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NEEDLE-FREE HOPE: IONTOPHORESIS FOR BETTER QUALITY OF LIFE IN ORAL SUBMUCOUS FIBROSIS

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ABSTRACT

Background: Oral submucous fibrosis (OSMF) is a progressive, potentially malignant condition of the oral mucosa, linked chiefly to areca nut chewing and frequently to tobacco as well. Patients live with burning, mucosal stiffness and a mouth that opens a little less each year, and these changes touch eating, speech, social life and peace of mind. Medical management still leans heavily on intralesional injections given over many visits; they hurt, they work slowly, and a good number of patients give up before the course ends. Iontophoresis, in which a weak electric current carries a charged drug into tissue, offers a way of giving the same medicines without a needle. **Aim:** To trace how OSMF develops, describe what it does to a patient's quality of life (QoL), examine how conventional treatment adds to that burden, and judge whether iontophoresis can reasonably be expected to make patients' lives better. **Methods:** Narrative review of peer-reviewed literature on OSMF, quality of life, conventional treatment and iontophoretic drug delivery. **Results:** OHIP-14 scores in OSMF are close to five times those of healthy controls and worsen with stage. Fear of cancer, anxiety and depression are frequent. A course of injections can mean anywhere

from 6 to 26 visits, and in routine practice the gain in mouth opening is often small, with roughly a third of patients not completing treatment. Only two studies of iontophoresis in OSMF have been published. Both were carried out on animal tissue in the laboratory and recorded a 6.5- to 13-fold rise in mucosal drug uptake after 5 to 10 minutes of current. **Conclusion:** The main appeal of iontophoresis lies in easing the burden of treatment, a problem that has received little attention in OSMF care. Whether it actually improves patients' quality of life remains untested in humans, and trials that place QoL at the centre are required.

KEYWORDS: Oral submucous fibrosis; Quality of life; OHIP-14; Iontophoresis; Dexamethasone; Intralesional injection; Patient-reported outcomes.

1. INTRODUCTION

OSMF appears on the WHO Collaborating Centre for Oral Cancer list of oral potentially malignant disorders.[1] Its symptoms intrude heavily on daily living, and published estimates of malignant change vary from 1.5% to 15%.[2] Most oral medicine clinics in India will recognise the typical presentation: a young adult who has chewed areca nut, gutkha or mawa for years and now finds spicy food unbearable, struggles to bite an apple and can open the mouth only two or three fingers wide.

We, as clinicians, tend to record progress in millimetres. Our patients look at it differently. What they want is to sit down to a meal with the family, to stop worrying that a sore patch is turning into cancer, and to stop taking days off work for hospital visits. Intralesional corticosteroid, with or without hyaluronidase, is still the commonest medical treatment, and it involves a long series of injections. Many patients find these painful, lose patience when change comes slowly, and quietly stop coming.

Iontophoresis has been put forward as a way to deliver the same drugs without a needle. In this review we follow the patient from the first chew of areca nut, through the disease and its effect on everyday life, to the treatment chair. We then return to a plain question: if iontophoresis is adopted, are patients' lives genuinely better for it? Figure 1 outlines the journey.

