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ORIGINAL RESEARCH

Effectiveness of Aloe Vera and Antioxidant along with Physiotherapy in the Management of Oral Submucous Fibrosis

[1]Nisha Singh, [2]Manjula Hebbale, [3]Amit Mhapuskar, [4]Shams Ul Nisa, [5]Shameeka Thopte, [6]Saumya Singh

ABSTRACT

Background: Oral submucous fibrosis (OSMF) is a well-established precancerous condition affecting the oral mucosa. It is a disease that causes significant morbidity (in terms of loss of mouth function as tissues become rigid and mouth opening becomes difficult) and mortality (when transformation into squamous cell carcinoma occurs).

Aim: The aim of the study is to compare the efficacy of Aloe vera with antioxidant when given along with physiotherapy in the management of OSMF.

Materials and methods: Forty patients presenting with clinical signs and symptoms of OSMF were included for the study after informed consent. Group A included 20 patients who received Aloe vera gel (forever living gel) along with physiotherapy. Group B included 20 patients who received antioxidant capsules twice daily for 3 months along with physiotherapy exercises four times in a day. The following parameters, that is, burning sensation, mouth opening, tongue protrusion and cheek flexibility were recorded at each visit.

Results: Majority of the participant enrolled were in the age range of 30 to 35 years. Improvement in all the parameters was seen with the individuals receiving Aloe vera gel in comparison to antioxidants.

Conclusion: So, Aloe vera being a soothing, simple and safe mode of treatment along with proper habit restriction can be considered to be an effectual protocol in the management of OSMF. The analgesic effects of Aloe vera with the physiotherapy exercises provide better results in reducing burning sensation and improving mouth opening, tongue protrusion and cheek flexibility in comparison to antioxidants.

Keywords: Aloe vera, Antioxidant, Oral submucous fibrosis, Physiotherapy.

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[1-6]Department of Oral Medicine and Radiology, Bharati Vidyapeeth Deemed University, Dental College and Hospital Pune, Maharashtra, India

Corresponding Author: Nisha Singh, Postgraduate Student Department of Oral Medicine and Radiology, Bharati Vidyapeeth Deemed University, Dental College and Hospital, Pune 411043 Maharashtra, India, Phone: +8554857898, e-mail: dr.nish12oct@gmail.com

INTRODUCTION

Oral submucous fibrosis (OSMF) is a well-established potentially malignant disorder affecting the oral mucosa. Its literature dates back to as far as 2500 to 3000 BC when a renowned Indian physician Sushrutha mentioned about a condition, 'Vidari features that simulate OSMF. In 1952, Schwartz described five Indian women from Kenya with a condition of the oral mucosa including the palate and pillars of the fauces, which he called 'atrophiaidiopathica (tropica) mucosae oris'. Later, it was termed OSMF; other names are 'Diffuse Oral Submucous Fibrosis', 'Idiopathic Scleroderma of the Mouth', 'Idiopathic Palatal Fibrosis', 'Sclerosing Stomatitis' and 'Juxta-Epithelial Fibrosis'. The pathogenesis of the disease is thought to be multifactorial, with chewing of betel quid/areca nut being recognized as one of the most significant risk factors for OSMF.[1]

A wide range of treatment modalities both medical and surgical have been proposed for OSMF, but none have proved curative or reduced the morbidity significantly. Many authors are of the opinion that conservative

treatment is preferable than the conventional ones. Hence, the search for an effective treatment modality still continues. Plants have been a major source of medicine since the time immemorial and many incurable oral diseases when treated with alternate medicine such as Ayurveda had a good prognosis, which has been well documented in the literature. One such ayurvedic medicine is Aloe vera. It is a mannoprotein containing many amino acids called 'wound healing hormones'. The polysaccharides are contained in the gel of the leaves, which induce the promotion of wound healing, and also have anti-inflammatory, immunomodulators and antioxidant properties. Further, sterols in the Aloe vera have a strong ability to inhibit inflammation similar to the action of cortisone without any side effects. All such properties of Aloe vera suggests its possible benefits in treating OSMF.[3]

