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CKJ Review

CKJ REVIEW

Comparative efficacy of non-pharmacological interventions on xerostomia and salivary flow rate among haemodialysis patients: A systematic review and network meta-analysis

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ABSTRACT

Background. Xerostomia is a distressing symptom experienced by patients undergoing dialysis. We sought to compare and rank the efficacy of different non-pharmacological interventions on xerostomia and salivary flow rate among dialysis patients.

Methods. A systematic search was conducted in six English-language databases: PubMed, CINAHL, Scopus, Web of Science, Embase and Cochrane Central Register of Controlled Trials, in April 2023. Screening, quality appraisal and data extraction were undertaken by two independent reviewers. A network meta-analysis was performed to assess the relative efficacy of different non-pharmacological interventions.

Results. The analysis included 11 randomized controlled trials involving 739 patients and eight non-pharmacological interventions. The pairwise analysis indicated that compared with the control group, sugarless candy, chewing sugarless gum, acupressure auricular and licorice mouthwash had a significant positive effect on reducing the severity of xerostomia; also, transcutaneous electrical nerve stimulation (TENS), licorice mouthwash, sugarless chewing gum, photobiomodulation and pure water mouthwash significantly improved the saliva flow rate. The network analysis indicated that sugarless chewing gum significantly reduced the symptoms of xerostomia, while TENS and sugarless chewing gum were effective in improving the unstimulated whole salivary rate. Among dialysis patients, chewing sugarless gum and using TENS were the top-ranked interventions for relieving xerostomia and enhancing saliva flow rate, respectively.

Conclusions. Several non-pharmacological interventions have demonstrated effectiveness in relieving xerostomia and enhancing saliva flow rate. While further research may be needed to confirm and refine these findings, the interventions used in this review offer promising results and should be incorporated into the standard care of dialysis patients experiencing these symptoms to enhance their quality of life and oral health.

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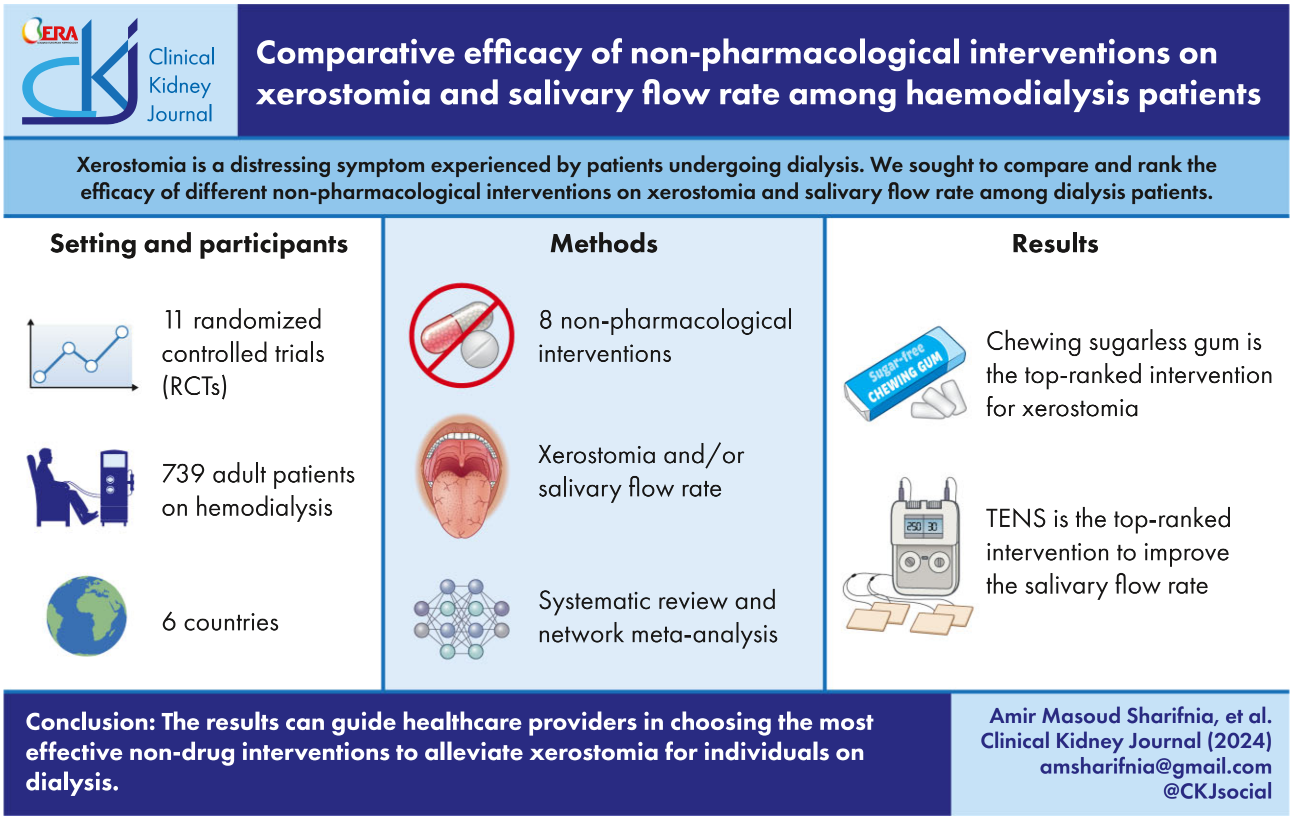
GRAPHICAL ABSTRACT



