Invited Review

Hyposalivation and oral candidiasis-A short review

N Aravindha Babu, N Anitha

Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Chennai, Tami Nadu, India

Abstract

Oral candidiasis is an opportunistic fungal infection commonly encountered in immunocompromised individuals. The oral cavity harbours numerous microbes and along with immunity saliva also maintains oral health. The Candida species form biofilm over the tissue and prosthetic surfaces. The biofilm formation results in persistent colonisation and persistent infection. The saliva in the oral cavity maintains the integrity of the oral environment by washing away the microbes through its flow and with its antimicrobial agents. The significant role of salivary histatins as an antifungal agent diminishes with hyposalivation. The importance of saliva in preventing fungal colonisation and infection is discussed in this review.

Keywords: Biofilm, candidiasis, hyposalivation

Address for correspondence: Dr. Anitha Nagarajan, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Chennai - 600 001, Tami Nadu, India.
E-mail:dranitha.nnr@gmail.com
Submitted: 06-Apr-2022, **Accepted:** 27-Apr-2022, **Published:** 28-Jun-2022

INTRODUCTION

Oral candidiasis being an opportunistic fungal infection is caused by Candida albicans. It is common in denture-wearing individuals, HIV-infected patients, bottle-fed infants and those under immunosuppressive therapy and anticancer therapy.[1]

PATHOGENESIS OF CANDIDIASIS

Candidiasis has pathogenesis which has an association with certain factors such as Candida biofilm formation, transition to hyphal form and secretion of hydrolytic enzymes. The candida species adhere to tissue surface or dental prosthesis. Following attachment, it takes a hyphal form and secretes polysaccharides contributing to the formation of three-dimensional biofilm. The regulation between the above-said sequences significantly stands as pathogenesis of candidiasis.[2,3]

MICROBIAL BIOFILM

Biofilm is a community of microbes attached to the surface of prosthesis or living tissue being an extracellular structural matrix. Such microorganisms in biofilm show a lower growth rate and resistance to treatment.[4] The adherence of such microbial colonies (biofilm) over living tissue and prosthesis (dentures) or medical devices (catheters, prosthetic heart valves and joint replacements) results in persistent infection due to its persistent colonisation.[5] Though single microbial species have the ability to form a biofilm, the bacterial and fungal species can be involved in biofilm formation which makes it difficult to explore.[6]

Factors involved in biofilm formation[7]

Access this article online

Quick Response Code:

Website: www.jomfp.in

DOI: 10.4103/jomfp.jomfp_161_22

How to cite this article: Babu NA, Anitha N. Hyposalivation and oral candidiasis-A short review. J Oral Maxillofac Pathol 2022;26:144-6.

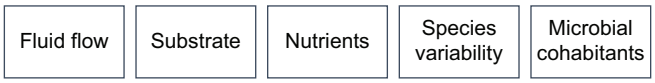

Figure 1: Factors involved in Biofilm formation

FORMATION OF CANDIDA BIOFILM

Candida biofilm formation commences with the adhesion of yeast cells to either living tissues or prostheses and forms a colony. Following this initial phase is the intermediate phase wherein the cells produce an extracellular polymeric substance (EPS). This extracellular polymeric substance is responsible for the maturation of the biofilm. The progeny biofilm cells may detach and form more biofilms on other surfaces.[7,8] Resistance to antifungal drugs is found in association with Candida biofilm. A study showed higher resistance to antifungal drugs by 48 h biofilms of Candida albicans compared to planktonic cells.[9]

SALIVA AND BIOFILM

Salivary flow influences the structural integrity and nutritional exchange of the biofilm.[7] A study on Candida albicans and Candida tropicalis biofilm formation over silicone rubber voice prosthesis with and without salivary film showed biofilms formed under salivary flow (salivary film) detached fast when compared to those formed directly without salivary flow.[10]

