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Is Topical Antifungal the Appropriate First Choice for Denture Stomatitis?

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Abstract

Background: Denture stomatitis (DS) is commonly diagnosed during the routine intraoral examination of prosthesis wearers. Episodes of DS relapse occur frequently.

Objective: This study aimed to investigate the therapeutic agents against DS lesions through a briefly review of the English literature on the comparison between topical and systemic protocols.

Materials and methods: A descriptive research was performed on articles published in PubMed/Medline using specific keywords following pre-established inclusion and exclusion criteria.

Results: Only two studies clinically compared topical and systemic protocols for DS treatment.

Conclusion: *In vivo* comparative studies on topical and systemic antifungal protocols against DS are extremely scarce. Thus, we recommend additional investigations on the drug principles, time of prescription, side effects and the best approach for choosing an antifungal drug. Finally, prosthesis care is a key factor to prevent DS lesions.

Keywords: Stomatitis; *Candida*; Denture hygiene; Treatment need

Introduction

Denture stomatitis (DS) is a common type of chronic oral candidiasis. DS clinically appeared as an atrophy of the mucosa restricted to tissue covered by a partial or total prosthesis [1-3]. DS prevalence in prosthesis wearers ranges from 27% to 65% [1-3]. Local and systemic predisposing factors account for this type of oral candidiasis.

Critical local risk factors are deficient oral hygiene, night-time prosthesis wearing, old dentures, prosthesis instability, and traumatism [4-11]. *Candida* spp., a normal commensal microorganism in oral cavity, can be the pathogenic agent because of the ability to adhere and proliferate through the tissues of oral cavity [2,6-8].

Systemic risk factors related to DS appearance are older age; intake of medications such as anxiolytics, antidepressants, antihypertensive drugs affecting the salivary flow rates, and broad-spectrum antibiotics; diabetes mellitus; nutritional deficiencies and endocrine dysfunctions (hypothyroidism) [9-15].

DS clinical aspects range from small or extensive erythematous dots to granular areas of the mucosa below the denture, generally asymptomatic and located more often on hard palate and alveolar ridge **(Figure 1)**. The English Literature lacks studies emphasizing DS treatment. The association of non-pharmacological methods with antifungal therapy is described as the main therapeutic approach [16,10]. Routinely, disinfection of the dental prostheses, renewal of dentures, and the removal of the prosthesis during the night are some of effective non-pharmacological methods [9,10,17,18]. Topical antifungal therapy is the widely prescribed protocol; systemic antifungal use is extremely rare, only in cases of recurrent DS [1,17,19,20]. However, failure and/or relapse is a daily event during topical antifungal therapy.

Thus, the dentists routinely face the clinical dilemma of selecting the correct antifungal therapy to treat DS. Therefore, this study aimed to investigate the therapeutic agents against DS through a briefly review of the English literature on the comparison between topical and systemic protocols.

Material and Methods

The descriptive review was performed based on articles searched in PubMed/Medline. The keywords selected were “oral candidiasis, chronic atrophic candidiasis, denture stomatitis, prosthesis, topic and systemic antifungal treatment”. The inclusion criteria were (1) articles published in English language; (2) experimental and/or review studies focusing on treatment of denture stomatitis; (3) *in vivo* comparative studies involving topical and systemic antifungal therapy against DS. The exclusion criteria were (1) manuscripts in other languages; (2) articles with no access to full text; (3) studies with no focus on DS treatment or on the comparison between the topical and systemic drugs (4) case reports. A

complete reading of the included articles was performed and the main results were discussed.

Results

Considering the proposed keywords, eight studies on antifungal DS treatment were found. The number was reduced to two articles after strictly applying the inclusion criteria [1,21]. Of the eight articles, one study was not written in English, the full text of 4 articles was not available [18,22-24] and 6 articles did not fulfill the review subject (DS diagnosis and/or the comparison between topical and systemic antifungal protocols) [17,19,22-24]. A complete list of all revised manuscripts is showed in **Table 1**.