Homeopathy is the alternative therapy that has been used over 200 years. It was presented for the first time by Samuel Hanemen (1755–1843), who used a plant from which quinine was derived in the treatment of malaria. In dentistry, homeopathic remedies have been proposed for oral ulcers, sialorrhea, neuralgia, temporomandibular joint disorders, xerostomia, lichen plan and bruxism.[2]

MATERIALS AND METHODS

The study was conducted at the Department Of Oral Medicine and Radiology, Bharati Vidyapeeth Deemed University, Dental College and Hospital, Pune. The study consisted of 40 clinically proven individuals with OSMF. Forty patients presenting with clinical signs and symptoms of OSMF reporting to Department of Oral Medicine and Radiology after informed consent were included for the study. These patients were randomly divided into two groups:

- Group A: 20 patients with OSMF applying Aloe Vera gel (Forever Living Gel) along with physiotherapy.
- Group B: 20 patients with OSMF taking Antoxid (Antoxid™ Capsule: Dr. Reddy's Product along with physiotherapy.

Criteria for Patient Selection

Inclusion criteria for the study shall be as follows:

- Patients with clinically diagnosed cases of OSMF.
- Patients who have not taken any treatment earlier for OSMF.
- Patients who are ready to quit the associated various habits and accept for regular follow ups.
- Patients with mouth opening between 20 and 39 mm.

Exclusion criteria for the study shall be as follows:

- Patients with OSMF coexisting with other oral lesion.
- History of hypersensitivity to Aloe vera.
- Pregnant women and lactating mothers.
- Oral submucous fibrosis patients with a history of associated systemic illness.

Method of Data Collection

A detailed history of patient was recorded regarding chief complaint along with the habit history.

Group A included 20 patients with OSMF who received Aloe vera gel (forever living gel) along with physiotherapy. Detailed procedure about the placement of cotton rolls and application of Aloe vera was explained to the patient. Aloe vera gel was applied topically on each side of oral mucosa three times daily for 3 months, which will be quantified approximately with a scoop. Patients were instructed to avoid solid and liquid diet for 15 minutes after application. Physiotherapy was advised using ice-cream stick four times in a day for 3 months.

Group B included 20 patients with OSMF who received antioxidant capsules twice daily for 3 months along with physiotherapy exercises (ice-cream stick exercise) four times in a day for 3 months.

The following oral findings were recorded each time the patient visits the department [baseline1st visit (2 week-4 week-6 week-8 week-10 week-12 week) respectively].

Clinical Parameters

Soluble irritants, such as capsaicin present in chilies and alkaloids of areca nut, act as initiating factors causing a juxta-epithelial inflammatory reaction, which is leading to burning sensation, vesiculation and ulceration of the oral mucosa. An atrophic epithelium makes the oral mucosa vulnerable to the soluble irritants and causes improper vascular channel formation resulting in decreased vascularity. This results in defective healing and scarification. Thus, the cumulative effect of these initiating and promoting factors leads to further fibrosis, which is a hallmark of OSMF. This fibrosis leads to reduced mouth opening, restricted tongue mobility and difficulty in blowing cheek.

So, the following parameters, that is, burning sensation, mouth opening, tongue protrusion and cheek flexibility were recorded each time the patient visited at [baseline1st visit (2 week-4 week-6 week-8 week-10 week-12 week] respectively.

Burning Sensation

The intensity of burning sensation was determined using a Numerical Rating Visual Analogue Scale (VAS) graded

on a 10 point scale from 0 to 10, where 0 represented no burning sensation while 10 represented the worst burning sensation possible.

Interincisal Opening

The inter-incisal mouth opening was measured using a Vernier Caliper from the mesio-incisal angle of upper central incisor to the mesio-incisal angle of lower central incisor and was recorded in millimeters.