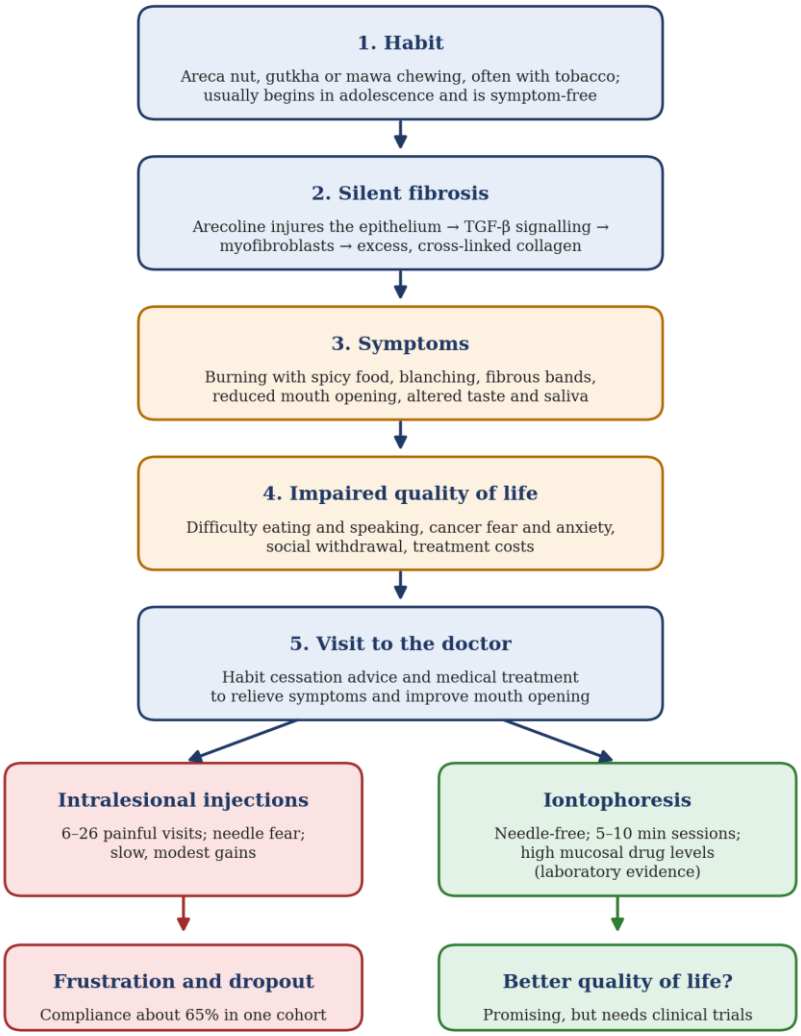


Figure 1: The OSMF patient journey: from habit to disease, impaired quality of life and the two treatment paths.

Flowchart prepared by the authors from the literature reviewed.

2. METHODOLOGY

Literature was identified by combining the terms "oral submucous fibrosis", "quality of life", "OHIP-14", "anxiety", "intralesional", "dexamethasone", "hyaluronidase" and "iontophoresis" with Boolean operators. Systematic reviews, meta-analyses, randomised trials, QoL surveys and laboratory work on mucosal drug delivery were considered. Only peer-reviewed articles from indexed journals were retained, and the citation details of each were verified; conference abstracts, theses and preprints were left out.

One finding stood out early: only two published studies have examined iontophoresis in OSMF, and both were laboratory studies.[3,4]

3. History: How Oral Submucous Fibrosis Develops

3.1 Burden of the disease

Roughly 600 million people chew areca nut, and about one in twenty of them goes on to develop OSMF.[5] In India the reported prevalence lies between 0.62% and 6.42%, parts of Taiwan report figures as high as 17.6%, and the worldwide total is thought to exceed five million.[6] Men are affected more often than women.[6]

3.2 Areca nut and tobacco

Patients often call OSMF a "tobacco disease". That is only partly right, because the principal culprit is areca nut. The International Agency for Research on Cancer regards the long-term chemical and mechanical irritation produced by chewing it as a major cause of the condition.[5] Tobacco makes matters worse. Areca nut, smokeless tobacco and cigarette smoke all damage the oral epithelium and, at the same time, push fibroblasts to lay down more matrix.[7] Gutkha and mawa deliver both insults together. In one Nepalese cohort, 45% of patients used such a product, typically seven or eight times a day for about a decade, and those who chewed more often reported poorer quality of life.[8]