Keywords: chronic kidney disease, non-pharmacological intervention, salivary flow rate, systematic review, xerostomia

KEY LEARNING POINTS

What was known:

- Patients undergoing dialysis frequently exhibit diminished saliva production and experience xerostomia as a distressing symptom.
- Non-pharmacological interventions have emerged as the preferred treatment options for addressing xerostomia in dialysis patients.
- Traditional pairwise meta-analysis only provides a direct comparison of two interventions. The most effective non-pharmacological interventions for alleviating xerostomia and enhancing saliva flow rate among dialysis patients remain unknown.

This study adds:

- Sugarless chewing gum is the most effective intervention for alleviating xerostomia in dialysis patients.
- Transcutaneous electrical nerve stimulation (TENS) and sugarless chewing gum can significantly enhance the saliva flow rate among dialysis patients.
- Sugarless chewing gum and TENS are the top-ranked interventions for relieving xerostomia and improving saliva flow rate, respectively, among dialysis patients.

Potential impact:

- This information can guide healthcare providers in choosing the most effective non-drug interventions to alleviate xerostomia and enhance saliva flow for individuals undergoing dialysis.
- These interventions can be implemented safely and at a low cost and will improve the quality of life of patients experiencing xerostomia.

INTRODUCTION

Kidney disease is a global health issue that affects >10% of the global population, accounting for >800 million people worldwide [1]. Without interventions such as dialysis or transplantation, chronic kidney disease (CKD) can be fatal. Individuals affected by CKD, particularly those receiving dialysis, not only face increased mortality risks, but also experience a significant burden of symptoms [2]. Among these, xerostomia is reported as one of the distressing symptoms [3], with up to 74% of people undergoing dialysis experiencing it [4].

Xerostomia, commonly referred to as dry mouth, is a condition that has considerable health implications, including an increased risk of oral infections and difficulties in eating, swallowing and speaking, as well as an unpleasant taste [5]. The underlying pathophysiology of xerostomia in people receiving dialysis remains unclear, however, studies have reported a reduced saliva flow rate in dialysis patients compared with their healthy counterparts [6, 7]. Diminished salivary flow due to atrophy and fibrosis of the salivary glands, together with other risk factors associated with CKD, such as polypharmacy, restriction of fluid intake and advanced age, collectively contribute to the development of xerostomia [8]. People receiving dialysis typically take a median of 19 medications daily [9]. In considering the already high pill burden and the correlation between polypharmacy and the risk of xerostomia, non-pharmacological interventions emerge as the preferred treatment options for addressing xerostomia in the dialysis population.

To date, several clinical trials have investigated the impact of non-pharmacological interventions, including products such as liquorice or gum and methods such as transcutaneous electrical nerve stimulation (TENS) or acupuncture that stimulate saliva glands, as well as the use of saliva substitutes. A saliva substitute is a synthetic solution designed to provide temporary moisture and lubrication to the mouth. It creates a protective film, helping reduce the risk of mechanical trauma commonly linked to chronic dry mouth [10]. Saliva stimulants attempt to increase the natural flow of saliva via mechanical or gustatory stimulation, such as chewing or sucking [11]. These non-pharmaceutical procedures offer a relatively simple, economical, non-invasive and low-complication option compared with pharmaceutical medications. However, no review has yet summarised these interventions comprehensively.

A primary search identified two publications on the effect of chewing gum [12] and acupressure [13], reported traditional meta-analyses comparing the same type of intervention using pooled head-to-head data. However, none of these studies undertook a quantitative evaluation and ranking of various non-pharmacological interventions. To address this gap, we conducted a network meta-analysis to allow comparisons of different non-pharmacological interventions in xerostomia and salivary flow rate and to rank the best intervention options for dialysis patients. This study aims to identify the most suitable treatment option that optimizes the management of xerostomia in patients receiving dialysis.

MATERIALS AND METHODS

Design

Network meta-analysis is an analytical approach that visualizes an overview of evidence by accommodating direct and indirect evidence between three or more interventions to understand the comparative effectiveness of different interventions and rank these interventions based on different outcomes to make evidence-based patient-care decisions [14]. This study was undertaken according to the Preferred Reporting Item for Systematic Review and Meta-analysis (PRISMA) guidelines extension statement for reporting of systematic reviews, including network meta-analysis of healthcare interventions [15] and guided by the Cochrane Handbook for Systematic Reviews of Interventions [14]. The protocol of this systematic review was registered at the International Prospective Register of Systematic Reviews (CRD42023415094).