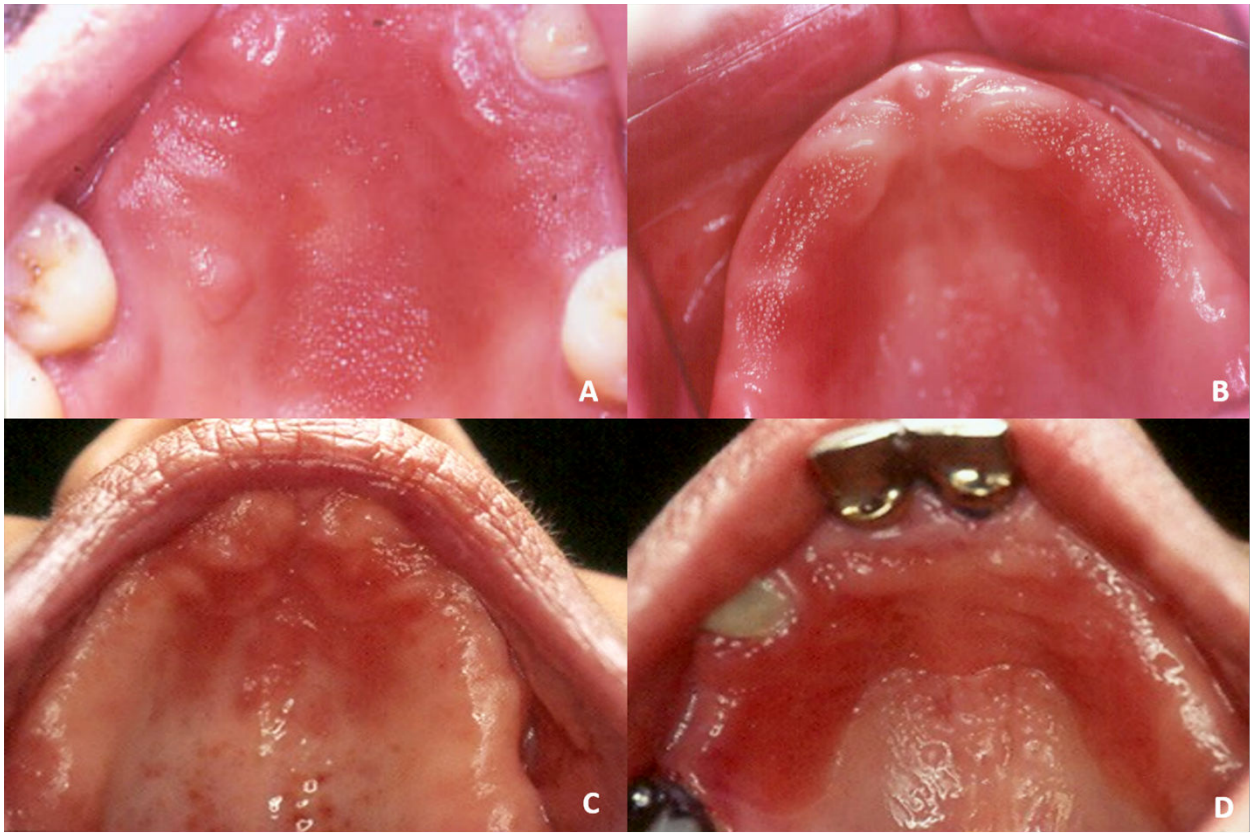

Figure 1 Sequence of clinical aspects of denture stomatitis. Extensive erythematous area on the hard palate and maxillary alveolar ridge (A). Bilateral erythematous aspect on the maxillary alveolar bridge extending towards anterior hard palate (B). Erythematous area on the palate; observe the dotted aspect on the posterior hard palate (C). A marked bilateral erythematous area on the maxillary alveolar bridge up to hard palate. Note that this area matched the same site of mucosa covered by removable prosthesis (D). The discreet granular aspect can be observed on the surface of all lesions.

Table 1 Complete list of reviewed articles on denture stomatitis (DS) and antifungal treatment.

Author	Year	Type of Study	Therapeutic Antifungal protocol	Main Result
Haessler	1978	Experimental research	Topical Clotrimazole	Improvement followed by recurrence after drug suspension
Bissel et al.	1993	Experimental research	Systemic fluconazole 50 mg X Amphotericin lozenges and cream	Similar clinical results, uncommon side effects and recurrence for both treatments
Banting et al.	1995	Experimental research	Topical liquid nystatin 100,000 IU/mL associated with nystatin vaginal lozenge 100,000 IU/g × Tap water	Reduction of recurrence rate of clinical signs and symptoms
Salonen et al.	1996	Experimental research (case-control study)	Topical miconazole 2% gel X Systemic fluconazole 50 mg	Positive results for both regimens with better findings for systemic antifungal
Muzyka	2005	Literature review	Antifungal medications commonly used by dentists	Topical medications are the first line of therapy Disinfection of the dental prostheses during the

