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Therapeutic Effects of Photobiomodulation and Electrical Stimulation on Xerostomia: A Recent Evidence-Based Review

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ABSTRACT

Objective: This study compared and analyzed the effectiveness of recent interventions for xerostomia, including photobiomodulation (PBM), electrical stimulation, and pharmacotherapy.

Methods: A systematic review of clinical trials and randomized controlled trials (RCTs) published between 2023 and 2025 was conducted, summarizing protocols (wavelength, session number, treatment duration) and clinical outcomes (symptom improvement rate, changes in salivary flow).

Results: PBM and electrical stimulation were highly safe and demonstrated significant improvements in salivary flow and symptom relief, whereas pharmacotherapy showed the greatest overall improvement. These findings provide a foundation for patient-tailored treatment strategies.

Conclusion: Etiology-specific customization and multimodal combination therapy are key, with protocol standardization and accumulation of long-term evidence critical for clinical guideline advancement.

Keywords: Xerostomia; Photobiomodulation; Electrical stimulation; Salivary secretion; Clinical intervention

INTRODUCTION

Xerostomia, defined as reduced salivary secretion (hyposalivation) or subjective oral dryness, frequently occurs with aging, anticholinergic medication use, systemic diseases (especially Sjögren's syndrome), and post-radiotherapy for head and neck cancer. It negatively impacts quality of life (QoL), causes oral pain, dysphagia, speech impairment, increased caries risk, denture retention issues, and heightened susceptibility to oral infections (e.g., candidiasis), thereby affecting systemic health. Despite its clinical importance, "fundamental recovery" remains challenging. Current treatments are stratified into salivary stimulation (muscarinic agonists, electrical/acupuncture therapy, PBM), replacement (saliva substitutes, moisturizers), etiology-targeted therapy (immunomodulation, radiation complication management), and regenerative medicine (gene and cell therapy).

In the last 2–3 years, clinical evidence has rapidly accumulated, particularly for post-radiation xerostomia (RIX), supporting acupuncture, PBM, and salivary/nerve electrical stimulation. A 2024 JAMA Network Open RCT showed that acupuncture significantly improved oral dryness and QoL compared to standard oral care in RIX patients,

highlighting the need for treatment standardization [1]. PBM studies from 2024-2025 demonstrated increased stimulated salivary flow, decreased subjective dryness, and preventive effects, although protocols (wavelength, energy density) varied [2]. Electrical stimulation, delivered via transcutaneous TENS or intraoral microelectrodes (lingual nerve/salivary gland neurostimulation), showed potential benefits in both post-radiation and Sjögren's patients [3].

Pharmacotherapy remains first-line, with muscarinic agonists (pilocarpine, cevimeline) confirmed effective in meta-analyses [4,5]. Topical stimulants such as 1% malic acid spray showed significant salivary increases and symptom relief in RCTs and meta-analyses, offering alternatives for elderly polypharmacy or contraindicated patients [6]. Manuka honey mouth rinses in 2025 suggested moisturizing and anti-inflammatory benefits in elderly patients [6].

Procedural approaches, including sialendoscopy and intraductal steroid injections, improved salivary flow and symptoms in Sjögren's or chronic sialadenitis, with effects reported for up to 60 weeks [7]. In regenerative medicine, AAV2-hAQP1 gene therapy (MeiraGTX AAV-AQP1) targeting damaged salivary duct water channels is in phase II trials for moderate-to-severe post-radiation xerostomia, with ongoing long-term follow-up, representing an innovative strategy targeting core pathophysiology [13].

Recent trends emphasize (i) multimodal, non-pharmacologic combinations, (ii) standardized protocols, (iii) etiology-specific customization (post-radiation vs. Sjögren vs. drug-induced), and (iv) clinical translation of regenerative medicine. This review integrates RCTs, systematic reviews/meta-analyses, and trial registries (2023–2025) to propose practical recommendations for domestic clinical application.

METHODS

This rapid, scalable review systematically collected and synthesized recent evidence on xerostomia treatment. Searches were conducted in PubMed/MEDLINE, Scopus, Cochrane Library, JAMA Network, ScienceDirect, SpringerLink, and ClinicalTrials.gov for publications from January 1, 2023, to August 20, 2025. Keywords included: "xerostomia," "dry mouth," "radiation-induced xerostomia," "Sjögren," "photobiomodulation OR low-level laser," "acupuncture," "electrostimulation OR TENS OR neurostimulation," "malic acid spray," "honey mouth rinse," "cevimeline," "pilocarpine," "sialendoscopy," "AAV2-hAQP1 OR AQP1 gene therapy."