Data sources and search methods

A three-step systematized search strategy was incorporated to identify studies from six electronic English-language databases (PubMed, CINAHL, Scopus, Web of Science, Embase and Cochrane Central Register of Controlled Trials). First, a preliminary search was conducted in MEDLINE to identify initial subject headings and keywords from titles and abstracts of relevant papers (see the supplementary file, search terms). A comprehensive search strategy that incorporated Medical Subject Headings terms and keywords was developed through collaboration with all the reviewers. Subsequently, a thorough search across all databases using the final search strategy was implemented by two reviewers (G.C. and A.S.) (Supplementary Item S1). In the last step, a backward search was performed by examining the reference lists of the included studies and Google Scholar was manually searched to uncover any additional relevant records.

Study selection

All the search records were uploaded into EndNote 20.3 (Clarivate, London, UK). After removing any duplications, two reviewers (A.S. and X.Z.) independently screened all titles and abstracts following the inclusion criteria. Both reviewers also retrieved and checked the full text of potentially relevant studies. Any disagreement was resolved through consultation with the third reviewer (R.F.).

Inclusion and exclusion criteria

This review included randomized controlled trials (RCTs) that were published in English from database inception until April 2023. The target studies were defined using the PICOS process (Box 1). Studies were included if they assessed the effect of non-pharmacological interventions that stimulate salivary glands, as well as the use of saliva substitutes (Supplementary Table S3). Diet and medicinal compounds with systemic or local effects without using mechanical stimulation methods of salivary glands were excluded from the review. To be included in the review, the studies had to evaluate xerostomia and/or unstimulated whole saliva (UWS) flow rates using the following instruments and procedures:

- Xerostomia: Visual Analogue Scale (VAS), Summated Xerostomia Inventory (SXI), Xerostomia Inventory (XI) and Xerostomia Questionnaire (XQ).
- UWS flow rate: UWS collected using oral cotton or spitting technique.

Data extraction

A standardized data extraction table was developed, including the first author, year of publication, country, study design,

Box 1. Inclusion criteria (PICOS format).

Inclusion criteria

Population	Adults ≥18 years of age with CKD undergoing dialysis
Intervention	Non-pharmacological interventions, specifically salivary substitutes and stimulants
Comparator	Other types of non-pharmacological interventions or control groups that were on usual treatment or placebo
Outcomes	Xerostomia and/or salivary flow rate
Study type	RCTs

intervention and control groups, characteristics of the participants and changes in outcomes. If the study evaluated outcomes at multiple follow-up periods, only the assessment immediately following the intervention was included. The data were extracted independently by two reviewers (A.S. and X.Z.) and if there were missing data, the authors were contacted to provide the data.

Methodological quality assessment

Study quality was assessed by two independent reviewers (H.G. and A.S.) using the Joanna Briggs Institute (JBI) critical appraisal checklist for RCTs [16]. JBI's critical assessment tool includes 13 criteria, each scored with four options (yes = 2, unclear = 1, no, and not applicable = 0). Due to the paucity of research in this field, studies were not excluded due to methodological weakness. Any discrepancy between reviewers regarding the study inclusion was resolved by consensus.

Statistical analysis

Meta-analysis was conducted using Stata MP version 16 (StataCorp, College Station, TX, USA). A traditional pairwise meta-analysis using a random effects model and restricted maximum likelihood method was performed to compare each intervention with the control group. The pooled effect sizes were calculated as standardized mean differences (SMDs) ± 95% confidence intervals (CIs). The SMDs of 0.2, 0.5 and 0.8 were interpreted as low, moderate and high effect sizes, respectively [17]. The heterogeneity was assessed using I^2 statistics and was rated as low ($I^2 < 25\%$), moderate ($I^2 = 25–50\%$) and high ($I^2 > 50\%$) [18].

Network meta-analysis was performed using frequentist approaches and a random effects model. The network of comparisons was graphically represented by a network map [19]. In the network map plot, interventions were represented by nodes and direct comparisons between interventions were shown with edges (lines). The width of treatment nodes and comparison edges were indicative of the number of studies containing each treatment or comparison [19, 20]. The study and population baselines (descriptive statistics) were assessed for the transitivity assumption. Inconsistency was assessed by the global approach using the Wald test and the local approach (node splitting), and a P-value <.05 was considered statistically significant [21]. The league table presented the relative effects of different treatments. The surface under the cumulative ranking (SCURA) was used to determine the relative ranking of order treatments and identify superiority between treatments [19, 22].

Sensitivity network meta-analysis was performed separately by excluding multi-arm trials and trials with control groups defined by brief interventions (e.g. placebo).

