

## Original Research

### Denture stomatitis: A systematic review

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#### ABSTRACT:

**Aim:** To assess the denture stomatitis as well as effectiveness of different interventions for treating or preventing denture stomatitis (DS). **Methodology:** Randomized controlled trials (RCTs) comparing any agent or procedure prescribed to treat or prevent DS in adults. There were two main outcomes reported in the trials included in this review: clinical signs of DS and remaining presence of yeast. **Results:** Thirty-five studies were included in the systematic review, with 32 judged as having high risk of bias. Three RCTs compared nystatin with placebo and found a significant effect on the reduction of clinical signs of stomatitis (risk ratio (RR) = 0.51, 95% confidence interval (CI) = 0.36–0.72), four RCTs compared nystatin with placebo and found a significant effect on mycological assessment (RR = 0.61, 95% CI = 0.46–0.80). Five studies of disinfectant agents also showed a significant effect in comparison with an inactive agent (RR = 0.52, 95% CI = 0.30–0.92) in clinical assessment. No evidence was found of an effect of miconazole, amphotericin, or imidazolic drugs. No RCT evaluated the effectiveness of preventive approaches. **Conclusion:** The results are supportive of the use of nystatin and disinfecting agents in the treatment of DS, but clinicians need to be aware that individual studies had high risk of bias and that the overall quality of the individual reports was judged to be low.

**Keywords:** denture stomatitis; meta-analysis; randomized controlled trial; oral health.

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#### INTRODUCTION

Denture stomatitis is a chronic inflammation in mucous membrane under prosthodontics which may be of local or general nature.<sup>1</sup> This inflammation is a common nation and sometimes pain or burning.<sup>2</sup> Various studies have been reported vast spectrum of spread between 11 to 60%, in different part of the world.<sup>3</sup> In a study in Chile, denture stomatitis was shown as the most common oral mucosal lesions in people older than 65 years (22.3%).<sup>4</sup> Another study in Germany indicated a prevalence of 18.3% in 65-74 years of old population.<sup>5</sup> In a study made in Tehran on those elderly people over 65 who were using dentures, spread of denture stomatitis was 18.2%.<sup>6</sup> However,

multi-factorial causes have been reported for this long-term mucosal lesion: trauma resulted from inappropriate denture, low hygiene of mouth and denture, microbes, nutritional deficiency, diabetes, immune deficiency, and some other systemic factors.<sup>7</sup> A review on etiology, diagnosis, and treatment of denture stomatitis indicates a combination of inflectional causes, trauma, and probable immune deficiency in host, as the etiology of the disease.<sup>8</sup> Numerous studies have emphasized the main role of candida albicans as primary pathogen in creating denture stomatitis, in a way that this type of candida has initiated, stabilized and exacerbated the disease in 93% of those stricken.<sup>9</sup> In the study of

Berdicevesky et al. the percentage of spread of candida on denture and in the mouth of those using denture was compared to a control group not using denture. The spread in the former group was 88%, while in control group, it was 52%.<sup>10</sup> A study on individuals using full dentures, showed 63.3% of spread of candida albicans.<sup>11</sup> 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.<sup>12</sup> 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.<sup>13</sup> Further- more, high recurrence rates of denture-related erythematous stomatitis and re-colonization of Candida after the cessation of antifungal treatment have been reported.<sup>14</sup> 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.<sup>15</sup> These guidelines are needed in order to direct the healthcare professional in treatment decision-making. 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.<sup>16</sup>

**AIM OF THE PRESENT STUDY**

To assess the denture stomatitis as well as effectiveness of different interventions for treating or preventing denture stomatitis (DS).

