



## EFFICACY OF ISOXSUPRINE AS AN ADJUVANT IN MANAGEMENT OF OSMF: A RANDOMIZED CLINICAL TRIAL

### Oral Medicine & Radiology

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### ABSTRACT

**Introduction:** Oral submucous fibrosis is a persistent, insidious mucosal condition that is primarily brought on by areca nut use. It can also be brought on by excessive use of peppers, dietary deficiencies, autoimmune, genetics, and environmental factors. **Aim Of The Study:** The aim of the study was to evaluate the effectiveness of vasodilator isoxsuprine as an adjuvant in the oral submucous fibrosis management. **Study Design:** Twenty patients with OSMF were recruited and randomly two groups were divided. Group A: Patients got treated with Isoxsuprine hydrochloride 10 mg thrice daily and antioxidants (Lycopene) twice daily for 3 months. Whereas, in the Group B, antioxidants two times a day for 3 months were given. Both were instructed for mouth opening exercises. All individuals, mouth opening, burning sensation were recorded and reassessment was done at every 15 days during the treatment and after 3 months follow-up and followed by statistical analysis. **Results:** Visual Analogue Scale (VAS) score for severity of burning sensation was observed in both the groups A & B was statistically significant whereas interincisal opening was higher in group A patients. **Conclusion:** Isoxsuprine Hydrochloride can be suggested as an adjunctive therapy in oral submucous fibrosis management.

### KEYWORDS

oral submucous fibrosis, Isoxsuprine Hydrochloride, Lycopene

### INTRODUCTION

Oral submucous fibrosis is a persistent, insidious mucosal condition that is primarily associated with areca nut use. It can also be initiated by excessive use of peppers, dietary deficiencies, autoimmune, genetics, and environmental factors.<sup>1</sup> The history of a burning sensation, altered salivation, and clinically observable phenomenon of mucosal blanching with a marble-like appearance are its early-stage features. Later, the extent of mouth opening and tongue protrusion gradually decrease as the mucosa turns leathery and develops palpable fibrous bands. Towards lateral stages, it may be associated with gustatory dysfunction, speech and hearing impairments, and difficulty in swallowing.<sup>2</sup> Squamous cell carcinoma might result from oncogenic changes cases which are not treated or ignored.

The rate of malignant transformation of OSMF has been reported as between 7 and 12%.<sup>3</sup> Currently, almost 10–20% of the World's population consumes areca nut in a huge range of formulations. Prevalence in India was estimated to range from 0.2–2.3% in males & 1.2–4.6% in females.<sup>4</sup> It can be seen in any age but more commonly in young adults between 25 and 35 years. There have been numerous studies trying to evaluate various methods of OSMF treatment including intralesional steroids, antioxidants, surgical therapy, physiotherapy till date.<sup>5</sup> Yet, none have been successful in demonstrating the complete regression of the condition. Thus, the quest for an effective treatment modality with a better outcome continues.

Around 10–20% of people worldwide are presently using areca nut in many formulations like raw arecanut, arecanut scrapings, scented supari, flavored supari, gutka and pan masala. Male prevalence in India was estimated to be 0.2–2.3% and female prevalence of the same was assessed to be 1.2–4.6%.<sup>4</sup>

It is of paramount to conduct randomized trials aimed at the means of regulating this chronic progressive illness because of its precancerous condition, prevalence across a wide geographic area, and debilitating nature. Lycopene, a potent antioxidant generated from tomato extract,

It has been proven to be an efficient radical scavenger in many in-vivo and in-vitro studies. Its anti-oxidant qualities have been researched. for use in other health-related illnesses in addition to being utilized to treat OSMF.<sup>6</sup>

Isoxsuprine is an epinephrine phenylalanine derivative. It's a -adrenoreceptor agonist that raises cytosolic calcium levels generally, which in turn triggers endothelium-derived vasodilators production and release in large number. Isoxsuprine also lowers blood viscosity and prevents platelet aggregation. Based on these properties, a few research studies done to assess effectiveness of isoxsuprine as a therapeutic adjuvant of the management of OSMF.<sup>7</sup>

According to Chetan J. Bhadage et al., those patients who got treatment with isoxsuprine, a vasodilator, together with physical therapy had a better result in OSMF management regarding reducing the burning sensation and improving the mouth opening without observable adverse effects. This study's aim was to assess isoxsuprine's performance as an adjuvant in OSMF treatment.<sup>8</sup>

### MATERIALS AND METHODS:

The study was carried out in the department of oral medicine and radiology. Inclusion criteria considered were patients clinically diagnosed to have OSMF stages I or II. Based on their willingness to participate in the study and came for regular follow-up were informed of the study's procedure and patients' objectives and study protocol. Patients on alternative treatments for OSMF, stage III&IV OSMF patients, patients with oral carcinoma, pregnant women, people taking immunosuppressant medications, people who had difficulty opening their mouths for reasons other than OSMF, and people with fibrotic lesions other than OSMF were excluded. After discussing the study & treatment methods with every patient, informed consent was taken from each patient. A thorough case history was taken, which focused on adverse habits. Based on the criteria provided by Babu S et al., the final diagnosis of OSMF was made.<sup>9</sup>

Patients were assigned in two groups. Group A included 10 OSMF

patients those who were given Isoxsuprine hydrochloride 10 mg three times daily and antioxidants twice daily. for 3 months. Group B consists of 10 OSMF patients who got treated with same as the Group A patient's antioxidants twice daily for three months. For both the instructions for mouth physiotherapy exercises were given.

#### Drugs used:

1. Tab. Duvadilan 10 mg (isoxsuprine hydrochloride).
2. SM FIBRO TABLETS: Lycopene Antioxidant capsules: Twice per day for 3 months.

