Minimum inhibitory/efficacious concentrations (μg/ml) were as follows in increasing order: terbinafine 0.25, amphotericin B 1, itraconazole 4, voriconazole 16, and posaconazole 36. To evaluate the interaction between antifungal drugs, the activity of the posaconazole in combination with terbinafine was also evaluated. A zoe-fu was using agar diffusion test. A combination of posaconazole and terbinafine, significantly inhibited the mycelial growth, which indicates synergy. The patient’s treatment was started on terbinafine in combination with posaconazole. On several follow-up examinations following treatment on day 30, 90 and 120, the infection had not recurred.

Conclusion: The species of M. scrofa is an environmental mold belonging to the order Mortierellales within the subphylum Mortierellomycota of the Kingdom Fungi. The fungus has been mostly associated with fungal infections leading to abortion in dairy cows feeding moldy hay and silage.

Although posaconazole exhibited high MICs against M. scrofa, our in vitro combination study demonstrated that posaconazole and terbinafine combined are significantly more potent than either drug alone. As a suggestion, combination therapy could provide an option for the treatment of severe cases of M. scrofa in patients with underlying primary immunodeficiencies.

As molecular identification and sequencing techniques continue to develop and become more available, we will likely see more diverse pathogens emerge in patients with underlying primary immunodeficiencies. In this current case. Additional study is warranted to explore insights into human immunity and the efficacy of combination therapy against these fungal species in CGD patients.

P001 Characteristics and dynamics of azole-resistant Aspergillus fumigatus variants emerging over a 28-year period in the Netherlands

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Background: Aspergillus fumigatus, a globally distributed opportunistic pathogen, is the main cause of invasive aspergillosis, especially in immunocompromised patients with high mortality. The emergence of azole-resistant A. fumigatus isolates has been a significant concern worldwide and an important clinical problem.

Objective: We aim to determine the presence of variants in a large collection of clinical A. fumigatus isolates from the Netherlands, if the number of variants increased over time and if the presence of additional single nucleotide polymorphisms (SNPs) or tandem repeats (TR) variants impacted on the isolate phenotype.

Methods: The Radboud University Medical Center has collected 11,813 clinical A. fumigatus isolates since 1994. The collection includes isolates cultured from patients admitted to our own center, isolates sent from other hospitals for identification and in vitro susceptibility testing, and isolates sent from five university medical centers and five national hospitals that contribute to the national Aspergillus resistance surveillance. The genotypes were detected by Cyp51A fingerprints. All isolates were subjected to in vitro susceptibility testing using the EUCAST microdilution reference method. Minimal inhibitory concentrations (MICs) were determined for terbinafine, voriconazole, posaconazole, in isolates and for in vitro susceptibility in clinical isolates in 2015 and thereafter.

Results: In total, 1926 A. fumigatus isolates harbored azole-resistant mutations in the Cyp51A gene with 92 genotypes.

We identified new mutations in Cyp51A and the promoter region. In addition, we observed a significant increase in azole-resistant variants over time, as well as a significant increase in TR and SNP variants. The number of azole-resistant isolates increased from 1 in 1999 to 64 in 2021. The majority of azole-resistant isolates harbored mutations in the TR46/Y121F/T289A, TR92/Y121F/M172I/T289A, and TR34/L98H genotypes. The TR46/Y121F/T289A mutation was detected in 92% of the azole-resistant isolates, while the TR92/Y121F/M172I/T289A mutation was detected in 16% of the azole-resistant isolates. The TR34/L98H mutation was detected in 2% of the azole-resistant isolates.

Conclusion: Our survey showed a significant increase in resistance genotypes in clinical A. fumigatus over a period of 28 years. Azole-resistant phenotypes vary from resistant variants in clinical isolates; it is an implication for clinical A. fumigatus infection treatment options and antifungal stewardship.
Background: Candida is one of the most frequent opportunistic infections in immunocompromised and/or hospitalized patients. In countries like Colombia, candidiasis is associated with a mortality rate of ~ 46%. Growing pharmacological resistance of Candida spp., and the appearance of the emerging pathogen Candida auris, have turned candidiasis into a major public health problem. Different types of antimicrobial peptides have been investigated as a therapeutic alternative to control candidiasis effectively and safely.

Objective: This work aimed at evaluating the in vitro antifungal activity of three synthetic antimicrobial peptides (35 409, 1409, and 29 009) obtained from Plantococcus (platelet rich) protein against C. auris, C. albicans, C. glabrata, C. parapsilosis, C. tropicalis, and C. krusei, species with worldwide clinical importance.

Methods: The minimum inhibitory concentrations (MIC) of the three peptides against Candida species were determined by the plate microdilution method, the peptide’s effect on biofilm formation in C. auris and C. albicans species was also evaluated through the XTT metabolic activity assay. Additionally, the structural damages in C. auris and C. albicans caused by the action of the peptides were observed by transmission electron microscopy (TEM) and finally, the peptides’ cytotoxicity against L929 mouse fibroblasts was verified.

Results: Our findings showed that these three peptides, based on the evaluated, displayed antifungal activity in both planktonic and sessile Candida cells. Likewise, the TEM evidenced morphological alterations induced by the peptides, both in the membrane and at the intracellular level of the yeast. As well, total safety against the mouse cell line L929 with 24 h of treatment was observed.

Conclusions: From these results, we conclude that the antimicrobial peptide 35 409, 1409, and 29 009 are potential therapeutic alternatives against the most important Candida species in Colombia and the world.