

REVIEW

Management of denture stomatitis: An overview

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Denture stomatitis is a common inflammation of the palatal mucosa beneath removable dentures. The objective of this article was to examine the systematic reviews and clinical trials pertaining to the treatment of denture stomatitis. For this research, electronic databases (PubMed, Embase, Scopus, and ISI Web of Science) were searched from January 2000 to June 2021 using specified MESH keywords. Irrelevant articles were eliminated in three steps based on their titles, abstracts, and body texts. In the final analysis, 47 papers were selected, which included 12 systematic reviews and 35 clinical trials. Herbal compounds and denture disinfection were the interventions most commonly indicated. We concluded that, possibly due to the complex nature of this lesion's etiology, there is no present definitive therapy guideline for this prevalent lesion.

Keywords: denture stomatitis, clinical trial, management

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Introduction

Because dentures are foreign objects in the mouth, they can cause damage to the underlying tissues, which are not intended to withstand the pressure they exert. Some mucosal lesions are caused by the acute or chronic stimulation of dentures. These lesions are known as denture-related mucosal lesions (DMLs). Denture stomatitis (DS) is one of the most common DMLs [1]; it is a benign, chronic, inflammatory pathological change that manifests as shiny erythema in tissues covered by removable acrylic-based prostheses in the palatal mucosa and maxillary alveolar ridge. This condition is also known as denture-induced stomatitis or denture-related stomatitis [2–5]. According to the Newton classification and clinical signs, there are three types of DS:

- Type I: Simple inflammation with pinpoint petechia.
- Type II: Erythema and edema are more widespread in denture-covered areas.
- Type III: Erythematous areas with inflamed, red papules (granular level); this condition is also known as inflammatory papillary hyperplasia (IPH), and the inflammation is often more severe in the hard palate [6].

Due to its asymptomatic nature, DS remains undetected in nearly all patients, despite its high prevalence; only a small percentage of patients report mild bleeding, burning, itching, or pain in the affected area [7]. If this lesion is found quickly and correctly, it can lead to more efficient care, the right treatment, and a better quality of life for older people with full dentures.

The prevalence of DS among denture wearers ranges from 15 to 70 percent (mean=50 percent) [8]. It is more prevalent among older adults (those over 60) and women. The etiology of DS is unknown despite its high prevalence,

and its pathogenesis is multifactorial. *Candida albicans* is considered the primary etiological factor in DS. However, other factors such as opium use, diabetes mellitus, poor denture hygiene, denture-related tissue injuries, and constant denture use have also been implicated [1–8].

In this regard, we should take *Candida albicans* into consideration. This increases the likelihood that DS patients will develop dysplasia and premalignant changes. It has also been shown that DS kills cells in the oral mucosa. This means that even DS with no symptoms needs to be treated. Due to the complexity of the etiology of DS, there is no standard treatment protocol for DS patients. Various recommendations, such as using antifungal drugs and disinfectant compounds, constantly cleaning the denture, and replacing it, have been made. In addition, the increase in the number of elderly people is resulting in an increase in the prevalence of edentulism and the number of individuals with complete dentures. Because of this, it is important to know what causes DS for sure and to have an effective treatment plan for this condition. The inconsistencies in the studies conducted on DS treatment have made it difficult for dentists to interpret clinical data [1–11]. As a result, the goal of this review was to put together reliable evidence about effective ways to treat DS.

Materials and Methods

This study was a structured review. The research question (PICO) was as follows:

- Population: denture-related stomatitis patients
- Intervention: DS prevention or treatment (gathered via Method A)
- Comparison: comparison of the proposed treatment with the gold standard
- Outcome: improvement of the lesion following the proposed treatment

Four databases (PubMed, Embase, Scopus and ISI Web of Science) were searched for the relevant papers.

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All papers written in English between January 1, 2000 and June 30, 2021 were considered. MeSH was used to choose the keywords based on the goals of the study. The papers' titles, abstracts, and full texts were scanned for the following keywords:

"Candida-associated denture stomatitis, candida-related denture stomatitis, denture-related stomatitis, sub-prosthetic stomatitis, prosthetic stomatitis, stomatitis prosthética, denture-related erythematous stomatitis, granular stomatitis" and "etiology, prevalence, treatment, prevention, epidemiology, and management".