Assessment of certainty of evidence

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework for network meta-analysis to evaluate the certainty of evidence [19, 23]. The certainty of evidence for each direct comparison was rated following the GRADE framework for pairwise meta-analyses. Issues related to the risk of bias, inconsistency, indirectness and imprecision were considered when assessing the certainty of evidence [23]. Subsequently, the certainty of the network estimation was assessed. The process commenced with determining the certainty of direct or indirect evidence that dominated the comparison for network estimates. Following this, consideration was given to potentially downgrading the certainty in network estimates due to inconsistencies between direct and indirect estimates. Instances of inconsistency or imprecision between direct and indirect estimates prompted contemplation of reducing the certainty of the network estimates [24].

RESULTS

Study selection

The search identified 1303 studies, of which 833 remained after duplicates were removed. Following the review of titles and abstracts, 805 studies were excluded, with 28 studies included for a full-text review. A total of 11 studies met the eligibility criteria and were included in the analysis. The study selection process is presented in Fig. 1.

Methodological quality

The included studies had moderate to high methodological quality, with scores ranging from 69.2% to 92.3% of the quality items in the JBI quality assessment tools. Most studies failed to address the blinding process and the outcome assessors (Supplementary Tables S1 and S2).

Characteristics of included studies

Of 11 RCTs [25–34] published between 2013 and 2021, 2 were three-arm trials [34, 35]. These studies were conducted in six countries: Iran, Brazil, Turkey, South Korea, Egypt and Taiwan. A total of 739 participants were included in these studies, with a mean age of 44–67 years and a mean dialysis vintage of 42–139 months. Eight types of non-pharmacological interventions were identified: acupressure auricular ($n = 2$), sugarless chewing gum ($n = 4$), aroma gargling solution ($n = 1$), licorice mouthwash ($n = 2$), pure water mouthwash ($n = 1$), sugarless candy ($n = 1$), photobiomodulation (PBMT) ($n = 1$) and TENS ($n = 2$). The duration of the interventions in the studies ranged from 15 sec to 3 months. The full characteristics of trials included in this review are presented in Table 1.

Analysis of outcomes

Pairwise meta-analysis

The direct comparison demonstrated that sugarless candy, sugarless chewing gum, licorice mouthwash and auricular acupressure had a significant positive effect on reducing the severity

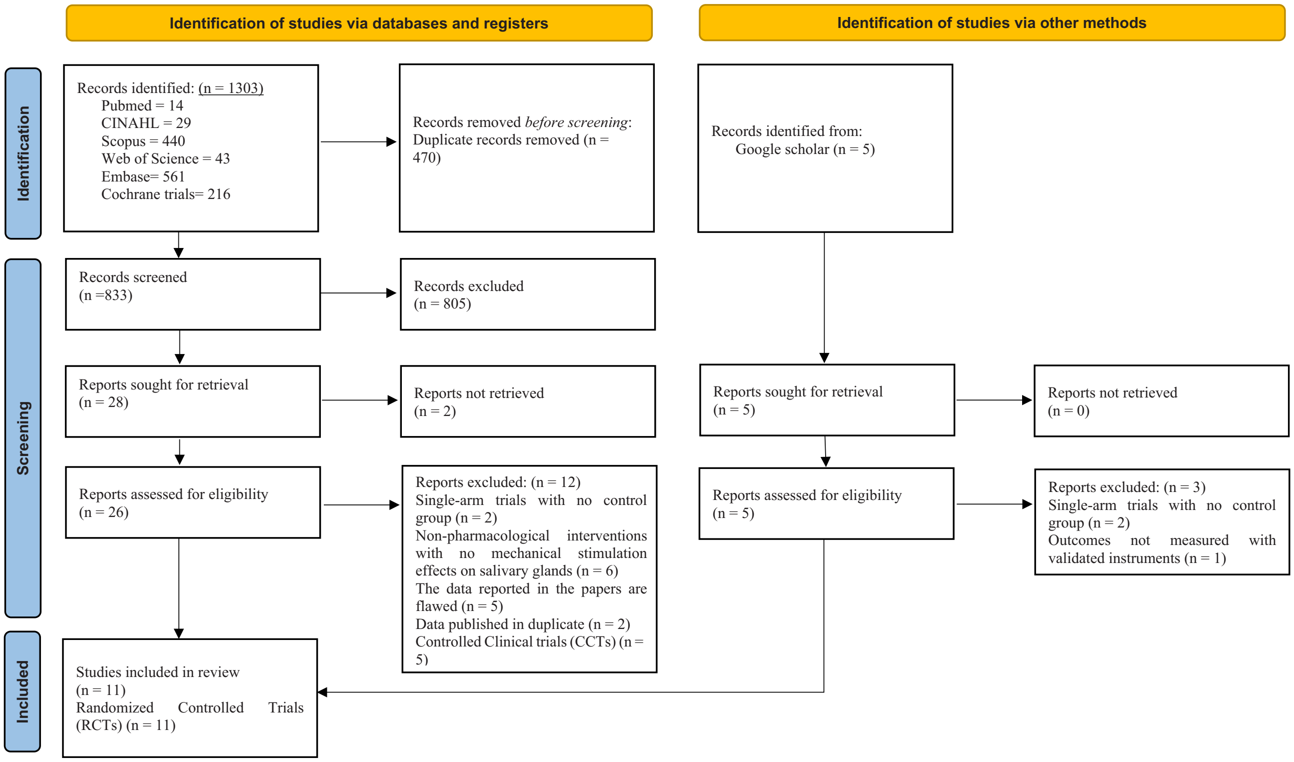


Figure 1: PRISMA 2021 flow diagram [46].

