

# Lack of reliable evidence for oral submucous fibrosis treatments

## Abstracted from

**Fedorowicz Z, Chan Shih-Yen E, Dorri M, Nasser M, Newton T, Shi L.**

Interventions for the management of oral submucous fibrosis. *Cochrane Database Syst Rev* 2008; issue 4

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## What treatments are effective in managing restricted jaw opening or movement in people who have oral submucous fibrosis?

**Data Sources** Searches were made for relevant studies using the Cochrane Oral Health Group Trials Register, Cochrane Central Register of Controlled Trials, Medline, Embase and IndMED (bibliographic database of Indian biomedical journals). There were no language restrictions.

**Study selection** Randomised controlled trials were to be selected if they compared surgery, systemic or topical medicines, or other interventions, to manage the symptoms of oral submucous fibrosis (OSF).

**Data extraction and synthesis** Two authors independently assessed trial quality and extracted trial data. Disagreements were resolved by consultation with a third author. Attempts were made to contact study authors where necessary for clarification and for additional information. Because of limited poor quality data, only a descriptive summary of the results of the included trials was carried out.

**Results** Two trials, involving 87 participants, evaluated either lycopene in conjunction with intralesional injections of a steroid, and pentoxifylline in combination with mouth-stretching exercises and heat. There were no reports of toxicity to the interventions but some side-effects, which were mostly gastric irritation to pentoxifylline, were noted.

**Conclusions** The lack of reliable evidence for the effectiveness of any specific interventions for the management of OSF is illustrated by the paucity, and poor methodological quality, of trials retrieved for this review.

## Commentary

This article provides a basic review of OSF and focuses on nonsurgical management. OSF is an insidious disease affecting the oral cavity, pharynx and upper digestive tract. Its aetiology is directly linked to betel nut usage, which is common to the Indian subcontinent, Far East and Pacific Rim. Betel nut usage is thought to be the primary cause of the condition. OSF's morbidity and mortality is associated with significant masticatory dysfunction (trismus) and an increased risk of developing squamous cell carcinoma, with a malignant transformation rate of 7–30%.<sup>1,2</sup>

Indian studies indicate that over 5 million people in India suffer from OSF (0.5% of the population of India). It is estimated that, in addition, up to 20% of the world's population use betel nut in some form, so the incidence of OSF is probably higher than

figures in the published literature suggest. Currently, OSF is considered a public health issue in the Indian subcontinent, UK and South Africa.<sup>3</sup> With the migration of peoples of the Indian subcontinent to all corners of the world, the general practitioner will certainly encounter this disorder at some point of their career.

OSF is thought to be a disease of collagen metabolism secondary to betel nut usage. Betel nut contains alkaloids, flavonoids and copper, all of which are thought to affect collagen synthesis and breakdown, so that there is a significant increase in collagen production and maintenance.

Treatment of OSF is a challenge, especially as the disease progresses. To aid in treatment planning, Khanna and Andrade developed a classification system of OSF based on interincisal opening (MIO), as follows.<sup>4</sup>

Group 1. Early OSF without trismus (MIO >35 mm).

Group 2. Mild to moderate disease (MIO 26–35 mm).

Group 3. Moderate to severe disease (MIO 15–26 mm).

Group 4a. Severe disease (MIO <15).

Group 4b. Extremely severe; malignant or premalignant lesions noted intra-orally.

Treatment is based on severity of disease. Typically, if the disease is noted prior to development of trismus, cessation of the betel habit will often resolve the disease. Once trismus has developed and disease is classified as mild to moderate, OSF is irreversible. Then, the goal of medical and surgical therapy is to maintain oral function and limit progression of disease. Treatment at this stage is focused on restoring mandibular range of motion, oral cancer surveillance, and cessation of betel nut habit. Physical therapy combined with medical treatment is often utilised.

In this review, Fedorowicz and colleagues did not identify any randomised controlled trials of surgical procedures, only two studies examining nonsurgical treatment of OSF. One study used lycopene in conjunction with intralesional injections of a steroid, and the other pentoxifylline in combination with mouth-stretching exercises and heat, and the review authors note that both trials provided unreliable results. The lack of good quality trials of medical and surgical procedures for OSF is disappointing but unsurprising given that the largest burden of this disease is found in under-resourced countries

OSF is associated with significant morbidity, with restricted mouth opening causing eating difficulties so a range of surgical modalities have been attempted, from moderately to significantly invasive. The most common initial surgical intervention includes release of

intra-oral fibrous bands, coronoidotomies, muscle of mastication myotomies, and soft tissue reconstruction with split thickness skin graft or allograft.<sup>5</sup> Aggressive physical therapy postsurgery is essential: without physical therapy compliance, the risk of recurrent trismus is possible. Patients should be aware that, although the trismus has resolved postsurgery, their OSF has not been cured. As such, continued physical therapy for the rest of their life is the best way to prevent recurrence of trismus. In addition, cessation of betel nut use is essential to minimise disease progression. Finally, oral cancer surveillance is necessary for the rest of the patient's life.

For cases in which initial surgical intervention is unsuccessful (recurrent trismus; usually secondary to lack of compliance with physical therapy), more aggressive surgical therapy is indicated. Again, excision of any fibrous bands intra-orally and repeated masticatory muscle myotomy is required. Often, in this situation, a larger soft tissue buccal defect is created, needing large soft tissue reconstruction. This can include a temporalis pedicled flap, pedicled superficial temporalis fascial flap or a radial forearm free flap combined with split thickness skin graft-coverage.<sup>6</sup>

The review found no reliable RCT evidence for medical or surgical interventions, surgical procedures have been used to relieve the

problems caused by restricted mouth opening but robust trials are required to identify the most effective treatment approaches to this debilitating condition.

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*Evidence-Based Dentistry* (2009) **10**, 8–9. doi:10.1038/sj.ebd.6400625