Based on the mouth opening, the study subjects will be grouped as (given by Lai DR{1995})[3]

- Group A: Mouth opening greater than 35 mm.
- Group B: Mouth opening greater than 30 to 35 mm.
- Group C: Mouth opening greater than 20 to 30 mm.
- Group D: Mouth opening less than 20 mm.

Group D is not included in the present study.

Cheek Flexibility

Cheek flexibility was measured according to the method by Mathur and Jha:

Cheek flexibility = V1-V2

Two points were measured between:

V2 = is marked at one-third the distance from the angle of the mouth on a line joining the tragus of the ear and the angle of the mouth.

V1 = the subject is then asked to blow his cheeks fully and the distance measured between the two points marked on the cheek.

Tongue Protrusion

Tongue protrusion was assessed from normal mesio-incisal angle of upper central incisor to the tip of tongue when maximally extended with mouth wide open.[2]

All the four parameters were measured and recorded during patient's every visit.

RESULTS

The results were expressed as mean ± SD values. Inter group comparisons are performed using Mann-Whitney U test and intra group comparisons are performed using Wilcoxon's signed rank test. So, the following parameters, that is burning sensation, mouth opening, tongue protrusion and cheek flexibility, were recorded every time the patient visited at [baseline 1st visit (2 week-4 week-6 week-8 week-10 week-12 week] respectively.

The above-noted parameters were assessed and entered in a pre-designed proforma.

The age distribution of the cases treated did not differ significantly between two study groups ($p > 0.05$) (Table 1). In the present study, the youngest participant enrolled was aged 18 years. Majority of the participant enrolled were in the age range of 30 to 35 years, which was similar to studies done earlier.

Table 1: The age distribution of the cases treated across two study groups

Age Group (years)	*Group A (n = 19) [Aloe vera with physiotherapy group]*	*Group B (n = 18) [Antioxidant with physiotherapy group]*	*Intergroup comparison (p)*
<25.0	7 (36.8)	3 (16.7)	0.392 (NS)
25–30	3 (15.8)	2 (11.1)	
30–35	8 (42.1)	10 (55.6)	
>35	1 (5.3)	3 (16.7)	

Values are n (%). Chi-square test. p value <0.05 is considered to be statistically significant; NS: statistically nonsignificant

The gender distribution of the cases treated did not differ significantly between two study groups ($p > 0.05$) (Table 2). In the present study, majority of the participants enrolled were male in comparison to female, which was similar to studies done earlier.

In the present study, 67% patient has the habit of gutka chewing alone, while 33% used to eat bothgutka and tobacco (Graph 1).

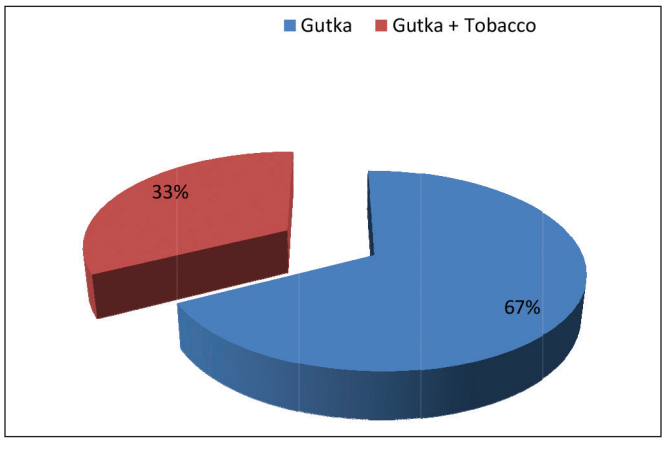
In the present study, maximum duration of habit was between 5 and 10 years and frequency of intake was in between five and eight times (Graph 2).

