

FOCUS ON RESEARCH

ANTIFUNGAL RESISTANCE AND PATHOGENESIS OF *CANDIDA ALBICANS* BIOFILMS: A SOCIOECONOMIC PROBLEM IN ELDERLY DENTURE STOMATITIS PATIENTS

Researchers

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Aim

Elderly patients who wear dentures are susceptible to denture stomatitis, a disease caused by the yeast *Candida albicans*. This causes inflammation of the oral cavity due to a slime layer of yeast cells on the denture, which is commonly referred to as a biofilm. This study aimed to examine how this organism causes infection as a biofilm, and evaluate suitable ways to treat these established infections.

Project Outline/Methodology

Forty one patients, including non-infected controls, were evaluated for their level of inflammation (0 – 3). Microbiological assessment was performed by direct sampling from the denture biofilms using mild agitation to remove adherent cells. *Candida* cells were grown and identified on agar and by biochemical tests. These cells were treated with antifungal agents to assess the most effective treatment available. This was performed against free-floating (planktonic) and biofilm cells using commonly used antifungal agents. Molecular analysis was subsequently performed on the cells removed from the denture to examine gene expression. Genes involved in adhesion, structural composition and virulence were examined qualitatively and quantitatively.

Key Results

C. albicans was the predominant yeast isolated (83%), followed by *C. glabrata* (37%). Mild agitation proved to be an efficient sampling technique. Patients with the highest levels of inflammation possessed quantitatively more yeasts. Denture stomatitis patients with more severe disease did not exhibit good oral hygiene practices compared to uninfected patients with dentures. Treatment of the yeasts with commonly used antifungal agents (azoles) using standard techniques was effective, except against *C. glabrata*. However, when the yeasts were grown as biofilms then the antifungal agents were ineffective. Cell wall active antifungals exhibited good activity using standard techniques, and against biofilms. Molecular analysis demonstrated that key secreted enzymes were likely responsible for the severity of

inflammation, as indicated by their expression levels from these patients. Morphological and adhesion genes were similar in the samples tested.

Conclusions

We conclude that *C. albicans* is the key pathogen associated with denture stomatitis, and the emergence of the resistant yeast *C. glabrata* may be problematic. Whilst genes responsible for adhesion and structural composition are important for colonisation in the oral cavity, degradative enzymes play the key role in causing inflammation. Treatment of intact biofilms with azoles is ineffective, but caspofungin can be used to successfully treat *C. albicans* biofilms where the clinical response is poor or recurrent infections occur.

What does this study add to the field?

This study confirms that *C. albicans* is an important pathogen in the oral cavity of elderly immunocompromised individuals. We have shown that the denture is an important reservoir for infection, indicating the need for stringent oral hygiene. Biofilms are highly resistant to most antifungal agents, but the use of caspofungin or antifungal agents with a similar activity profile will provide a suitable means of treating denture stomatitis patients. This includes treating the emerging pathogen *C. glabrata*.

Implications for Practice or Policy

To increase efforts to improve denture hygiene, such as implementing alternative methods of cleaning, for example, the wider use of ultrasonic baths. To reduce the prescription of traditional antifungals.

Where to next?

To develop clinically effective and cost effective alternatives to traditional antifungal agents for managing fungal biofilm associated infections. Caspofungin provides a model to develop this from. Also, to understand the interactions between different yeast species within a biofilm.

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