Included studies: RCTs, prospective cohorts, meta-analyses/systematic reviews, and ongoing registered trials; single-case or retrospective studies were supplementary. Exclusion criteria: (1) xerostomia as a secondary outcome, (2) duplicate reports, (3) non-dental primary targets (ophthalmology, non-salivary organs), (4) pre-2022 reviews without updates. Two reviewers independently screened titles/abstracts and assessed full texts. Primary and secondary outcomes extracted: (a) subjective dryness (questionnaires/visual analog scale), (b) unstimulated/stimulated salivary flow, (c) oral QoL (OHIP-14), (d) safety (adverse events/withdrawals), (e) durability (follow-up duration). Interventions were categorized as (i) pharmacologic (muscarinic agonists, topical stimulants), (ii) physical/procedural (PBM, acupuncture, electrical stimulation, sialendoscopy), (iii) regenerative medicine (gene therapy). High heterogeneity led to narrative synthesis; RCTs and meta-analyses were summarized qualitatively with effect direction (increase/decrease). Trial registry data described design, population, endpoints, and status. Core literature prioritized: 2024 JAMA acupuncture RCT, 2024–2025 PBM clinical studies/reviews, 2023–2025 electrical stimulation studies,

malic acid spray meta-analysis, 2025 Manuka honey RCT, 2021–2025 sialendoscopy RCT/review, AAV2-hAQP1 phase II/long-term follow-up [13,14].

Results

3.1 Acupuncture:The 2024 JAMA Network Open RCT demonstrated significant improvement in oral dryness and overall QoL in post-radiation chronic xerostomia patients with minimal adverse effects. Short-term intensive sessions (1–2/week) followed by maintenance are suggested [1].

3.2 Photobiomodulation (PBM/LLLT):2024–2025 studies showed PBM increased stimulated salivary flow, reduced subjective dryness, and improved QoL during and after radiation. Protocol standardization (wavelength 650–980 nm, energy 2–8 J/cm², major salivary gland targeting) remains necessary [2].

3.3 Electrical Stimulation (TENS/intraoral neurostimulation):Multi-center RCTs and prospective studies demonstrated increased natural salivary flow and symptom relief in post-radiation and Sjögren's patients. Recent 2025 studies confirmed safety and efficacy, though optimal parameters and long-term durability are still under investigation [3-5].

3.4 Pharmacotherapy:Cevimeline/pilocarpine and topical malic acid sprays were effective in symptom reduction and salivary flow increase. Cholinergic side effects require monitoring. 1% malic acid spray is useful for short-term symptom relief in elderly or polypharmacy patients [5].

3.5 Natural/Adjunct Therapies:2025 RCT in elderly patients showed Manuka honey rinses reduced dryness; plant-based interventions may also increase salivary flow, though standardization is needed [6,7].

3.6 Sialendoscopy and Intraductal Steroids:In Sjögren's/chronic sialadenitis patients, sialendoscopy maintained salivary flow and reduced dryness for over one year, with procedural skill and re-stenosis management being critical [7].

3.7 Gene Therapy (AAV2-hAQP1):Phase II and long-term studies in moderate-to-severe post-radiation xerostomia are ongoing, with potential to shift paradigms by restoring ductal water transport [13].

DISCUSSION

Recent evidence supports etiology-specific, multimodal approaches. In post-radiation xerostomia (RIX), acupuncture, PBM, and electrical stimulation provide first-line adjunctive strategies with minimal pharmacologic burden. PBM and acupuncture showed clear symptom improvement, while electrical stimulation offers potential for home-based management [1].

In Sjögren's/chronic sialadenitis, sialendoscopy with intraductal steroids addresses structural and inflammatory pathophysiology, supported by 60-week RCT follow-up. Standardization and patient selection (duct preservation, fibrosis stage) remain key [7].

Pharmacotherapy remains central, but systemic side effects limit use. Topical 1% malic acid provides short-term symptom relief as a low-burden adjunct, with fluoride application and usage guidance mitigating enamel risk [12]. Natural products (Manuka honey) show promise but require further high-quality RCTs for recommendation upgrades [10-12].

Gene therapy (AAV2-hAQP1) targets the core pathophysiologic bottleneck of salivary duct water transport. Positive long-term results could complement or replace symptom-focused treatments, though cost, infrastructure, immune response, repeat dosing, and insurance coverage remain practical considerations [13,14].

Proposed Clinical Algorithm:Etiology assessment: medication history (anticholinergics), systemic disease (Sjögren), radiation, oral hygiene/denture status. Supportive care: hydration, humidification, sugar-free stimulants, fluoride management. Pharmacologic: muscarinic agonists (check contraindications) ± 1% malic acid short-term. Non-pharmacologic multimodal: for RIX, combine standardized PBM + acupuncture + electrical stimulation based on patient preference/accessibility. Structural intervention: sialendoscopy ± steroid irrigation for Sjögren/chronic sialadenitis. Regenerative medicine: offer clinical trial enrollment (AAV2-hAQP1). Monitoring: unstimulated/stimulated salivary flow, OHIP-14, oral environment (caries/candidiasis), adverse effects, follow-up 3–12 months. Limitations:Small RCT sample sizes, heterogeneous protocols (acupuncture points/frequency, PBM parameters, electrical stimulation settings), mixed outcome measures, difficulty in blinding device-based interventions, variability in natural product formulation and quality. Future research should include (i) stratified randomization by etiology, (ii) standardized protocols and core outcome sets, (iii) ≥12-month follow-up, (iv) cost-effectiveness analysis, and (v) synergistic evaluation of multimodal therapy.

CONCLUSION

Recent xerostomia management has expanded to pharmacologic (cevimeline/malic acid), non-pharmacologic (PBM, acupuncture, electrical stimulation), procedural (sialendoscopy), and regenerative (AAV2-hAQP1) strategies. Etiology-specific customization and multimodal combination are essential, while protocol standardization and long-term evidence accumulation are critical for clinical guideline advancement.

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