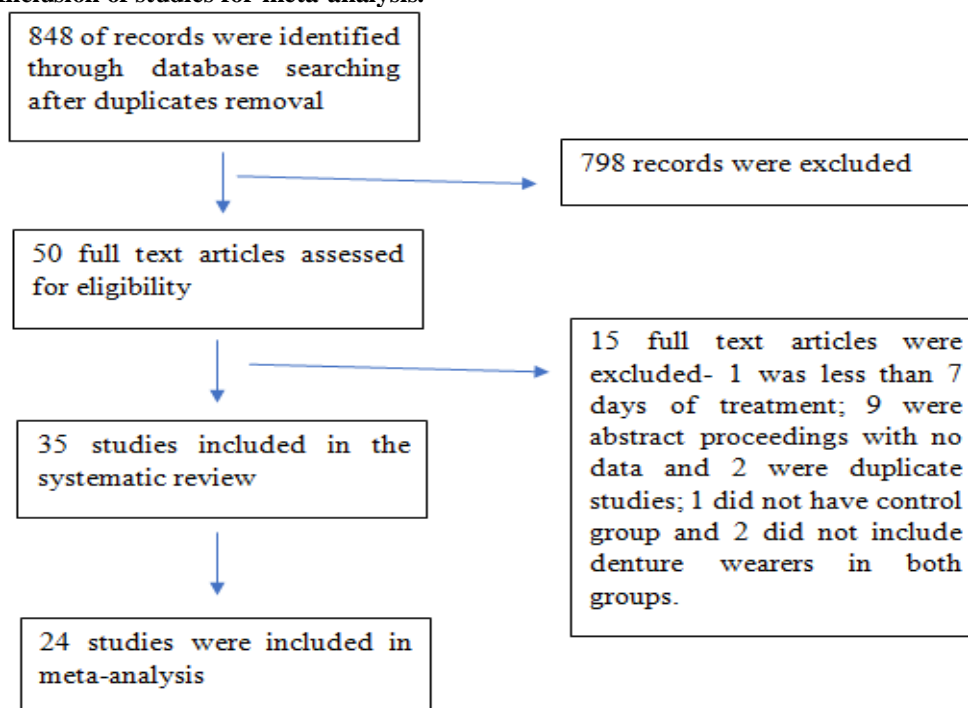
**METHODOLOGY**

All randomized controlled clinical trials (RCTs) that compared agents prescribed to treat or prevent DS were eligible for this review. A period of at least 7 days of treatment was required for including a clinical trial in the review. All individuals who wore dentures were included. There were two types of interventions. Active agents: any agent or procedure prescribed to treat or prevent DS. Control: an inactive comparator (e.g., placebo or no treatment) or another active intervention (e.g., positive control). Two main outcomes were reported in the trials included in this review: clinical signs of DS and remaining presence of yeast.

**SEARCH STRATEGY AND STUDY SELECTION**

For the identification of studies included or considered for this review, detailed search strategies we redeveloped for each database searched. These were based on the search strategy developed for MEDLINE (OVID) but revised appropriately for each database. All trials that met the inclusion criteria were evaluated in full. Authors were contacted when the trial had insufficient information to make a decision about eligibility. Outcome data were collected using a predetermined form designed for this purpose. The evaluations were compared, and any inconsistencies between the review authors were discussed and resolved in a consensus meeting. Risk of bias of seven domains was evaluated, and each domain was assessed as low, unclear, or high risk of bias. Trials were judged as low risk if all domains were classified as such, whereas a single domain judged to be inappropriate resulted in a high-risk classification for the article being assessed. (Table 1)

**Table 1- Inclusion of studies for meta-analysis.**



## DATA ANALYSIS

The estimate of effect of an intervention was expressed as risk ratios (RRs) with their respective 95% confidence intervals. The subgroup analyses were undertaken to compare the results for different types of interventions. For categorical outcomes, the numbers reporting an outcome to each group were related. Results for each study were expressed as risk ratios (RRs) with 95% confidence intervals (CIs) and combined using the Mantel- Haenszel method. An increase in the risk of a particular outcome was displayed graphically in the meta-analysis to the right of the centerline, and a decrease in the risk of an outcome was displayed graphically to the left of the center line. Clinical heterogeneity was assessed by examining the characteristics of the studies, the similarities of the types of participants, the interventions and the outcomes as specified in the criteria for included studies. The  $I^2$  statistic describes the percentage of variation across studies that is due to heterogeneity as opposed to chance. Heterogeneity was considered to be significant at  $P < .10$ . As a general rule, a fixed-effects model was used for calculation of summary estimates and their 95% CIs unless there was significant heterogeneity (variations), in which case results were confirmed using a random-effects statistical model.