				treatment to avoid reinfection. Systemic therapy is applied in resistant cases that donot respond to topical therapy
Milillo et al.	2005	Experimental research	Topical varnish containing 5% amorolfine	The varnish suppressed the nystatin resistance
Koray et al.	2005	Experimental research	Systemic fluconazole 50 mg X Hexetidine mouthrinses 1% X Fluconazole 50 mg plus hexetidine mouthrinses	No statistically significant difference was observed among the regimens. Hexetidine presented fewer side effects
Khozeimeh et al.	2010	Experimental research	Systemic ketoconazole tablet 200 mg X Topical ketoconazole 2% in orabase	Topical ketoconazole 2% in orabase had efficacy similar to ketoconazole tablet and fewer side effects

Discussion

Because of the high relapse rates of classical topical antifungals, we hypothesized which antifungal protocol would be better for DS treatment [25,26]. According to the inclusion criteria, only two study trials on patients with DS focused on the treatment with topical and systemic antifungal [1]. One study observed similar efficacy between topical and systemic antifungals using two forms of ketoconazole: orabase (topical) and tablet (systemic) [1]. At long-term administration, the ketoconazole tablet produced more side effects than topical ketoconazole, including gastrointestinal disturbances such as nausea, vomiting, diarrhea, constipation, and abdominal pain [1]. Also, these studies observed transient elevation of liver serum enzymes, hepatitis, adrenal cortex suppression, pruritus, rash, headache, dizziness, and somnolence [1,27]. Likewise, the comparison of amphotericin lozenges and topical cream with systemic fluconazole showed similar clinical response [21]. However, either uncommon or no side-effects occurred during the treatment with fluconazole and only one patient complained about nausea [21]. Thus, the administration of both topical and systemic antifungals showed positive results for DS treatment. From a clinical point of view, although the literature reports small number of side effects with fluconazole, the results observed in only two studies did not allow us to draw conclusions on side effects.

In the dental clinical routine, the polyene agents (including nystatin) are the most topical agent prescribed for patients with DS [17]. Systemically, Azole antifungals (ketoconazole and fluconazole) are the drugs most used [28-34]. Systemic therapy has been prescribed for DS in cases not responding to topical agents or in cases with presence of systemic factors, such as immunosuppression or diabetes [35-37]. Generally, the dentists are concerned about prescribing systemic antifungals because of the risk of side effects.36 Conversely, *in vivo* studies reported the efficacy of systemic antifungals with minimal or no side effects to treat patients with DS through [1,21,25,38]. Interestingly, a Spanish study on drug choice for oral candidiasis demonstrated the strong predilection for topical drugs (miconazole and nystatin) by general dentists while the experts, including stomatologists frequently chosen systemic antifungals in the same cases [16]. Therefore, the stomatologists' knowledge on time administration and side effects and large expertise in oral medicine led them to choose systemic antifungal.

Despite the availability of a number of antifungal drugs, the DS relapse after antifungal therapy is often noticed [21,23,26]. Nystatin is the first treatment choice for DS, but some articles reported lack of DS cure and yeasts recolonization after cessation of drug protocol [39,21]. A possible cause of the lesion relapse would be the persistence of Candida biofilms on the mucosa and on inert prosthesis surfaces [21]. Moreover, multiple daily doses for a relatively long period have been associated with lower patient compliance, immunodeficiency, and drug resistance, which are additional factors against complete recovery [26]. The aspects associated with the prosthesis, including poor hygiene, habit of sleeping with prosthesis, and no replacement of old prostheses play a role in the lesion relapse, regardless of DS treatment type.

Conclusion

Due to the high DS relapse frequency, *in vivo* comparative studies on topical and systemic antifungals are urgently required to evaluate the efficacy, advantages, and disadvantages related to both protocols. To the best of our knowledge, this present short review was the first study to search this topic aiming to reach some reliable conclusions and guide the dentists during the choice for antifungals. The few studies on this topic limited our assumptions. Nevertheless, we recommend further studies on the drug principles, time of administration, side effects, and best practice to choose an antifungal drug. Finally, prosthesis care is a key strategy for the complete healing of DS lesions.

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