of xerostomia compared with a control group. TENS, licorice mouthwash, sugarless chewing gum, PBMT and pure water mouthwash significantly enhanced UWS flow rates compared with the control group (Supplementary Figs. S1–S12 demonstrate the direct comparisons).

Network meta-analysis

Xerostomia. A total of nine RCTs ($n = 641$ participants) assessed the effect of 7 non pharmacological interventions on the symptoms of xerostomia. The network map plot indicates that sugarless chewing gum was the most frequently used intervention (Fig. 2a). Overall, sugarless chewing gum [$n = 4$; SMD $= -1.97$ (95% CI -3.28 to -0.66)] significantly reduced the symptoms of xerostomia (Fig. 2b). The confidence of the evidence for sugarless chewing gum and auricular acupressure was moderate and for the remaining interventions was low to very low (Supplementary Table S5). When considering the interval estimation of both direct and indirect comparisons, no superiority was found between interventions (Supplementary Table S3). Supplementary Table S4 demonstrates the ranking of interventions. Cumulative ranking probability plots indicated that sugarless chewing gum is the top-ranked intervention for xerostomia (Supplementary Fig. S13).

UWS flow rate. A total of 8 RCTs ($n = 579$) assessed the effect of six non-pharmacological interventions on UWS. The network meta-analysis results are shown in Fig. 3. The network map plot indicates the most frequent interventions were auricular acupressure and sugarless chewing gum (Fig. 3a). TENS [$n = 1$; SMD $= 2.41$ (95% CI 0.75–4.06)] and sugarless chewing gum [$n = 3$; SMD $= 1.12$ (95% CI 0.17–2.08)] were effective in improving UWS (Fig. 3b). The confidence of the evidence was moderate for sugarless chewing gum and low and very low for the remaining interventions (Supplementary Table S6). According to the internal estimation of both direct and indirect comparisons (Supplementary Table S3), no intervention was found to be superior to the others. TENS was the top-ranked intervention to enhance UWS (Supplementary Table S4 and Supplementary Fig. S14).

Transitivity and consistency assessment

The assumption of transitivity was accepted because the distribution of study and population baselines were similar between trials. The global inconsistency levels for xerostomia indicated statistically non-significant results ($\chi^2 = 3.12$, $P = .0774$) and the local inconsistency level showed no significant differences in direct and indirect comparisons (all P-values $>.05$). The node split results were consistent for all the loops (all P-values $>.05$) (Supplementary Table S7). The global inconsistency could not be explained for UWS because there was no source of inconsistency. In addition, the local inconsistency level was not indicative of the significance of the direct and indirect effects (all P-values $>.05$) (Supplementary Table S8).

Sensitivity analysis

The sensitivity analysis was conducted by excluding the three-arm trials. The result reduced the effect sizes of sugarless chewing gum for xerostomia but the effect values for UWS remained unchanged (Supplementary Table S9). When sensitivity analysis was performed by excluding studies using placebo as a control group, we found no difference in the effect sizes for both xerostomia and UWS (Supplementary Table S10).

Table 1: Characteristics of the studies included in the network meta-analysis.