## RESULTS

After de-duplication, 848 citations were identified from electronic searches performed in February 2021. After examining titles and abstracts, 50 articles were identified for further examination. The other studies were excluded because they were not relevant to the question under study or did not meet inclusion criteria. Studies that were not in English, Portuguese, Spanish, German, or French were translated for

further evaluation of eligibility when necessary. After screening the full text of the selected articles, 35 were included in the systematic review and 24 in the meta-analysis. Of the 35 trials selected for full-text assessment, two had a crossover design. Only 24 studies had available data to enter in the meta-analysis. The total number of participants included in the systematic review was 1,635, with a range of 12 to 100 per study. The duration of the intervention in the majority of the studies was 14 to 15 days. Some were 7 to 8 days, and the rest were longer than 15 days, with a maximum of 90 days of the 24 studies entered into the meta-analysis, compared an active intervention with placebo, five compared two active interventions, and the three remaining trials compared an intervention with no treatment. Three trials compared miconazole with placebo in the form of lacquer or gel. Mycological assessment was performed by counting the number of yeast colonies. In the pooled results, using a fixed-effects model, miconazole did not differ from placebo (RR = 0.73, 95% CI = 0.48–1.10). presence of *Candida* spp. with that of placebo were analyzed. Amphotericin B was in the form of a powder that adheres to mucous membranes and open wounds (2% amphotericin) and lozenges (10 mg). Mycological assessment showed no significant heterogeneity between studies ( $P = .40$ ;  $I^2 = 0\%$ ), and no differences were found between amphotericin and control (RR = 1.17, 95% CI = 0.96–1.43). Three articles compared nystatin with placebo regarding clinical stomatitis. When the results of the three studies were pooled in a meta-analysis using fixed-effects methods, fewer subjects who used nystatin were found to have clinical stomatitis (RR = 0.51, 95% CI = 0.36–0.72), with no heterogeneity between studies ( $P = .31$ ;  $I^2 = 15\%$ ). (Table 2)

**Table 2- Evaluation of Effects of Interventions, Statistical Method, and Assessment of Heterogeneity of All Outcomes for Assessment**

Comparison	Outcome or Subgroup	Risk Ratio (95% Confidence Interval)	$I^2$ (P-Value) for Heterogeneity
Miconazole (n = 45) vs control (n = 49)	Mycological assessment (2 weeks of follow-up)	0.73 (0.48–1.10)	0 (.84)
Nystatin (n = 44) vs control (n = 47)	Clinical stomatitis (14–28 days of treatment)	0.51 (0.36–0.72)	15 (.31)
Amphotericin (n = 68) vs control (n = 60)	Mycological assessment (14–28 days of Treatment)	1.17 (0.96–1.43)	0 (.4)
Imidazole (n = 75) vs control (n = 74)	Clinical stomatitis	0.98 (0.85–1.13)	26 (.26)

## DISCUSSION

The findings of this review present an overall comparison of different therapeutic options for the treatment of DS. In general, some medications containing nystatin appeared to be more effective than inactive controls. Based on the results of some included studies, nystatin appeared to be more effective than placebo in terms of clinical signs and *Candida* counts.<sup>17</sup> Nevertheless, no evidence of effect

was found for amphotericin B, considering the presence of *Candida* counts,<sup>18</sup> or for miconazole, regarding oral microbial counts of edentulous individuals. Another intervention that seems to be more effective than placebo is the immersion of dentures in disinfectants such as chlorhexidine, glutaraldehyde, and octapinol. Included studies provided inconclusive evidence regarding other interventions such as denture brushing, use of

itraconazole, and soaking in mouthwashes, precluding comparison of different therapeutic modalities. Most included studies enrolled complete denture wearers from university clinics, who may not have been representative of individuals from other settings (e.g., institutionalized elderly adults, partial denture wearers, individuals in primary health care). Moreover, the results should be interpreted with caution because of the small number of studies for most comparisons. This review included 32 studies with high risk of and 34 with unclear risk in at least one of the domains in bias evaluation. Only one of the reports provided satisfactory information regarding important methodological aspects of RCTs such as sequence generation and allocation concealment, and 20 described high risk of adequate blinding of participants. Only 13 studies addressed incomplete outcome data (low risk of bias). In summary, risk of bias was a major concern for most studies. One systematic review was found that addressed the treatment of DS by comparing antifungal treatments with other alternatives. It found results similar to those of the current study regarding the effectiveness of antifungals and disinfectants, as well as regarding the quality of studies. As in the present review, included studies seem to prioritize secondary outcomes instead of solely addressing major aspects such as normal or pathogenic oral tissues or self-reported outcomes.

## CONCLUSION

Current evidence suggests that nystatin and disinfecting agents can reduce the inflammation associated with DS and the presence of *Candida* better than inactive treatment methods, but there is no evidence that any therapy is better than any other for the treatment of DS. Decisions regarding antifungals or disinfecting methods should be made based on clinical experience.

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