The intensity of burning sensation was determined using a VAS graded on a 10-point scale from 0 to 10, where

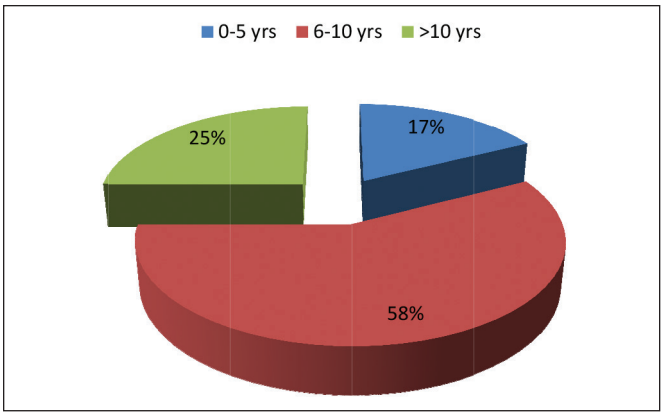
Table 2: The gender distribution of the cases treated across two study groups

Sex	*Group A (n = 19) [Aloe vera with physiotherapy group]*	*Group B (n = 18) [Antioxidant with physiotherapy group]*	*Intergroup comparison (p)*
Male	19 (100.0)	16 (88.9)	0.135 (NS)
Female	0	2 (11.1)	

Values are n (%). Chi-square test. p < 0.05 is considered to be statistically significant; NS: statistically nonsignificant



Graph 1: Tissue abuse habit



Graph 2: Duration of habit

0 represented no burning sensation while 10 represented the worst burning sensation possible. In the present study, there was 93.8% reduction in burning sensation in the Group A as compared with Group B in which there was 71.2% reduction. Significant improvement was seen with the individuals receiving Aloe vera gel in comparison to antioxidants (Table 3).

The average mouth opening score significantly increased at 1-month, 2-month and 3-month post-treatment follow-ups compared with the baseline mouth opening in group A ($p < 0.001$ for all). The average mouth opening score significantly increased at 1-month, 2-month and 3-month post-treatment follow-ups compared with the baseline mouth opening in group B ($p < 0.01$ for all). The average baseline, 1-month, 2-month and 3-month post-treatment mouth opening did not differ significantly between two study groups ($p > 0.05$ for all). The average post-treatment % increase in mouth opening is significantly higher in Group A than in Group B ($p < 0.001$) (Table 4).

The average tongue protrusion score significantly increased at 2-month and 3-month post-treatment follow-ups compared with the baseline tongue protrusion in group B ($p < 0.001$ for all). The average tongue protrusion did not differ significantly at 1-month post-treatment follow-up and baseline tongue protrusion in group B ($p > 0.05$). The average baseline, 1-month, 2-month and 3-month post-treatment tongue protrusion did not differ significantly between two study groups ($p > 0.05$ for all). The average post-treatment % increase in tongue protrusion is significantly higher in Group A than in Group B ($p < 0.001$) (Table 5).

The average cheek flexibility score significantly increased at 2-month and 3-month post-treatment follow-ups ($p < 0.05$ for all). The average cheek flexibility did not differ significantly at 1-month post-treatment follow-up and baseline cheek flexibility in both group A and group B ($p > 0.05$). The average baseline, 1-month, 2-month and 3-month post-treatment cheek flexibility

Table 3: The inter- and intragroup comparison of burning sensation score in each study group

Burning sensation	*Group A (n = 19) [Aloe vera with physiotherapy group]*	*Group B (n = 18) [Antioxidant with physiotherapy group]*	*Intergroup comparison (p)*
Pre-treatment (Baseline)	7.21 ± 1.27	6.83 ± 1.29	0.408 (NS)
1-month post-treatment	4.74 ± 0.99	5.33 ± 1.46	0.284 (NS)
2-month post-treatment	2.79 ± 1.03	3.78 ± 1.22	0.022 (NS)
3-month post-treatment	0.53 ± 0.49	2.06 ± 1.16	0.001 (S)
% Reduction at 3 months	93.8%	71.2%	0.001 (S)
Intragroup comparisons			
Pre v/s 1-month post treat	0.001 (S)	0.001 (S)	–
Pre v/s 2-month post treat	0.001 (S)	0.001 (S)	–
Pre v/s 3-month post treat	0.001 (S)	0.001 (S)	–

