R517
Publication Only
Mycology: Resistance and mechanisms of action of antifungals

Azole resistance in a general hospital in Madrid: *A. fumigatus 'sensu stricto'* and cryptic species: two sides of the same problem

T. Pelaez Garcia[1], S. Álvarez-Pérez[2], V. García-Gil[3], M.E. García[2], J.L. Blanco[2], B. Gama[1], P. Muñoz[1], E. Bouza[1], E. Mellado[3]

[1]Microbiology, Hospital Gregorio Marañon, Madrid, Spain ; [2]Patologia, Facultad de Veterinaria, Madrid, Spain ; [3]Microbiology, National Center for Microbiology ISCIII, Madrid, Spain

Objectives: The emergence and spread of azole resistance in the *A. fumigatus* species complex (AFSC) gives cause for concern worldwide. The AFSC comprises *A. fumigatus* 'sensu stricto' and other cryptic species that are intrinsically resistant to azoles. We studied the frequency and evolution of azole resistance in clinical AFSC isolates in a general hospital in Madrid (Spain) from 2000 to 2012.

Material and methods: The study included all patients with a positive AFSC culture. Isolates were identified by classic and molecular methods and screened for possible triazole resistance by culture on agar media containing itraconazole, posaconazole or voriconazole. The prevalence of cryptic species was also determined. Susceptibility testing was performed and breakpoints interpreted using CLSI methodology.

Results: We retrospectively studied 1662 AFSC isolates from 878 patients. Of these, 846 (96.3%) were infected or colonised by *A. fumigatus* 'sensu stricto' and 32 (3.7%) by cryptic species. The yearly evolution of *A. fumigatus* 'sensu stricto' and cryptic species was as follows: 2000 (56/1), 2001 (35/0), 2002 (70/1), 2003 (56/2), 2004 (54/3), 2005 (46/3), 2006 (71/2), 2007 (112/1), 2008 (83/1), 2009 (97/6), 2010 (67/5), 2011 (54/3), 2012 (77/4). The cryptic species identified were: *A. lentulus* (16), *Neosartorya udagawae* (9), *A. fumigatiaffinis* (5), *A. novofumigatus* (1) and *A. felis* (1). Since 2009, a significant increase has been observed in the number of patients infected by cryptic species ($p<0.001$) and four *A. fumigatus* 'sensu stricto' isolates exhibited resistance to azoles (three had the TR34/L98H mutation in the *cyp*51A gene and one the G448S point mutation). Of the 878 patients, 36 (4.1%) had one or more isolates with resistance to triazoles.

Conclusions: During the study period, we recorded a significant increase in the isolation of cryptic AFSC species that were intrinsically resistant to azoles. We also observed the emergence of multiazole-resistant *A. fumigatus* 'sensu stricto' isolates. Further surveillance is justified.