The logical operators "AND" and "OR" were then applied between the keywords of the aforementioned two series to locate papers. The result was saved as an EndNote document. The paper's citations were reviewed to identify grey literature. Two researchers screened the collected papers in three consecutive stages after eliminating duplicates using EndNote. In the initial phase, titles were examined and irrelevant papers were eliminated. In the subsequent step, the remaining papers were obtained and read by two researchers, while irrelevant papers were eliminated. The full texts of the papers that progressed to the next phase were prepared, and the two researchers read them; the papers that would enter the final review were then determined.

Structured reviews and randomized clinical trials (single or double-blinded) entered the final review; as a result, studies with low evidence levels (case reports, case series,

experimental studies, animal studies, case-control studies, preliminary studies, and non-randomized interventions) were excluded. In addition, studies proposing the elimination of underlying factors as a treatment for DS were not considered to present a particular treatment. The selected papers' data were then extracted and imported into an Excel spreadsheet [12].

The information that was taken from the chosen papers was the names of the researchers, the year the paper was published, the therapeutic methods that were compared in the paper, the more effective method, and the important results that were relevant to the paper.

Results

In the databases chosen for this structured review, 1460 papers were found. After removing 698 papers that were duplicates, 558 papers with irrelevant titles, 118 papers after reading the abstracts, and 39 papers after reading the full texts, the final review included 35 clinical trials and 12 systematic reviews (Figure 1).

The explanation of the 12 structured reviews on DS treatment is provided in Table I. Systematically reviewed DS treatments included microwave therapy (two reviews), chemicals and denture cleaners (five reviews), natural compounds (one review), antifungals (two reviews), nanotechnology (one review), and low-level laser therapy (one review) [13–24].

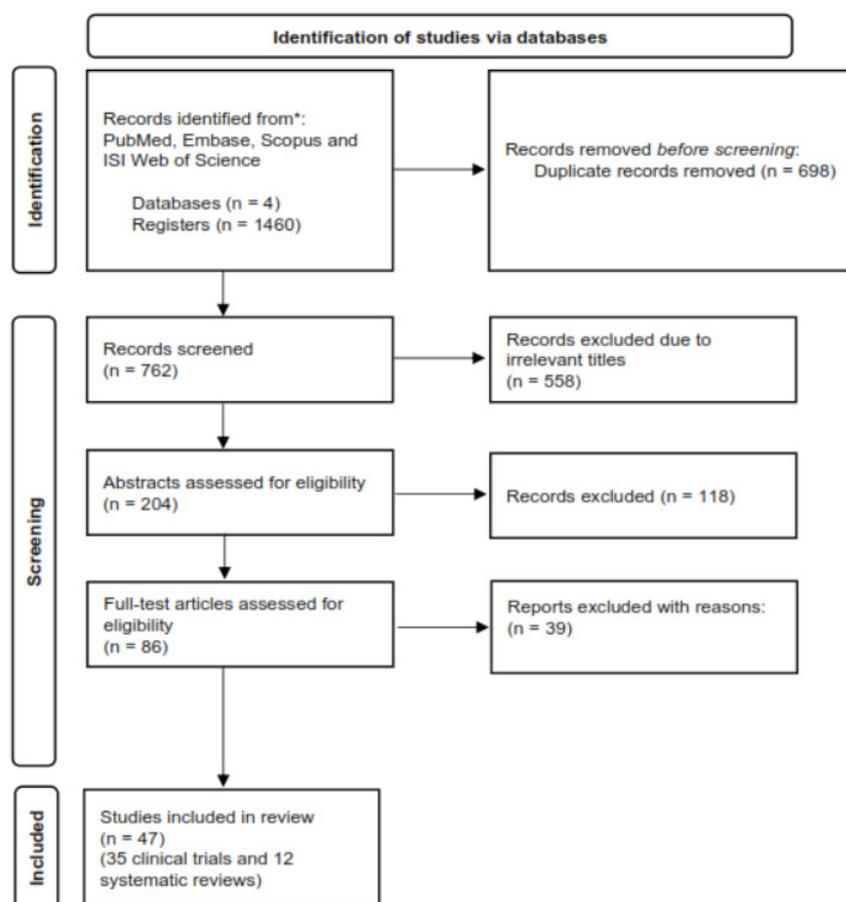


Fig. 1. Diagram illustrating the study selection procedure used to identify papers for this review.