Intervention types	Study author (year)	Country	Study design	Population	Sample size, *n*	Age (years), mean ± SD	Time on dialysis (months), mean ± SD	Frequency and duration of intervention	Intervention methods	Outcome measures	
										Xerostomia	UWS
Acupressure auricular	Jung and Chang, 2020 [25]	South Korea	RCT	HD patients	IG: 26 CG: 27	IG: 67.30 ± 10.60 CG: 61.50 ± 1.31	IG: 61.04 ± 63.36 CG: 72.15 ± 48.94	4 weeks	IG: auricular acupressure CG: placebo	VAS	Absorbed in oral cotton (ml/min)
	Keskin and Tasci, 2021 [26]	Turkey	RCT	HD patients	IG: 30 CG: 30	NR	NR	6 weeks, three times a week, 15 min each time	IG: auricular acupressure CG: placebo	NR	Collected using the spitting technique (ml)
Licorice mouthwash	Khatab, 2019 [27]	Egypt	RCT	HD patients	IG: 22 CG: 22	IG: 51.5 ± 10.6 CG: 54.4 ± 10.5	NR	5 days, three times per day after each meal	IG: licorice mouthwash CG: usual care	Xerostomia inventory	NR
Gargling aroma solution	Oh and Cho, 2019 [28]	South Korea	RCT	HD patients	IG: 28 CG: 28	IG: 61.96 ± 8.84 CG: 56.82 ± 12.24	NR	15 sec	IG: gargling aroma solution CG: usual care	VAS	NR
Chewing sugar-free gum	Ozen *et al.*, 2021 [29]	Turkey	RCT	HD patients	IG: 22 CG: 22	IG: 61.72 ± 15.21 CG: 61.40 ± 16.64	IG: 42.00 CG: 48.00	3 months, 10 min six times a day	IG: chewing sugar-free gum CG: usual care	VAS	Collected using the spitting technique (ml/min)
	Said and Mohammed, 2013 [30]	Egypt	RCT	HD patients	IG: 30 CG: 30	NR	NR	2 weeks, six times a day, each time >10 min	IG: chewing sugar-free gum CG: usual care	Xerostomia inventory	Collected using the spitting technique (ml)
	Duruk and Eşer, 2016 [31]	Turkey	RCT (crossover)	HD patients	IG: 61 CG: 61	NR	NR	1 day, four times a day, each time 15 min	IG: chewing sugar-free gum CG: usual care	VAS	Collected using the spitting technique (ml/min)
PBMT	Pavesi *et al.*, 2021 [32]	Brazil	RCT	HD patients	IG: 21 CG: 17	IG: 44.2 CG: 47.0	IG: 139.56 CG: 120.6	14 days, three sessions	IG: PBMT CG: placebo	NR	Collected using the spitting technique (ml/min)
TENS	Yang *et al.*, 2019 [33]	Taiwan	RCT	HD patients	IG: 40 CG: 40	IG: 57.8 ± 13.8 CG: 57.6 ± 11.9	IG: 69.6 ± 68.7 CG: 100.8 ± 60.4	3 weeks, three times a week	IG: TENS CG: placebo	10-point scale for dry mouth intensity	Absorbed in oral cotton (ml/min)
Multi-arm trials	Mansouri *et al.*, 2018 [34]	Iran	RCT	HD patients	IG: 20 CG1: 20 CG2: 20	IG: 52.17 CG1: 51.93 CG2: 53.07	NR	1 week, at the time of dry mouth	IG: chewing sugarless gum CG1: sucking sugarless candy CG2: usual care	Xerostomia index	NR
	Yu *et al.*, 2016 [35]	Taiwan	RCT	HD patients	IG: 41 CG1: 44 CG2: 37	IG: 65.5 ± 13.1 CG1: 59.3 ± 11.5 CG2: 57.3 ± 12.2	NR	10 days, 30–60 min after each meal	IG: pure water mouthwash CG1: licorice mouthwash CG2: usual care	Summed xerostomia inventory	Collected using the spitting technique (ml/min)

IG: intervention group; CG: control group; SD: standard deviation; NR: not reported.