3.3 How the habit becomes fibrosis

For years the process causes no symptoms. It begins in the epithelium, where arecoline, the main alkaloid in areca nut, thins the lining and drives cells into senescence and death;[7] at higher concentrations it also generates reactive oxygen species and damages DNA.[6] The injured epithelial cells then send transforming growth factor-β (TGF-β) signals to the fibroblasts lying beneath them.[7] Under this stimulus fibroblasts change into contractile myofibroblasts, which produce TGF-β1 together with CCN2, a mediator that has been tied to malignant progression.[5] Collagen synthesis rises while its breakdown slows, and extra cross-linking leaves the new tissue tough and hard to remodel.[6,7]

Over time the soft, pliable lamina propria gives way to dense, poorly perfused fibrous bands. This is worth keeping in mind for what follows, since the lamina propria is exactly where any drug has to arrive if it is to do some good.

3.4 Symptoms and risk of cancer

Most patients first notice a burning feeling when they eat spicy food. Later the mucosa turns pale, firm bands can be felt in the cheeks, and the mouth opens less and less, so that chewing, talking, swallowing and even brushing become an effort. Saliva and taste change as well:

salivary flow drops in advanced disease, salivary pH shifts, and sweet, salty and sour tastes may be dulled or distorted.[9] A meta-analysis put the overall rate of malignant transformation at 6%, and at 8% for Indian cohorts.[10]

4. Quality of Life of Patients Living with OSMF

4.1 Physical and functional impact

When 115 men with OSMF were compared with 115 healthy men, their mean OHIP-14 scores were 19.10 and 3.98 respectively. Patients scored worse in all seven domains, every one of them reported at least one negative effect, and those with stage 4 disease fared worst.[11] Put simply, the oral health burden carried by these patients was nearly five times that of healthy men of the same age. A study of 120 patients published in 2025 found the same pattern, with quality of life falling as mouth opening became more restricted.[12]

4.2 Psychological impact

Hearing the word "precancerous" is frightening for anyone. In a Nagpur study every patient showed some level of cancer phobia and anxiety, 65% had severe scores, and scores rose with the grade of disease; women, homemakers and patients with less schooling were hit hardest.[13] Anxiety and depression in OSMF have also been linked with raised serum cortisol, and the investigators advised that psychological assessment should become part of routine care.[14]

Treatment does not lift this weight evenly. Among 130 patients given intralesional injections, OHIP-14 scores improved at six months in every domain but one, and the exception was psychological disability.[15] Gaining a few millimetres of mouth opening, it seems, does not by itself give patients back their sense of well-being.

4.3 Social and financial impact

In India, food is closely bound up with family and community life. A patient who has to skip most dishes, or cut everything into tiny pieces, misses out on far more than nutrition, and the social domains of OHIP-14 reflect this.[11] Treatment is costly too. Drawing on 72 studies, one analysis calculated a median cost of INR 1,906 for each millimetre of mouth opening gained.[16] Daily-wage earners must add bus fares and lost wages for every visit.

4.4 Measuring quality of life

OHIP-14 is the instrument most commonly used in OSMF research and has proved reliable, with a Cronbach's alpha of 0.90.[8] It was not built, however, to capture fear of cancer or the strain of repeated injections. The first core outcome set for OSMF trials (OSFCOS) appeared in 2026. Patient interviews and focus groups generated 31 candidate outcomes, whereas a review of published trials yielded only 20,[17] a reminder of how much of the patient's experience earlier studies overlooked.

Table 1: Evidence on quality of life in OSMF.