Table I. A summary of the 12 systematic reviews on the treatment of denture stomatitis

Author, Year	Number of reviewed studies	Main Conclusion
Skupien et al, 2013 [13]	38	Using sodium hypochlorite at a concentration of 0.5% can help disinfect denture liners and tissue conditioners. Incorporating nystatin into these substances also has the ability to treat or prevent oral candidiasis.
Emami et al, 2014 [14]	15	In the treatment of denture stomatitis, disinfection methods could be considered as an adjunct or alternative to antifungal medications.
Ferreira et al, 2015 [15]	3	At this time, it is not possible to confirm the existence of scientific evidence for the use of natural products in the treatment of oral candidiasis.
Hilgert et al, 2016 [16]	35	The findings support the use of nystatin and disinfectants for the treatment of DS.
Robeiro Rocha, 2016 [17]	5	Only chlorhexidine and chlorine dioxide demonstrated some evidence of a reduction in <i>Candida</i> spp
Yarborough et al, 2016 [18]	67	Clinical strategies frequently involved multiple approaches with the combined objective of eradicating pathogenic microorganisms and preventing the re-establishment of a pathogenic biofilm through preventive hygiene measures.
Davoudi et al, 2018 [19]	4	LLLT plays an important role in the clinical treatment of Down syndrome. However, PDT outcomes were comparable to those of conventional antifungal treatments.
Ahmad et al, 2020 [20]	27	Nanomaterials composed of metal oxides demonstrated cytotoxicity against <i>Candida</i> and other microorganisms present in oral biofilm, including PMMA denture surface.
An et al, 2020 [21]	28	Incorporating antimicrobial agents into Denture Base Resins has not been conclusively demonstrated to be effective.
De Costa et al, 2020 [22]	5	For the treatment of denture stomatitis caused by <i>Candida</i> , microwave disinfection produced comparable outcomes to conventional therapies.
Santos Sousa et al, 2020 [23]	3	Microwave sterilisation of complete dentures is as effective as antifungal treatment for the treatment of denture stomatitis.
Shui et al, 2021 [24]	19	Most studies showed phytomedicines had fewer side effects and higher patient satisfaction than antifungals or disinfectants. To verify the clinical efficacy of phytotherapy as an alternative or adjunctive therapy for denture stomatitis, more RCTs with standard herbal formulations are needed.

Table II and Table III provide a summary of the data extracted from the 35 clinical trials pertaining to DS treatment. Herbal remedies (ginger, propolis gel, vinegar, garlic, etc.) and disinfecting the denture using different methods, such as antiseptic mixtures (sodium hypochlorite, chlorhexidine, etc.), brushing, and microwaving, were the most common methods studied. Consideration should also be given to the seven papers on the efficacy of photodynamic therapy and low-level laser therapy. The use of antifungals (nystatin and miconazole) was considered the treatment standard and benchmark in clinical trials related to this field [25–59].

Discussion

This study examined 47 systematic reviews to provide a structured overview of DS treatment. The significant number of structured reviews (12 studies) conducted in this field was the first significant observation made during the analysis of the chosen studies [26–42]. Skupien and Hilgert highlighted the importance of nystatin in DS treatment in the results of their structured review [13,16]. The colonization of *Candida albicans* on the impression surface of maxillary dentures is the primary cause of DS. DS is categorized as chronic atrophic candidiasis or a lesion induced by candida. Consequently, the primary treatment for this lesion is a topical antifungal medication, and nystatin is frequently the first choice of treatment. The unpleasant and bitter taste of topical (oral) nystatin is a significant disadvantage. In their systematic review [17], Robeiro Rocha et al. noted the beneficial effects of prescribing chlorhexidine mouthwash in the treatment of DS. However, the antifungal properties of chlorhexidine are described as “mild” in the majority of texts, and it should be noted that prolonged use can result in complications such as tooth discoloration, increased dental tartar, and a

burning sensation in the mouth. In addition to prescribing topical nystatin, Skupien and Hilgert emphasized the efficacy of disinfecting dentures with substances such as sodium hypochlorite [13,16]. In their structured review, Emami et al. suggested that the use of such compounds as a supplement or alternative to nystatin should be considered [14]. In addition to disinfecting dentures with antiseptic compounds, their use in the denture resin base to prevent candida colonization on the denture surface has been discussed. However, the systematic review by An et al. did not confirm the efficacy of these disinfectants [21]. Denture hygiene and daily brushing of denture impression surfaces are unquestionably effective in reducing the risk of DS. However, these studies raise the issue of a higher level of routine “cleaning” and, in fact, “disinfection” of the denture. Because the proposed methods for disinfecting dentures are so diverse, De Costa and Santos Souza conducted a systematic review on the use of microwaves [22,23]. Due to insufficient evidence, the application of this method has remained a suggestion.