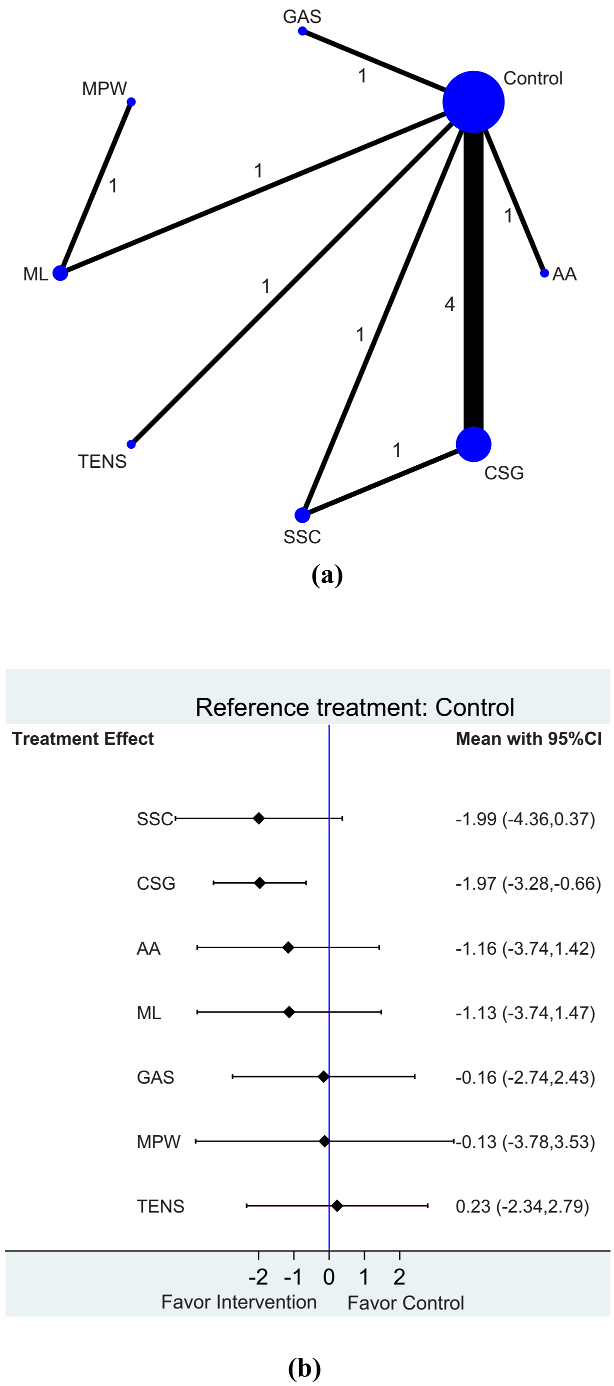


Figure 2: (a) Network map and (b) forest plot of analysis results for xerostomia. AA: auricular acupressure; CSG: chewing sugarless gum; GAS: gargling aroma solution; ML; mouthwash licorice; MPW: mouthwash pure water; SSC: sucking sugarless candy; TENS: transcutaneous electrical nerve stimulation.

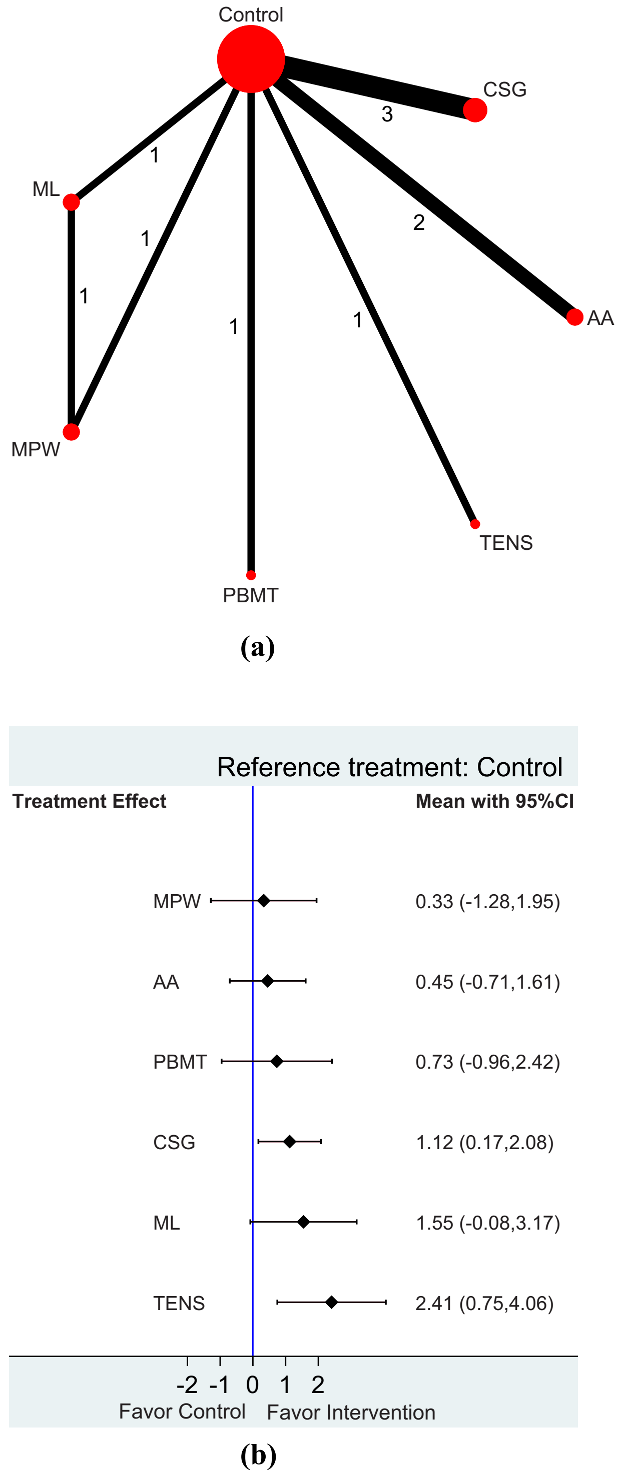


Figure 3: Network map (a) and forest plot of analysis results (b) for salivary flow rate. Abbreviations: AA: Acupressure auricular; CSG: Chewing sugarless gum; ML; Mouthwash licorice; MPW: Mouthwash pure water; PBMT: Photobiomodulation; TENS: Transcutaneous electrical nerve stimulation.

Adverse event data analysis

None of the studies reported any adverse outcomes related to the non-pharmacological interventions.

DISCUSSION

Patients undergoing dialysis frequently exhibit diminished saliva production and changes in its composition, which leads to xerostomia. This network meta-analysis compared eight different non-pharmacological interventions with effects on salivary glands and the symptoms of xerostomia. The findings demonstrated that sugarless chewing gum and TENS were the top-ranked interventions for relieving xerostomia and improving saliva flow rate, respectively, among dialysis patients. Sugarless chewing gum is a simple yet effective approach that may provide patients with a convenient means of managing dry mouth symptoms.