Table 4: The inter- and intragroup comparison of mouth opening in each study group

Mouth opening	*Group A (n = 19) [Aloe vera with physiotherapy group]*	*Group B (n = 18) [Antioxidant with physiotherapy group]*	*Intergroup comparison (p)*
Pre treatment (Baseline)	30.4 ± 4.5	29.9 ± 3.3	0.822 (NS)
1-month post treatment	30.8 ± 4.5	30.2 ± 3.2	0.730 (NS)
2-month post treatment	31.8 ± 4.5	30.9 ± 3.3	0.590 (NS)
3-month post treatment	33.1 ± 4.4	31.4 ± 3.4	0.245 (NS)
% improvement at 3 months	9.1%	5.3%	0.004 (S)
Intragroup comparisons			
Pre vs 1-month post-treat	0.001 (S)	0.004 (S)	–
Pre v/s 2-month post-treat	0.001 (S)	0.001 (S)	–
Pre v/s 3-month post-treat	0.001 (S)	0.001 (S)	–

NS: statistically nonsignificant; S: statistically significant

Table 5: The inter- and intragroup comparison of tongue protrusion in each study group

Tongue protrusion	*Group A (n = 19) [Aloe vera with physiotherapy group]*	*Group B (n = 18) [Antioxidant with physiotherapy group]*	*Intergroup comparison (p)*
Pre-treatment (Baseline)	42.9 ± 7.3	43.8 ± 3.6	0.976 (NS)
1-month post-treatment	43.1 ± 7.2	43.9 ± 3.5	0.988 (NS)
2-month post-treatment	43.9 ± 7.3	44.4 ± 3.5	0.855 (NS)
3-month post-treatment	44.6 ± 7.6	44.7 ± 3.6	0.879 (NS)
% Improvement at 3 months	3.9%	2.2%	0.001 (S)
Intragroup comparisons			
Pre v/s 1-month post-treat	0.020 (S)	0.102 (NS)	–
Pre v/s 2-month post-treat	0.001 (S)	0.001 (S)	–
Pre v/s 3-month post-treat	0.001 (S)	0.001 (S)	–

NS: statistically nonsignificant; S: statistically significant

did not differ significantly between two study groups ($p > 0.05$ for all).The average post-treatment % increase in cheek flexibility did not differ significantly between two study groups ($p > 0.05$). In the present study, there was 80.8% improvement in cheek flexibility in the Group A as compared with Group B in which there was 61.4% improvement (Table 6).

DISCUSSION

Oral submucous fibrosis was defined as an 'insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. it is associated with vesicle formation and juxta-epithelial inflammatory reaction followed by progressive hyalinization of the lamina propria and later sub-epithelial and sub-mucosal myo-fibrosis leads to stiffness of the oral mucosa and deeper tissues with progressive limitation in opening of the mouth and protrusion of the tongue, thus causing difficulty in eating, swallowing and phonation'.[5, 6]

There is evident that patient with OSMF has increased free radicals and decreased antioxidant levels. A variety of etiologic factors including capsaicin, betel nut alkaloids, hypersensitivity, autoimmunity, genetic predisposition and chronic iron and vitamin B-complex deficiency have been suggested by various authors, the most common of which is chewing areca nut.[7]

Early OSMF includes a burning sensation in the mouth when consuming spicy food followed by either hypersalivation or dryness of the mouth (25%). The oral mucosa is involved symmetrically and the fibrous bands in the buccal mucosa run in a vertical direction. The density of the fibrous deposit varies from a slight whitish area on the soft palate causing no symptoms to a dense fibrosis causing fixation and shortening or even deviation of the uvula and soft palate.[8,9]

Narayan et al[10] in their study found that there was no correlation between clinical staging and histopathological grading of OSMF.