HYPOSALIVATION AND ORAL CANDIDIASIS

The saliva in the oral cavity plays a vital role in maintaining oral health. The saliva has various functions like neutralising acidic environment, antimicrobial properties, tissue repair and digestive function.[11] Hyposalivation is the reduced production of saliva and salivary flow rate.[12] The protective environment set by saliva in the oral cavity diminishes with hyposalivation. Pertaining to our discussion, the antifungal property of salivary histatins is found to be very efficient even against azole-resistant Candida species with regards to their specific mechanism of action.[13] With significant antifungal activity histatin 5 provides an immune response in the oral cavity. Histatin 5 binds with a specific target site of the fungal cell wall and crosses the cell wall and accumulates in the mitochondria. Histatin 5 has mitochondrial presequences (basic peptides) that target mitochondria. Cardiolipin in mitochondrial membrane attracts histatin 5 and following binding releases Adenosine triphosphate (ATP). The intracellular ATP was found to be lower than extracellular ATP in Candida albicans exposed to histatin 5.[14] The loss of ATP leads to cell death by activation of purigenic-like receptor which is due to extracellular ATP.[15] The adhesion of Candida species and its colonisation over the mucosal surface or prosthesis is required for causing infection. The washing away property of saliva prevents such adhesion and colonisation of Candida albicans, thereby, providing protection against infection. The whole saliva (unstimulated), which is resting salivary flow, coats the oral mucosa and is responsible for the maintenance of the integrity of oral mucosa. The submandibular and sublingual salivary glands are predominantly mucin and more protective compared to parotid secretion which is enzymatic and corresponds to stimulated saliva.[13]

CONCLUSION

Candida albicans being an opportunistic infection finds an opportunity to invade and cause infection. Such an infection can occur when the protective environment of the oral cavity is lost due to hyposalivation. It is usually a sign and could be recognised by a dentist. Certain clinical manifestations of hyposalivation are also noticeable. Apart from lowered immune response, the low salivary flow rate and amount (hyposalivation) also give an opportunity to the Candida species to cause an infection. Thus, the underlying cause of hyposalivation should be explored and with appropriate management, the Candida infection can be prevented. Also, it is the responsibility of every practitioner to educate patients about the importance of saliva with regards to a healthy oral environment.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Dos Santos JD, Fugisaki LRO, Medina RP, Scorzoni L, Alves MS, de Barros PP, *et al.* Streptococcus mutans secreted products inhibit Candida albicans induced oral candidiasis. Front Microbiol 2020;11:1605. doi: 10.3389/fmicb. 2020.01605.
2. Breger J, Fuchs BB, Aperis G, Moy TI, Ausubel FM, Mylonakis E. Antifungal chemical compounds identified using a C.elegans pathogenicity assay. PLoS Pathog 2007;3:e18.
3. Costa AC, Pereira CA, Friere F, Junqueira JC, Jorge AO. Methods for obtaining reliable and reproducible results in studies of Candida biofilms formed *in vitro*. Mycosis 2013;56:614-22.
4. Cavalheiro M, Teixeira MC. Candida biofilms: Threats challenges and promising strategies. Front Med 2018;5. doi: 10.3389/fmed. 2018.00028.
5. Potera C. Forging a link between biofilms and disease. Science 1999;283:1837-9.
6. O'Toole G, Kaplan HB, Kolter R. Biofilm formation as microbial development. Annu Rev Microbiol 2000;54:49-79.
7. Chandra J, Mukherjee P. Candida biofilms: Development, architecture and resistance. Microbiol Spectr 2015:3:157-76.
8. Seneviratne CJ, Jin L, Samaranayake LP. Biofilm lifestyle of Candida: A mini review. Oral Dis 2008;14:582-90.

9. Hawser SP, Douglas LJ. Resistance of Candida albicans biofilm to antifungal agents in vitro. Antimicrob Agents Chemother 1995;39:2128-31.
10. Busscher HJ, Geertsema-Doornbusch GI, Va der Mei HC. Adhesion to silicone rubber of yeast and bacteria isolated from voice prosthesis: Influence of salivary conditioning films. J Biomed Mater Res 1999;34:201-9.
11. Wiener RC, Wu B, Crout R, Wiener M, Plassman B, Kao E, McNeil D. Hyposalivation and Xerostomia in dentate older adults. J Am Dent Assoc 2010;141:279-84.
12. Wu B, Plassman BL, Liang J, Wei L. Cognitive function and dental care utilisation among community-dwelling older adults. Am J Public Health 2007;97:2216-21.
13. Billings M, Dye BA, Lafolla T, Grisius M, Alevizos I. Elucidating role of hyposalivation and autoimmunity in oral candidiasis. Oral Dis 2017;23:387-94.
14. Kavanagh K, Dowd S. Histatins: Antimicrobial peptides with therapeutic potential. J Pharm Pharmacol 2004;56:285-9.
15. Koshlukova S, Lloyd T, Araujo M, Edgerton M. Salivary histatin 5 induces nonlytic release of ATP from Candida albicans leading to cell death. J Biol Chem 1999;274:18872-9.