In this review, eleven randomized clinical trials on the treatment of DS with different disinfection methods were compiled. Regarding the effect of tooth brushing, Kabawat et al. found that routine palatal brushing is beneficial in preventing DS [40]. According to the findings of clinical trials conducted by Araujo, Badaro, Aoun, Nittayananta, and Uludamar, the proposed antiseptic compounds include sodium hypochlorite, triclosan, cetylpyridinium, chlorhexidine immersion, lawsone methyl ether (LME) (a naphthoquinone compound with potent antifungal properties), and alkaline peroxide tablets [25, 28, 37, 38, 44, 53]. In addition to the variety of proposed antiseptic compounds, which renders it difficult to choose a single treatment option, the routine use of some of these compounds is ambiguous. Denture immersion in chlorhexidine, for in-

Table II. A brief summary of the interventions and results discussed in the selected clinical trials.

Author	Year	Sample Size	Intervention	Result
Araujo, et al. (25)	2021	108	Sodium hypochlorite 0.25% / 0.15% Triclosan/ Denture Cleanser Tablets	All Groups had similar disinfecting effects.
Gonoudi, et al. (26)	2021	28	Nystatin Suspension / Zataria Multiflora (ZM) Droplet	Droplet Zataria Multiflora (ZM) was as effective as Nystatin Suspension in D.S treatment.
Alves, et al. (27)	2020	65	Nystatin/ Antimicrobial Photodynamic Therapy (aPDT) via photodithazine(PDZ) with 660 nm Lasertherapy	This method of implementing PDT can be a considerable treatment for D.S.
Badaro, et al. (28)	2020	60	Ricinus communis 10% / chloramine-T 0.5% Control (Water) / Control (Sodium hypochlorite 0.25%)	Sodium hypochlorite is more effective than other disinfecting agents.
Afroozi, et al. (29)	2019	66	Nystatin + photodynamic therapy (PDT)/ Nystatin	Adding PDT to Nystatin enhances the treatment effect.
Mustafa, et al. (30)	2019	30	Mouthwash Chitosan-Curcuminoid (CHI-CUR) / Chlorhexidine / Chitosan with polyethylene glycol (PEG) 400	CHI-CUR Mouthwash has an acceptable alternative topical effect.
Alrabiah, et al. (31)	2019	36	photodynamic inactivation (PDI) and Nystatin	PDI is as effective as nystatin in D.S treatment
Lee, et al. (32)	2019	36	Partial Denture Users Consuming milk with or without Lactobacillus rhamnosus SP1 probiotic	This Probiotic decreases the severity of D.S in elders residing in nursing homes.
De Senna, et al. (33)	2018	-	Miconazole 2% Gel / Methylene blue + Photodynamic inactivation (PDI) with 660 nm Low Level Lasertherapy	This method of applying PDI can decrease the load of fungal infection and inflammation.
Pina, et al. (34)	2017	40	Miconazole 20mg/g Gel / 2% Brazilian Propolis Gel	The effect of propolis gel is not inferior to miconazole and it could be considered an alternative treatment.
Maciel, et al. (35)	2016	40	methylene blue-mediated PDT with Low Level Lasertherapy / Miconazole	The effect of miconazole in the treatment of D.S was more prominent than PDT with low-level laser therapy.
Alizadeh, et al. (36)	2016	50	Mouthwash ginger / Mouthwash Nystatin	Both treatments had the same results.
Aoun, et al. (37)	2015	40	% /0.05 cetylpyridinium chloride Chlorhexidine 0.12% / Control (Water)	Both solutions were effective in denture disinfection
Aoun, et al. (38)	2015	60	Chlorhexidine 0.12% / 0.1%hexetidide / Distilled water (Control)	Submerging the denture in hexetidide had a lesser effect than disinfecting with chlorhexidine.