The treatment of OSMF is based on severity of disease. If the disease is noted prior to development of trismus, cessation of the betel habit will often resolve the disease. Once trismus has developed, the goal of therapy is to maintain oral function and limit progression of disease. Recent data suggest that Aloe vera also exerts anti-inflammatory effects through the reduction of leukocyte adhesion and tumor necrosis factor (TNF)-a levels.[3] It contains carboxypeptidase that inactivates bradykinins and produces an anti-inflammatory effect. Aloe vera gel improved wound healing by increased blood supply, which increased oxygenation as a result. A mannose-6-phosphate component of the gel has been credited with a wound healing effect. It also has soothing and cooling

Table 6: The inter- and intragroup comparison of cheek flexibility in each study group

Cheek flexibility	*Group A (n = 19) [Aloe vera with physiotherapy group]*	*Group B (n = 18) [Antioxidant with physiotherapy group]*	*Intergroup comparison (p)*
Pre-treatment (Baseline)	0.097 ± 0.04	0.098 ± 0.04	0.852 (NS)
1-month post-treatment	0.11 ± 0.06	0.10 ± 0.06	0.988 (NS)
2-month post-treatment	0.16 ± 0.09	0.14 ± 0.11	0.517 (NS)
3-month post-treatment	0.19 ± 0.17	0.18 ± 0.16	0.677 (NS)
% Improvement at 3 months	80.8%	61.4%	0.244 (NS)
Intragroup comparisons			
Pre v/s 1-month post-treat	0.102 (NS)	0.317 (NS)	–
Pre v/s 2-month post-treat	0.001 (S)	0.003 (S)	–
Pre v/s 3-month post-treat	0.001 (S)	0.001 (S)	–

NS: statistically nonsignificant; S: statistically significant

qualities. So, these could be the possible reasons for reducing pain and burning sensation in OSMF patients. Once the patient's burning sensation is reduced, they try to open the mouth. Aloe vera is an antioxidant-rich plant that contains vitamins such as A, C and E along with minerals, beta carotene, zinc, iron and selenium. Antioxidants help boost the immune system and combat free radicals in the body. During the inflammatory process, bradykinins produce pain associated with vasodilation and, therefore, its hydrolysis reduces these two components and produces an analgesic effect. So, these could be the possible reasons for reducing pain and improvement in mouth opening in patients with OSMF. Combinations of drugs have been used. But the lack of good quality trials of drug treatment for OSMF is disappointing.[3, 5, 8, 9]

In the present study, majority of the participant enrolled were in the age range of 30 to 35 years, which was similar to studies done earlier. Sudarshan et al,[3] Thakur and Keluskar[11] and Mehrotra et al[12] have also reported highest incidence between 3rd and 4th decades of life. This continuous rise in the incidence of OSMF has been attributed to increased popularity of commercially available areca nut preparations, that is, paan masala/gutkha in India and an increased uptake of this habit by young people due to easy access and marketing strategies.[7]

In the present study, majority of the participants enrolled were male in comparison to female, which was similar to studies done earlier. Sudarshan et al,[3] Mehrotra et al[12] and Patil and Halgatti[13] also found male predominance in their studies.

In the present study, 67% of patients have the habit of gutka chewing alone while 33% used to eat both gutka and tobacco. In the present study, maximum duration of habit was between 5 and 10 years and frequency of intake was in between five and eight times. Mehrotra et al[12] showed that maximum number of the patients were between 5 and 10 years duration, which was consistent with the present study.

