepared for EUCAST EDef 7.3.1 antifungal susceptibility to echinocandins and fluconazole was used for kinetic analysis.

Briefly, 100 µL of the suspension were added to double-concentrated RPMI 1640 medium in flat-bottomed microdilution trays and incubated with moderate shaking at 35ºC for 36 hours (performed in triplicate). The optical density in each well was measured every 15 minutes at 490 nm.

Differences among the kinetics parameters (average growth rate, time to maximum rate, maximum peak and, lag phase) were compared by Kruskal-Wallis and Mann–Whitney tests.

RESULTS

- Significant differences in kinetic parameters (average growth rate, time to maximum rate and, maximum peak) were found in *C. albicans* and *C. parapsilosis* (P<0.01) compared with the remaining susceptible species (Table). *C. glabrata* was the species showing the highest average growth rate and the highest maximum peak. However, *C. albicans* was the species showing the lowest average growth rate (Table).
- Average growth rate and time to maximum rate between susceptible *C. glabrata* isolates and fluconazole-resistant *C. glabrata* isolates were similar but higher than those found in echinocandin-resistant isolates (P<0.001). However, we did not found significant differences in the maximum peak between susceptible and resistant *C. glabrata* isolates (Table).
- Latent phase of *C. parapsilosis* isolates was significantly longer than that for the remaining species. *C. tropicalis* was the species with the shortest lag phase (Table). No differences were found between susceptible and resistant *C. glabrata* isolates.
- All species had an average growth rate that might mirror the time to positivity in blood cultures with the exception *C. glabrata* that paradoxically showed the fastest rate of growth.

Table. Kinetic parameters of susceptible and resistant species.

	Species	n	Average growth rate (s-1, mean)	Maximum peak (OD, mean)	Time to maximum rate (s, mean)	Lag Phase (h)
Susceptibles	*C. albicans*	351	3.87×10^{-6}	0.71	9.68×10^{4}	6.75
	C. parapsilosis	200	4.35×10^{-6}	0.66	9.52×10^{4}	8.75
	C. glabrata	83	7.50×10^{-6}	1.10	6.35×10^{4}	7
	C. tropicalis	54	6.90×10^{-6}	0.92	7.92×10^{4}	6
	C. krusei	17	6.08×10^{-6}	0.83	8.34×10^{4}	7.75
Echinocandin-resistant	*C. glabrata*	31	4.59×10^{-6}	1.05	1.04×10^{5}	7
Fluconazole-resistant	*C. glabrata*	10	7.98×10^{-6}	1.01	6.39×10^{4}	7.5

CONCLUSIONS

- Differences in the kinetics parameters among *Candida albicans* and *Candida parapsilosis* were found.
- The low average growth rate of *C. glabrata* echinocandin resistant isolates could have an impact on positivity time of blood culture.