Ishikawa, et al. (39)	2015	59	Placebo Group / Group Taking Probiotic Capsule Containing: lyophilized Lactobacillus rhamnosus HS111, Lactobacillus acidophilus HS101, and Bifidobacterium bifidum	This probiotic treatment can be considered as a possible alternative against candida infection in the elderly with dentures.
Kabawat, et al. (40)	2014	48	Palatal Brushing	Palatal brushing is an effective method for D.S treatment.
Dastjerdi, et al. (41)	2014	30	Nystatin / Homemade Mouthwash (Vinegar and Rose Water)	This homemade mouthwash could be an alternative to nystatin in DS treatment.
Tay, et al. (42)	2014	50	Placebo/ Miconazole 2% / Uncaria tomentosa 2% Gel	Uncaria tomentosa gel could be used as an supplemental treatment for DS.
Capistrano, et al. (43)	2013	45	Miconazole 2% Gel / 2.5% Propolis Gel / 24% Propolis Mouthwash	Propolis was found as effective as miconazole.
Nittayananta, et al. (44)	2013	67	Lawson methyl ether (LME) Mouthwash / Chlorhexidine Mouthwash	The application of IME in HIV and DS patients may be effective in persistent cases.
Pinelli, et al. (45)	2013	30	Ricinius Communis / Nystatin / Miconazole	Treating with Ricinius Communis may clinically improve denture stomatitis in elderly patients residing in nursing homes. Additionally, this treatment has the same effect in comparison with miconazole.
Bakhshi, et al. (46)	2012	40	Nystatin Mouthwash/ Garlic Extract Solution	The therapeutic effects of garlic extra solution are similar to nystatin.
Sabzghabae, et al. (47)	2012	80	Placerbo / 1% S. hortensis essential oil Gel	The topical application of S. hortensis could be effective in treating DS.
Silva , et al. (48)	2012	60	Nystatin / Microwave/ Control Group	Disinfection with microwave was as effective as nystatin in DS treatment.
Mima, et al. (49)	2012	40	Nystatin / Photodynamic Therapy (PDT)	PDT method was as effective as nystatin in DS treatment.
Sanita, et al. (50)	2012	40	Nystatin / Microwave	the application of microwave was as effective as nystatin in DS treatment in controlled type II diabetes patients.
Sabzghabae, et al. (51)	2011	80	Placebo/ Pelargonium 1% Gel	This gel was found to be more effective than placebo
Sefidgar, et al. (52)	2010	30	Nystatin Mouthwash / Mouthwash Artemisia 1%	artemisia extract could be used as a treatment option for DS.
Uludamar, et al. (53)	2010	90	Three Brand of Alkaline Peroxide Tablets (Polident, Efferdent, and Fittydent) CloSYS II and Corsodyl Mouthwashes Control Group Distilled water	The application of this mouthwash was effective in treating DS. (This article's method was centered around disinfecting dentures)
Neppelenbroek, et al. (54)	2008	60	Microwave with Miconazole / Miconazole / Microwave Control Group	disinfecting the denture with microwave is effective in DS treatment and decreases the recurrence of candida.
Amanlou, et al. (55)	2006	24	Miconazole 2% Gel / Zataria multiflora 0.1% Gel	Zataria multiflora gel was better at alleviating palatal erythema. While miconazole had a better effect in decreasing the number of colonies on the denture surface.
Webb, et al. (56)	2005	60	Sodium hypochlorite / Microwave / Control Group	Both disinfecting methods were found effective.
Maver-Biscanin, et al. (57)	2004	70	685 nm Diode Laser / 830 nm Diode Laser /Anti-Fungal Gel and Disinfection Solution / Placebo	The application of low-power laser could be valuable in treating DS.
De Souza Vasconcelos, et al. (58)	2003	60	Miconazole Gel / Punica granatum	P.granatum could be considered as a topical antifungal agent in DS treatment.
Cross, et al. (59)	2000	40	Itraconazole in Liquid and Capsule form	These two drug forms could be used equally as supplemental therapy.

