European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

Impact of biofilm formation and azoles' susceptibility in *Scedosporium/Lomentospora* species using an in vitro model that mimics the cystic fibrosis patients' airway environment

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What was your research question?

The lungs of cystic fibrosis (CF) people present a peculiar characteristic: they are rich in mucus containing a high amount of a protein called mucin, which forms a sticky and viscous material that favours the microbial colonization/infection in these individuals. Moreover, the antimicrobial drugs administered to CF persons, when reach this mucus-rich environment, soon become ineffective that permits the invading microbes to proliferate and to form biofilm structures, leading to serious and recurrent infections. Biofilms are classically defined as complex microbial communities that consist of microbial cells attached to a surface and to one another, enclosed in a protective cover, which provides several advantages for the microorganisms, including protection against host immune attack and resistance to antimicrobial agents. Based on these premises, in our work, we aimed to describe the impact of cystic fibrosis environment on antifungal susceptibility profile and on biofilm formation ability of filamentous fungi belonging to *Scedosporium* and *Lomentospora* genera, which are microorganisms commonly isolated from the lungs of people with CF.

Why is this important?

Infections of the respiratory tract are the main cause of death in people with CF. *Scedosporium* and Lomentospora species are the second mostly usual filamentous fungi isolated from these people. However, the current treatment prescribed with antifungal drugs is quite ineffective due to the resistance profiles of these fungi. We have demonstrated that

the standardized susceptibility test using the classical culture medium as well as the use of only planktonic conidial cells (in other words, individual fungal cells) cannot estimate the veritable antifungal susceptibility profile of *Scedosporium/Lomentospora* infecting people with CF. So, the clinicians cannot obtain a realistic scenario of the antifungal susceptibility pattern and, as a consequence, it does not help the clinicians in the correct management of the patients.

What did you do?

We compared the susceptibility profile of several *Scedosporium/Lomentospora* isolates to different antifungal drugs in a classical culture medium with a culture medium that mimics the cystic fibrosis sputum. We also analysed the ability to form microbial communities, known as biofilms, and its susceptibility profile in the cystic fibrosis environment.

What did you find?

We found out that the resistance of *Scedosporium/Lomentospora* conidia to triazole drugs increase in a cystic fibrosis mimic environment. In addition, all isolates can form robust biofilms with enhanced resistance to antifungal drugs. All these results highlight the inefficacy of the antifungal treatment of cystic fibrosis patients infected with these multidrug-resistant fungi.

What does this mean and reasons for caution?

The present research has shown that the classical susceptibility tests can underestimate the resistance profile of *Scedosporium/Lomentospora* isolates obtained from people with CF, which can misguide the antifungal treatment prescription. In this context, a better understanding about those fungi in people with CF can help in the development of more effective treatments.

What's next?

The next steps in our research line are to: (i) investigate the effectiveness of the combination of antifungal drugs in a cystic fibrosis mimic environment, (ii) study the biofilm characteristics and mechanisms that lead to increase in resistance in such environment, and (iii) discover new antifungal drugs against these human opportunistic fungi.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/33334714/