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Review

# Linking evidence to treatment for denture stomatitis: A meta-analysis of randomized controlled trials

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ABSTRACT

*Objectives:* The aim of this meta-analysis was to compare the efficacy of antifungal therapy with any other alternative methods used for the treatment of denture stomatitis.

*Data sources:* MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews were searched, complemented by hand searching, until the first week of January 2013.

*Study selection:* Included studies consisted of randomized clinical trials published in English or French, which compared antifungals with any other alternative or placebo, used for the treatment of denture stomatitis. The remission of clinical signs of denture stomatitis, and the reduction in *Candida* colony counts were considered as the clinical and microbiological outcomes, respectively. Random effects models were used to conduct the statistical analyses.

*Results:* From 233 identified articles, a total of 15 manuscripts on 14 randomized controlled trials were included in systematic review and 8 in the meta-analysis. No statistically significant difference between antifungal treatment and disinfection methods was found for both clinical (OR = 0.7; 95% CI: 0.32–1.36; $Z = -1.14$; $p = 0.256$) and microbiological (OR = 0.8; 95% CI: 0.26–2.5; $Z = -0.35$; $p = 0.724$) outcomes. The meta-analysis showed a statistically significant difference between an antifungal and a placebo for the microbiological outcome (OR = 0.32; 95% CI: 0.12–0.89; $Z = -2.2$; $p = 0.028$), favouring the antifungals. However, there was no statistically significant difference between antifungal and placebo for the clinical outcome (OR = 0.2; 95% CI: 0.04–1.04; $Z = -1.9$; $p = 0.056$).

*Conclusions:* Disinfection agents, antiseptic mouthwashes, natural substances with antimicrobial properties, microwave disinfection and photodynamic therapy could be suggested as an adjunct or alternative to antifungal medications in the treatment of denture stomatitis.



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## 1. Introduction

Denture-related erythematous stomatitis (denture stomatitis), a chronic inflammatory response of the palatal mucosa to a harmful stimuli, is widespread in edentate individuals and is considered to be the determinant of oral health in this population.[1] It is also the most common mucosal lesion associated with removable prostheses,[2,3] affecting one in every three complete denture wearers.[4] Several risk factors have been reported to be associated with denture stomatitis, including trauma,[5] poor hygienic habits, continuous and nocturnal denture wear [6] and fungal infections (particularly *Candida albicans*).[7]

Antifungal medications are routinely used by clinicians for the management of this condition, based on some evidence that *Candida* is the main etiological factor in the onset of denture stomatitis.[8–11] However, a cause-and-effect relationship has never been shown, and some studies did not demonstrate an association between the presence of denture stomatitis and the presence of *Candida* infection.[12–14] Furthermore, high recurrence rates of denture-related erythematous stomatitis and re-colonization of *Candida* after the cessation of antifungal treatment have been reported.[15–17]

A meta-analysis of randomized controlled trials comparing the efficacy of antifungal therapies with other alternatives approaches and placebo will shed a light on the efficacy of these treatments and will guide the development of clinical practice guidelines.[18] These guidelines are needed in order to direct the healthcare professional in treatment decision-making.

We tested the null hypothesis that there is no difference between antifungals and other alternatives in the treatment of denture stomatitis.

## 2. Material and methods

This systematic review and meta-analysis was conducted according to the guidelines of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement.[19]

### 2.1. Search strategy and eligibility criteria

The following databases were used for the identification of studies: MEDLINE via OVID (1946 to January Week 1 2013), EMBASE (1996 to 2013 Week 02), Cochrane Central Register of Controlled Trials (until December 2012) and the Cochrane Database of Systematic Reviews (2005 to November 2012). We included all relevant randomized controlled trials that compared the efficacy of antifungal medications with other methods used in the treatment of denture-related erythematous stomatitis in adults wearing conventional acrylic removable complete dentures. Trials with a period of treatment of 7 days or less and quasi-experimental randomized trials were excluded.

An adapted search strategy for MEDLINE and EMBASE from a Cochrane systematic review protocol was used [20] (Appendix 1). The search was complemented by manual search of reference lists. No language restriction was considered. Titles and abstracts of the identified articles were screened independently by two reviewers. Full text articles were obtained for studies that appear to meet the inclusion criteria and were reassessed independently by three reviewers. Any disagreement was discussed and resolved by consensus. The study flow chart is depicted in Fig. 1.

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jdent.2013.11.021.

### 2.2. Data extraction and outcomes

The data collected from each study included the following: authors, year and country of the study, study design, population characteristics, intervention characteristics, type of measurement instrument and main outcomes (clinical and microbiological outcomes). The remission of clinical signs and severity of denture stomatitis were considered as the clinical outcome, while reduction in the level of *Candida* colony counts (CFUs) was used as the microbiological outcome.

### 2.3. Assessment of the methodological quality

The quality of included studies was assessed following the *Cochrane Handbook for Systematic Reviews of Interventions*.[21] This assessment included the following parameters: sequence generation, allocation concealment, blinding of care providers and participants, masking outcome assessors, reference to withdrawals or dropouts and intention-to-treat analysis (ITT). We graded each parameter of trial methodological quality as: 'adequate', 'inadequate' and 'unclear or not reported'.

### 2.4. Statistical analysis

All analyses were performed using Comprehensive Meta-Analysis, Version 2 (Biostat$^{TM}$) software. Only studies of similar comparisons reporting the same outcome measures were included in the meta-analysis.

Odds Ratios (OR) and 95% Confidence Interval (CI) were calculated to compare results across studies. Heterogeneity between studies was assessed by the Cochrane Q test and $I^2$. A $p$-value $\leq 0.20$ and $I^2$ of at least 50% were taken as indicators of heterogeneity between trials. *A-Priori* subgroup analysis was planned and random effect model were used to conduct the analyses. This approach accounted for inter-study variations and provided more conservative estimate comparing to a fixed model.[21] Due to the small number of studies within subgroups, a pooled estimate of tau-squared in a random-effects meta-analysis was given. A forest plot was used to show the point estimate of the results of each individual study and the pooled estimate for subgroups (antifungal vs. disinfection method and antifungal vs. placebo). The overall effect was not presented because a difference between the subgroups was expected (Figs. 2 and 3).

## 3. Results

### 3.1. Characteristics of studies

A total of 233 articles were identified. After duplicates elimination, 187 articles were searched by title and abstract. Only 24 were eligible for full-text searching (Fig. 1: flow chart).