Table III. The classification of all treatment methods discussed in the clinical trials under review.

Treatment Method	Number of Studies
Herbal Medicine / Phytotherapy	12
Denture Disinfection	11
Photodynamic and low-level laser therapy	7
Probiotics Application	3
Chitosan Based Materials	1

stance, can discolor the labial surface, resulting in patient dissatisfaction with the denture's appearance. Additionally, cetylpyridinium requires precise concentration control; otherwise, it can cause mucosal irritation and even chemical burns. In this review, three clinical trials conducted by Silva, Sanita, and Neppelenbroek on the use of microwaves in denture disinfection were discussed [48, 50, 54]. Silva and Sanita argued that microwaves are equally effective as nystatin for this purpose. It is important to note, though, that Sanita et al. did their research on people with type 2 diabetes [48, 50]. Overall, it is essential to emphasize that there is no universally acknowledged procedure for denture disinfection; hence, the difficulties associated with denture stomatitis continue. There are a variety of approaches and products dedicated to this issue now accessible on the market. However, it is recommended to adhere to best practices, such as the aforementioned procedures.

Ferreira and Shui conducted two systematic reviews that investigated the efficacy of herbal medicine in the treatment of DS. The results of both reviews indicated that although the reviewed studies have shown the positive impact of using such treatments to improve this complication, due to the lack of precise formulations and the probable side effects, their superiority over standard treatment options (such as nystatin) is questionable and in need of further research [15, 24]. Iranian traditional medicine is very popular among researchers, and the clinical trials examined in this review confirmed that Iranian researchers are interested in treating DS with traditional medicine. Seven studies conducted by Alizadeh, Dastjerdi, Bakhshi, Sefidgar, Sabzqabai, and Amanloo investigated the use of ginger, homemade vinegar and rose water, garlic, *Pelargonium graveolens*, *Satureja Hortensis*, *Artemisia Sieberi*, and *Zataria multiflora* in DS treatment, respectively [36, 41, 46, 47, 51, 52, 55]. Tay, Pinelli, and De Souza Vasconcelos noted the use of *Uncaria tomentosa*, *Ricinus communis*, and pomegranate herbal compounds for this purpose [42, 45, 58]. Tay et al. argued that *Uncaria tomentosa* extract could play a complementary role in the treatment of DS. Furthermore, Pinelli et al. argued that the effect of *Ricinus communis* in this instance is comparable to that of the well-known antifungal drug miconazole [42]. A country's culture, geography, and flora play a role in the selection of a herbal compound for the study of its effect or lack thereof on diseases. In the two clinical trials conducted in Brazil by Pina and Capistrano, for instance, the effect of a botanical compound called propolis, which appears to be regionally specific, was evaluated [34, 43]. Therefore, the inability to

generalize the use of herbal compounds for patients in different parts of the world appears to be an additional limitation of such compounds. Photodynamic therapy (PDT) and low-power laser therapy for the treatment of DS were the subjects of a systematic review by Davoodi et al. [19].

Seven clinical trials were compiled for this analysis, including studies by De Souza Alves, Afroozi, Alrabiah, Sena, Maciel, Mima, and Maver-Biscanin [27, 29, 31, 33, 35, 49, 57, 58]. Different methods were proposed by the aforementioned researchers to administer photodynamic therapy to patients with DS. Various compounds, such as photoditazine or methylene blue, were used for this purpose in these studies, resulting in heterogeneity. Due to the use of various wavelengths by researchers, the same is true for low-power lasers. Some researchers, including Maver-Biscanin et al., questioned the efficacy of low-power lasers in the treatment of DS [57]. However, Mima et al. noted that photodynamic therapy and drugs like nystatin have the same effect (49%). Additionally, Afroozi et al. argued that combining photodynamic therapy with nystatin improves the therapeutic effects [29]. Consequently, the precise status of treatments such as photodynamic therapy and low-power laser for the management of DS is uncertain. The fact that there are so many studies on DS can be seen as a weakness of this structured review since it made it harder to choose the final papers.

Due to the recurring nature of denture stomatitis, it becomes crucial to arrange follow-up appointments at regular intervals to verify that adequate cleaning and hygiene procedures are being followed. However, there is no generally agreed upon strategy for doing so. Therefore, a professional agreement is essential for patient recalls and follow-ups.

Conclusion

The present systematic review revealed that due to the multifactorial nature of DS incidence, the interpretation of its most likely causes varied greatly between studies. Possibly, for this reason, different treatments have been proposed in research, and no single treatment has been proposed for this complication to date. Therefore, the following recommendations are made to rectify the existing deficiencies:

Providing a valid treatment guideline for DS is an issue that should be considered by researchers. For example, should antifungal medications be administered topically or systemically to patients with DS who have an immune deficiency or dry mouth? What are the initial topical and systemic treatment options? What dosages should be used? How and for how long are they to be utilized? Up to this point, DS prevention has not been discussed seriously. This can be accomplished by educating patients when they begin using dentures. The patients should be given educational pamphlets, and their contents should be explained. Smoking cessation, frequent visits to clinicians to resolve denture problems, daily denture brushing, avoiding wearing dentures at night, and storing dentures in disinfecting solutions are all methods for preventing this complication.

Also necessary seems to be the education of clinicians in this field.

Authors' Contribution

NN contributed to the study's conception and design. PS was responsible for the literature search, study selection, and collection of data. NN and PS examined the gathered data. ARH was responsible for drafting the manuscript. All authors have read and approved the final manuscript version.

Conflict of Interest

None to declare.

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