Study	Design and sample	Main finding
Jena et al., 2018[11]	Cross-sectional; 115 patients vs 115 controls	OHIP-14: 19.10 vs 3.98; all domains worse; stage 4 worst
Shriram et al., 2025[12]	Cross-sectional; 120 patients	Poorer OHIP-14 with more restricted mouth opening
Mody et al., 2025[9]	Case-control; 80 subjects	Lower salivary flow, altered pH, taste disturbance
Kalaskar et al., 2025[13]	Cross-sectional; Nagpur	Cancer phobia in all patients; 65% severe
Manshi et al., 2023[14]	90 subjects	Anxiety and depression correlated with serum cortisol
Memon et al., 2022[15]	Randomised; 130 patients	All OHIP-14 domains improved except psychological disability
Rimal & Shrestha, 2015[8]	74 patients	Median OHIP-14 fell from 18 to 5 after treatment

5. When the Patient Visits the Doctor: Conventional Treatment and Its Burden

5.1 Current treatment

Giving up the habit comes first. Medical treatment usually follows in the form of intralesional corticosteroid, most often dexamethasone, frequently mixed with hyaluronidase. The steroid damps down inflammation and fibroblast activity, while hyaluronidase loosens the ground substance so the drug can spread. Several studies report benefit. Monthly methylprednisolone for six months improved mouth opening over a year of follow-up;[18] dexamethasone with hyaluronidase produced an average gain of 6 ± 2 mm in grade III disease;[19] hyaluronidase brought the fastest relief in a double-blind comparison;[20] and twelve weekly injections of placental extract, hyaluronidase and dexamethasone together added 7.30 mm.[21]

Taken as a whole, though, the evidence is thin. A Cochrane review could include only two trials and considered their data unreliable.[22] A systematic review counted 27 reported treatments but only four randomised trials among them,[23] and a network meta-analysis

covering 3,850 patients concluded in 2025 that no class of non-surgical therapy clearly outperformed the rest, placebo included.[24]

5.2 Why patients become frustrated

Trial results do not always carry over into ordinary clinics. In a 2026 series of 54 patients treated with six injections of triamcinolone and hyaluronidase, mouth opening rose by a mean of only 2.2 mm, just 11% of patients improved by 5 mm or more, quality of life did not change significantly, and compliance stood at 65%.[25] Most clinicians will know this story well. Patients arrive hopeful, find the injections painful, see little change from week to week, grow irritated and eventually drop out.

Part of the reason is the sheer number of visits, which ranges from 6 to 26 per course in published regimens.[18,21,25,26] Pain and fear add to it, as the needle goes repeatedly into tissue that is already sore, and between 20% and 30% of young adults are afraid of needles to the point that some avoid treatment altogether.[27] The slow pace of improvement then means that discomfort is felt for weeks before any real benefit shows.[25]

Not surprisingly, needle-free options have drawn attention. In one randomised study, curcumin used as a topical gel or a mucoadhesive patch improved mouth opening by 5.45 to 5.9 mm with no injections at all.[28] Topical treatments do face practical hurdles, however: they do not stay on the mucosa for long, they penetrate the lining poorly and saliva washes them away.[29] Iontophoresis is aimed squarely at the second of these problems.

6. Iontophoresis: A Needle-Free Way to Deliver Drugs

6.1 How it works

In iontophoresis, a low, carefully controlled current pushes charged drug molecules into tissue. A negatively charged drug such as dexamethasone sodium phosphate sits under the negative electrode, or cathode, and is repelled into the mucosa because like charges push apart. Depending on the drug and the conditions, this can raise delivery anywhere from 10 to 2,000 times over simple topical application.[30,31] The technique suits drugs that dissolve in water and ionise readily, and steroids are among the agents studied most often.[30,31]

6.2 Why dexamethasone is suitable

Dexamethasone sodium phosphate is negatively charged and is converted into active dexamethasone once inside the tissue. In laboratory and animal experiments, most of the compound stayed intact in tissue for several hours, the amount delivered rose in step with the

applied current, and the presence of competing chloride ions cut delivery roughly in half.[32] That last observation matters for the mouth, because saliva contains chloride. Any intraoral device will therefore need to keep the drug reservoir sealed off from saliva.