The following parameters were measured:

From the mesioincisal angle of the upper central incisor to the mesioincisal angle of the lower incisor, the interincisal mouth opening was measured with a vernier calliper in millimetres. The midline distance between the highest alveolar crest points on the maxilla and mandible was measured in the incisal region in patients who had missing central incisor. [Figure 1].



**Figure-1:** Interincisal mouth opening measurement with vernier caliper

With Visual analogue scale, the intensity of the burning sensation was assessed at the time of the visits (VAS). A 10 cm line with a zero cm line for "no burning sensation" and a ten cm line for "burning sensation as awful as it could be" was devised as the scale. The patients' burning sensation at the time of baseline treatment was measured on a VAS, and the number was recorded. At every appointment, patients' parameters were measured and documented. It was recorded based on the patient's response and checked on once every 15 days while undergoing treatment. All the clinical examinations were performed by single trained and calibrated examiner. Reassessment of all the participants was done after 3 months. statistical analysis was done on the collected data. at the conclusion of the study.

Data was collected and complied and enter into Microsoft excel, version 2013. Statistical analysis for the SPSS version 20 was used to analyse the data. To compare the results of the mouth opening and VAS score at various intervals in two groups Friedman test was used. Using the Mann Whitney U test, intergroup comparison were made. P value <0.05 were regarded as statistically significant.

#### RESULTS

Twenty participants, each group with 10 patients of which 6 males, 4 females in group A ;7 males, 3 females in group B with mean age of 35.28±5.93 and 36.7±6.92 respectively.

The mean values of burning sensation and mouth opening in group A and B before the treatment were 6.00±0.0, 26.85±4.01, and 7.00±1.3, 27.9±4.4 respectively. [Table-1,2]

Intragroup comparisons in Patients of both groups showed significant improvement in mouth opening and burning sensation from baseline treatment to the follow-up intervals (P<0.05). [FIGURE 2,3]



**Figure-2:** pretreatment photograph



**Figure-3:** post treatment photograph

**Table 1: comparison of mouth opening among Group A and B at various intervals**

| Groups                        | Baseline   | 1st       | 2nd       | 3rd      | 4th       | 5th       | Follo<br>w up | P<br>value |
|-------------------------------|------------|-----------|-----------|----------|-----------|-----------|---------------|------------|
| A                             | 26.85±4.01 | 27.2±4.15 | 27.7±4.06 | 28.7±4.7 | 29.2±4.52 | 29.7±4.41 | 29.0±4.4      | <0.001*    |
| B                             | 27.9±4.4   | 28.2±4.4  | 28.7±4.31 | 29±39    | 29.7±4.26 | 30.2±4.33 | 30.2±4.0      | <0.001*    |
| Intergro<br>up compari<br>son | 0.609      | 0.655     | 0.71      | 0.94     | 0.94      | 0.84      | 0.81          |            |

**Table 2: comparison of VAS scores among Group A and B at various intervals**

| Group<br>s | Baseline | 1st          | 2nd       | 3rd       | 4th       | 5th       | Follo<br>w up | P<br>value |
|------------|----------|--------------|-----------|-----------|-----------|-----------|---------------|------------|
| A          | 6.00±0.0 | 6.00±0.0     | 5.00±0.0  | 4.00±0.0  | 4.00±0.0  | 3.00±0.0  | 3.00±0.0      | <0.001*    |
| B          | 7.00±1.3 | 6.42±0.97    | 6.28±0.95 | 5.71±0.95 | 5.57±0.98 | 5.57±0.98 | 6.8±0.1       | <0.001*    |
|            | 0.05*    | 0.26(N<br>S) | 0.003*    | 0.003*    | 0.003*    | 0.001*    | 0.001*        |            |

On observing the intergroup comparisons, statistically significant difference in the P values between Group A compared with Group B at baseline to follow-up visit in burning sensation were found, whereas from baseline to follow up visit, mouth opening between the two groups, no statistical significance was observed.

#### DISCUSSION

OSMF is a chronic disease which mostly affects the soft palate, lips, retromolar regions, and buccal mucosa. The fibro-elastic change of the juxta-epithelial layer causes mucosal rigidity of varied intensity. This causes a limited opening of the mouth, and when the tongue is implicated, its protrusion may be compromised. Early lesions cause the buccal mucosa to blanch and appear marble-like, while later lesions present with palpable fibrous bands that cause the mucosa to become pale, thick, and stiff. Eventually, hearing loss result from the oropharyngeal involvement and involvement of eustachian tube. Prior to beginning any form of treatment, it is crucial to stop the areca nut and tobacco habits.<sup>15</sup>

When antioxidants combined with isoxsuprine was used, a maximum remission of burning sensation was achieved more quickly when compared with use of antioxidants as a stand-alone therapy. Increased fibrosis in the oral submucous with resultant obliteration of vascular lumen, lowers the vascularity and blood flow of the oropharyngeal region. Peripheral vasodilator is used to widen the capillaries so that the supply of necessary nutrients and antioxidants can be restored.

Earlier various vasodilators [pentoxifylline, nylidrin hydrochloride, buflomedical hydrochloride] have been studied with unsatisfactory results.<sup>10,11,12</sup> Of the various vasodilators, isoxsuprine seems to be both efficient and well tolerated with the current dosage.

The study was limited by the relatively small sample size. Generalisation of results of our study can be achieved multicentric trials using isoxsuprine in OSMF patients with a bigger sample size and longer periods of follow-up.

#### CONCLUSION:

There was no difference was seen significantly in the degree of improved mouth opening between the two groups. However, burning sensation was statistically reduced in the isoxsuprine group compared

to antioxidant group alone. Our study suggested that Isoxsuprine can be employed as an adjuvant therapeutic medication for the OSMF management.

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