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Comparison of Photodynamic Therapy versus conventional antifungal therapy for the treatment of denture stomatitis: a randomized clinical trial

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Abstract

In this randomized clinical trial, the clinical and mycological efficacy of Photodynamic Therapy (PDT) was compared with that of topical antifungal therapy for the treatment of denture stomatitis (DS) and the prevalence of *Candida* species was identified. Patients were randomly assigned to one of two groups (n = 20 each); in the nystatin (NYT) group patients received topical treatment with nystatin (100 000 IU) four times daily for 15 days and in the PDT group the denture and palate of patients were sprayed with 500 mg/L of Photogem®, and after 30 min of incubation, were illuminated by light emitting-diode light at 455 nm (37.5 and 122 J/cm^2, respectively) three times a week for 15 days. Mycological cultures taken from dentures and palates and standard photographs of the palates were taken at baseline (day 0), at the end of the treatment (day 15) and at the follow-up time intervals (days 30, 60 and 90). Colonies were quantified (CFU/mL) and identified by biochemical tests. Data were analysed by Fisher's exact test, analysis of variance and Tukey tests and κ test (α = 0.05). Both treatments significantly reduced the CFU/mL at the end of the treatments and on day 30 of the follow-up period ($p < 0.05$). The NYT and PDT groups showed clinical success rates of 53% and 45%, respectively. *Candida albicans* was the most prevalent species identified. PDT was as effective as topical nystatin in the treatment of DS.

Keywords: *Candida*, light-emitting diode, nystatin, oral candidiasis, photodynamic antimicrobial chemotherapy, porphyrin
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Introduction

Denture stomatitis (DS) is the most common form of oral candidiasis with an overall incidence of 11–65% in complete denture wearers. This recurring disease is characterized by different degrees of inflammation of the mucosa under the maxillary denture, ranging from petechiae to generalized inflammation with papillary hyperplasia [1]. The aetiology of this problem is multifactorial: decreased salivary flow, medication, endocrinopathies, immunosuppression, metabolic and nutritional factors, smoking, increased age of denture, denture trauma, continuous denture wearing, and poor denture hygiene have been implicated [2]. Nonetheless, the denture–palatal interface offers a unique ecological niche for microorganism colonization because of the relatively anaerobic and acidic environment favouring yeast proliferation without any other predisposing factor present.

Candida albicans is the yeast species most frequently isolated in significant quantities from subjects with DS [1–8]. This oral fungal pathogen is able to grow in a variety of morphological forms, ranging from blastospores to hyphae. The filamentous growth can promote tissue penetration during

the early stages of infection [9]. Moreover, on soft and hard surfaces within the oral cavity, *C. albicans* grows as a biofilm, which consists of a complex community of cells embedded in a matrix of extracellular polysaccharide. When cells exist in a biofilm they exhibit phenotypic properties that are distinct from those of planktonic cells and they have increased resistance to antimicrobial agents [10]. Although *C. albicans* is the most prevalent and virulent species of the genus *Candida*, other non-*C. albicans* species are often isolated from acrylic surfaces and the palatal mucosa, such as: *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, *C. pseudotropicalis*, *C. krusei* and *C. guilliermondii*. The emergence of other *Candida* species is important because they may exhibit higher denture surface adherence, and species such as *C. glabrata*, *C. krusei* and *C. lusitaniae* show inherent resistance or intrinsic reduced susceptibility to antifungal agents [11].

Antifungal agents are commonly used to treat DS, but improvement in denture hygiene, discontinuation of nocturnal denture wearing, and eventually relining or replacing the denture are also required. Topical agents such as nystatin and miconazole have been used effectively [12,13]. However, the diluent effect of saliva and the cleansing action of the oral musculature tend to reduce the concentration of these agents to sub-therapeutic levels. Hence, treatment regimens tend to be prolonged and recurrence rates are high. Systemic antifungal agents such as amphotericin B and fluconazole are also effective, but they do not eradicate the microorganisms that colonize the denture [12]. Nonetheless, the major problem associated with the prolonged or recurrent use of antifungal drugs is the development of resistant species [9,11,13].

This makes it necessary to seek new therapeutic approaches. A promising modality is Photodynamic Therapy (PDT), which uses a photosensitizing agent and light of appropriate wavelength. The interaction between the photosensitizer and light in the presence of oxygen produces reactive species, such as singlet oxygen and free radicals, which cause cell damage and death [14,15]. As a consequence of these non-specific oxidizing agents, organisms resistant to conventional antifungal agents could be successfully killed by PDT, and it seems unlikely that they will develop resistance to such a therapy. PDT is effective against oral species and may not promote damage to host cells and tissues [16,17].

Investigations have shown that *Candida* spp. are susceptible to photoinactivation [14–16,18], including resistant strains [19,20]. Previous studies have shown that PDT is effective in reducing *C. albicans* counts in a murine model of oral candidiasis [16] and for denture disinfection [21,22] when a porphyrin was associated with light-emitting diode (LED) light. In a recent case report, five patients with clinical and microbiological diagnoses of DS were successfully treated with PDT [5]. Nonetheless, the clinical effectiveness of PDT in comparison with conventional antifungal therapy in the treatment of DS is not yet known. Hence, the aims of the present randomized clinical trial were to compare the efficacy of PDT with that of topical nystatin in the treatment of DS and to identify the prevalence of *Candida* species.

Materials and Methods

Study design

This was a two group, parallel, randomized clinical trial comparing the effectiveness of PDT and nystatin in the treatment of patients with DS. The procedures carried out in the study were in compliance with the criteria of Resolution 196/96 of the Brazilian Health Ministry, which regulates research involving human subjects. This research was conducted in accordance with the Declaration of Helsinki, and the protocol of the entire project was approved by the Ethics Committee of the Araraquara Dental School (39/2005—1308. 0.199.000-05 SISNEP). All participants were made aware of the objectives of the study and of the probable risks and benefits. All subjects voluntarily entered the study and signed an informed consent form before their enrolment.

Participants and randomization

Edentulous denture-wearing patients attending the Araraquara Dental School for prosthetic treatment were examined for clinical evidence of DS. The exclusion criteria were based on the medical history of each individual, which was checked for factors known to affect carriage of *Candida* spp., such as diabetes, anaemia, immunosuppression and cancer therapy (radiotherapy or chemotherapy). Similarly, individuals who had received in the past 3 months or who were currently receiving treatment with antibiotics, antifungal agents or steroids were excluded. A total of 40 voluntary patients were selected for inclusion in the present study. Medical and dental histories of the patients were recorded, and comprehensive oral examinations were performed by the same investigator. DS was classified according to the criteria proposed by Newton [23]. To create groups of patients that were similar with regard to baseline characteristics that could influence prognosis other than the treatment being considered, namely risk factors, a stratified randomization was used. The following risk factors were considered in this study: age of the dentures, smoking habits, medication use, denture hygiene habits and nocturnal wearing of dentures.