6.3 Use in the oral cavity

A review of iontophoresis in the mouth reported that drug transport across the buccal mucosa was consistently better than with passive application, and that animal and human studies had not raised safety concerns under the conditions tested.[33] Dental uses so far include local anaesthesia and the treatment of tooth decalcification and hypersensitivity.[33] In one randomised trial, adding iontophoresis to desensitising pastes kept dentine hypersensitivity under control for as long as six months.[34]

6.4 Evidence in OSMF

Only two studies have looked at iontophoresis for OSMF, and both used pig mucosa in the laboratory. In the first, ten minutes of current delivered around 13 times more buflomedil, a drug with anti-fibrotic action, than passive application did, and levels in the lamina propria reached about 700 times the concentration needed to halt collagen production.[3] The second study gave dexamethasone and buflomedil together in a single session. Five minutes of current was enough to raise the uptake of each drug about 6.5-fold, which led the authors to suggest that the approach could make treatment of oral disease easier for patients.[4] No clinical study of iontophoresis in OSMF patients has been reported so far.

Table 2: Conventional injections compared with iontophoresis.

Feature	Intralesional injection	Iontophoresis
Needle	Yes, at every visit	No
Pain and fear	Common; needle fear in 20–30% of young adults[27]	Probably less (not yet measured in OSMF)
Visits and session time	Short sessions, but 6–26 visits per course[18,21,25,26]	5–10 minutes of current in laboratory work[3,4]
Drug reaching target tissue	Direct, though spread through fibrotic tissue may be patchy	High lamina propria levels in the laboratory[3]
Two drugs in one session	Possible as a mixed injection	Possible with paired electrodes[4]
Adherence in practice	About 65% in one cohort[25]	Not known
Evidence in OSMF	Clinical trials and cohorts	Laboratory studies only

7. Discussion: Are We Really Improving Patients' Lives?

What a treatment finally does for a patient depends on three things: how well the drug works, whether the patient sees the course through, and what the treatment itself costs in pain, fear, time and money. Injections perform reasonably in controlled trials,[18,21] but adherence in everyday practice is poor[25] and the burden placed on patients is considerable.[16,27] Iontophoresis brings no new drug to the table. Whatever value it has lies in the second and third of these factors, that is, in making treatment easier to bear so that more patients finish it.

The reasoning holds together, but it has not been put to the test, and several gaps remain. Both OSMF studies were done on healthy pig tissue,[3,4] and fibrosed human mucosa may take up drugs quite differently. Saliva dilutes anything placed on the mucosa and carries ions that compete with the drug.[29,32] Nobody has yet asked OSMF patients to compare the discomfort of an iontophoresis session with that of an injection. Electrodes must also fit inside a mouth that may open less than two centimetres, and the equipment has to be affordable for government clinics, where many of these patients are seen. Finally, no local treatment is likely to help for long if the patient keeps chewing.

Settling the question will need randomised trials comparing iontophoretic dexamethasone with standard intralesional injection. Quality of life (OHIP-14 or an OSMF-specific tool) and mouth opening should be primary outcomes, in keeping with the OSFCOS core outcome set.[17] Pain at each session, fear of cancer, number of visits, cost, completion rates and relapse at one year deserve recording too, and every participant should be offered help to quit.

Limitations of this review: Being narrative in design, the selection of studies involves a degree of judgement, and the data were not pooled. Only peer-reviewed articles from indexed journals were considered, so relevant work in non-indexed regional journals may have been missed.

8. CONCLUSION

For many patients, OSMF starts with a habit that seemed harmless and ends with a mouth that will not open, food that no longer tastes right and a constant worry about cancer. Quality of life suffers badly, and the psychological part of that burden responds poorly to the treatment we currently offer. Injections help in trials, yet in day-to-day practice the gains are modest, the demands on patients are heavy and a sizeable share never finish the course.

Iontophoresis speaks directly to this problem. It needs no needle, takes minutes, and in the laboratory delivers drug to the target layer far better than a gel or ointment can. It has not, however, been tried in patients with OSMF. For now it is best seen as a promising option that could improve patients' lives, provided well-designed clinical trials bear that out.

DECLARATIONS

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