Dry mouth creates oral problems such as tooth decay, bad breath and gum disease [36], resulting in sores, difficulty in chewing, altered taste perception and oral infections [37]. Timely dry mouth intervention is crucial, not just for oral health, but also for overall quality of life [38]. The considerable effect sizes associated with the interventions reviewed in this network meta-analysis hold promise as viable options for improving the quality of life for patients affected by xerostomia in the context of haemodialysis (HD) treatment. Nevertheless, healthcare professionals need to tailor these interventions to individual patient needs and preferences to maximize their effectiveness.

An overview of the literature identified two relevant published systematic reviews using simple pairwise meta-analyses that evaluated the effect of auricular acupressure and chewing sugar-free gum on dry mouth in HD patients. The first systematic review includes three RCTs of the effects of auricular acupressure [13], indicating the superiority of the intervention over controls. However, the evidence obtained from this review is limited, as among the three papers only one [25] evaluated the effect of an intervention on xerostomia and the other two focused on thirst symptoms. Although our network meta-analysis showed a non-significant effect of auricular acupressure on xerostomia, this type of analysis includes more data to incorporate direct and indirect evidence and could be interpreted as being as valid as pairwise meta-analysis if there is no imbalance in the effect modifiers (trial and patient characteristics associated with intervention effects) across different types of direct comparisons [39]. The second published meta-analysis [12] included five clinical trials for the effect of sugar-free gum on xerostomia. The results reported in this review are consistent with our network meta-analysis, showing a significant effect of chewing sugar-free gum in reducing xerostomia symptoms.

Currently there are no international guidelines to manage xerostomia in CKD patients, but several local procedures exist within Australia and the UK, each with different recommendations [40, 41]. In this study, we found a number of non-pharmacological interventions available for mitigating xerostomia symptoms in HD patients. Each of these approaches may offer distinct advantages, ranging from the use of remedies to stimulate saliva production to behavioural interventions with mechanical stimulation effects like sucking candy or chewing gum. The outcome of this network meta-analysis provides comprehensive, evidence-based interventions to effectively address xerostomia and should assist in developing a standardized approach in this patient population.

A strength of this study was the incorporation of publications in various English-language databases, which contributes to the overall robustness of the inclusion criteria and increases the generalizability of the findings. Notwithstanding the variations among the studies, synthesizing the results across different interventions and their varying outcomes has provided valuable insights for healthcare practitioners and researchers seeking to understand the differential effects of non-pharmacological interventions on xerostomia in patients receiving dialysis. Despite the benefits of the interventions, certain limitations should be acknowledged. First, it should be noted that the evidence is based on single trials with a small sample size, hence further research and clinical validation are also crucial to solidify these findings and refine treatment recommendations. Although the review encompassed a significant number of studies, there are still constraints in the available evidence for specific comparisons. Second, the studies were included despite their methodological weaknesses due to the paucity of research in this field. Despite the moderate to high methodological quality of the included studies as measured by the JBI instrument, the majority lacked clarity or failed to conceal random allocation or blind participants and outcome assessors. Based on the GRADE approach, this resulted in downgrading the quality of evidence for most comparisons. Discrepancies in how primary studies reported their methods and outcomes could impact the assumption of transitivity. Nonetheless, due to factors such as missing data and limitations in subgroup analyses, certain levels of uncertainty persist. Third, moderate to substantial heterogeneity was observed between studies. Consequently, it is imperative to exercise caution in interpreting the results, as uncontrolled or unmeasured factors could potentially produce bias. The majority of interventions had a low to very low confidence of evidence; the only ones with moderate evidence were chewing sugarless gum (for both outcomes) and auricular acupressure (for xerostomia). Finally, many of the included trials were conducted in developing countries. This could be because low-income countries often face significant health disparities and a higher burden of disease. Therefore, researchers are motivated to study these areas to address pressing health concerns and contribute to improving healthcare and quality of life among people in these regions. Future studies should evaluate the cost:benefit ratio of the products as well as explore the usability and acceptability perceived by patients receiving dialysis, representing an important first step in addressing health disparities.

In conclusion, our study offers a comprehensive assessment of interventions to address xerostomia in dialysis patients. The review compared the effect of eight non-pharmacological interventions on xerostomia and saliva flow rate in dialysis patients. Sugarless chewing gum and TENS were the top-ranked interventions for alleviating xerostomia and improving saliva flow rate, respectively. The results emphasize the effectiveness and safety of different non-pharmacological strategies, offering valuable guidance for clinical applications and shaping the course of future research priorities.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

Amir Masoud Sharifnia: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Visualization, Supervision; **Ginger Chu:** Investigation, Resources; **Xiaoming Zhang:** Formal analysis; **Heidi Green:** Resources; **Ritin Fernandez:** Investigation, Methodology, Project administration, Supervision. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

DATA AVAILABILITY STATEMENT

All data that support the findings appear in the article.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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