In the present study, there was 93.8% reduction in burning sensation, which was seen in the Group A as compared with Group B in which there was 71.2% reduction. Significant improvement was seen with the individuals receiving aloe vera gel in comparison to antioxidants. The study by Sudarshan et al[3] showed an improvement of 80% in burning sensation with aloe vera group, whereas 65.7% patients showed an improvement in burning sensation in the antioxidant group, which is near about consistent with the present study. In both the studies, an improvement was seen with the Aloe vera group.[3] Alam and Al Iqbal[14] in their study noticed considerable decrease in burning sensation in the medicinal group with Aloe vera (1.73 ± 1.01), and in the present study, it was (0.53 ± 0.49). Significant reduction was found in the Aloe vera group in comparison to non-Aloe vera group in both the studies. Patil and Halgatti[13] found no significant improvement in burning sensation among the two groups, that is, Group A (oxitard) and Group B (aloe vera). Reduction in burning sensation was seen earlier in individuals receiving aloe vera gel (Group A) in comparison to individuals receiving antioxidants (group B), which was taken systemically.

In the present study, there was 9.1% improvement in mouth opening in the Group A as compared with Group B in which there was 5.3% improvement, whereas Sudarshan et al[3] showed an improvement of 20% in the patients who were given aloe vera, whereas only 9% improvement in antioxidants group that was not consistent with our study, but an improvement was seen with the Aloe vera group in both the studies. Alam and Al Iqbal[14] in their study noticed a considerable improvement in mouth opening in the medicinal group with Aloe vera. Mouth opening is increased by 13.74 mm from initiation to the 6-month follow-up. Patil et al[13] showed that mouth opening improved 60.5% in Group A (oxitard), whereas Group B (aloe vera) showed 25% improvement. Both the medicaments showed an improvement at the end of the study. It was not consistent with the present study.

In the present study, there was 3.9% improvement in tongue protrusion in the Group A as compared with Group B in which there was 2.2% improvement, whereas Sudarshan et al[3] showed an improvement of 8.8% in the aloe vera group, while the antioxidant group showed 4.25% improvement. Improvement was more with the individuals receiving aloe vera gel in both the studies. Here, it is important to mention that the restriction of tongue mobility is not only because of the fibrosis of the tongue but also because of the involvement of the retromolar area and the floor of the mouth. Aloe vera with the physiotherapy exercises improved tongue protrusion to some extent in the OSMF patients.

There was 0.09 cm improvement in the present study, whereas Sudarshan et al[3] found 0.07 cm improvement in cheek flexibility in individuals receiving aloe vera gel. Improvement was more with the individuals receiving Aloe vera gel in both the studies.

In the present study, three patients did not turn up for the follow-up [one patient from group A (after 1 month) and two patients from group B (one after 1 month and second one after 2 months)], as they got relieved from the burning sensation and they were able to eat. This could

be due to the lack of perceptible improvement in the condition of these patients. Self- perceived improvement was found to be an important factor in the motivation of the patient toward treatment. So, they were not included in the study.

CONCLUSION

Since the appearance of OSMF, various treatment modalities such as medical and surgical are tried to improve the patient condition. But most of them failed to have success of 100%. The medical management includes submucosal injection of steroids, placental extracts and hyaluronidase. This may give temporary relief but aggravates fibrosis because of the multiple needle insertion and irritation from the drug. The medical management is palliative therapy, which is not going to reverse the condition completely. Patient has to quit the habit, along with long duration of medication that will benefit in a mild to moderate way, which is not up to the satisfaction of patient or original mouth opening.

Aloe vera being an ayurvedic medicine that is noninvasive is used to evaluate improvement in mouth opening, reduction in burning sensation, tongue protrusion and cheek flexibility and in comparison to administration of antioxidant, along with physiotherapy, so that it can be used as an alternative or adjunct to conventional therapies in the management of OSMF in future.

Homeopathy is an alternative therapy that seems to be effective in cases of treatment failure to conventional drugs. It is recommended that more research be done to evaluate the effectiveness of homeopathic remedies for treatment of conditions that seem to be dependent on spiritual and mental conditions of patients or the conventional drugs just have alleviative effect and poor response.[2]

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