



EVALUATION OF EFFICACY OF ALOE VERA JUICE IN OSMF PATIENTS

Oral Medicine & Radiology

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ABSTRACT

OSMF can be defined as a chronic, insidious disease which is extensively found in India and etiology is credited to the habit of betel nut and areca nut chewing. **AIM:** Our study aimed at evaluating the efficacy of aloe vera juice in OSMF patients bases on the burning sensation, inter incisal distance, cheek flexibility and tongue protrusion. **Material & Methods:** 50 Patients were administered with aloe vera juice systemically 30 ml two times a day with a regular interval of follow up after every fortnight. **Results:** significant improvement seen on the basis of all four parameters. **Conclusion:** Many treatment modalities since decades have been provided by many authors but no totally effective modality is available. We can conclude from our study that Aloe vera is effective in treating OSMF but not yet considered to be a proven cure for it.

KEYWORDS

Oral Submucous Fibrosis, Aloe vera, juice, burning, cheek flexibility, tongue protrusion, inter incisal distance

Oral Submucous Fibrosis (OSMF) has been a topic of study since years. It has been designated with various names by various authors and researchers. There are estimated to be 600 million people who chew betel nuts worldwide making it a very popular habit.^[1] The process of chewing releases several mineral components and alkaloids from the areca nut which is responsible for a range of effects on the body. It has catastrophic effects among which most significant is Oral Sub Mucous Fibrosis.

Various hypotheses have been put forward which suggest a multifactorial origin for the etiology of OSMF. The etiological factors include local irritants such as chili consumption, areca nut chewing, tobacco smoking and chewing.^[2]

The disease expansively occurs mostly in India and in South East Asia, but the cases have been reported worldwide like Kenya, China, UK, Saudi Arabia. Moreover, recent data suggests that prevalence of OSMF in India has increased from 0.03% to 6.42%. The prevalence in India is estimated to range from 0.2-2.3% for males and 1.2-4.6% for females. Age groups which it involves are quite broad ranging from 11 to 60 years.^[2,3,4]

Intralesional injections of corticosteroids, placental extracts, and hyaluronidase, IFN- α , oral administration of peripheral vasodilators, immune milk, turmeric, lycopene, and micronutrient supplementation are some modalities used. Various physiotherapeutic modalities have also shown favorable results. Steroids till date are the most accepted modality of treatment for OSMF.^[5]

Aloe vera is considered as an adaptogen. An adaptogen is a substance that invigorates or strengthens the system. Specifically, the term applies to herbs that maintain health by increasing the body's ability to adapt to environmental and internal stressors. Aloe vera contains 75 potentially active constituents : vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids. The vitamins present are vitamin A (beta-carotene), C, and E, which are antioxidants and help to neutralize free radicals. Henceforth such properties of aloe vera enables it to be used as a sole entity in treatment of this chronic insidious disease.^[5]

MATERIALS AND METHODS:

Source of data:

The study group consisted of 50 patients with OSMF. Patients selected were randomly among the out patients attending the Department of Oral Medicine and Radiology, CAREER POST GRADUATE INSTITUTE OF DENTAL SCIENCES AND HOSPITAL, LUCKNOW. A written informed consent was taken from the patients

before beginning of the treatment and before they participated in the study.

A ethical clearance by the committee constituted by the college of Career Post Graduate Institute of Dental Sciences & Hospital was given. Reference No. CPDISH/1162/2021.

AIM AND OBJECTIVES OF THE STUDY:

- To assess the efficacy of Aloe Vera Juice given systemically in OSMF patients.
- To assess improvement in burning sensation in patients with OSMF.
- To assess improvement in mouth opening of patient with OSMF.
- To assess improvement in tongue protrusion before and after treatment.
- To check improvement in cheek flexibility.

METHODOLOGY:

Aloe Vera juice manufactured by Gurukul Ayurved Pharmacy, India was provided to patients with clinically diagnosed with oral sub mucous fibrosis. A sample size of 50 patients diagnosed with OSMF were taken for the study and were advised to take the juice systemically, 30 ml twice daily empty stomach. Patients were periodically recalled for follow up for a period of six months. Approval from the institutional ethical committee was obtained for the study. Patients were evaluated on the basis of classification given by Chandramani More with OSMF. An informed consent was obtained from all the patients after the nature of the study, and its procedures were explained. A thorough clinical examination was carried out, and The parameters taken under account were consecutively measured and checked for from time to time.

The parameters recorded were-

- Intensity of Burning sensation was measured on the numerical VAS scale.
- The interincisal distance was measured using a metallic scale and divider. The distance was recorded from interincisal angle of upper central incisor to the interincisal distance of the lower central incisor in millimeters.
- Cheek flexibility was also measured. To measure this method described by Nagesh and Bailoor was taken. Ideally two points are marked on either side of face 1/3rd distance from angle of mouth, on a line joining the two points i.e. angle of the mouth and tragus of the ear. This is V2. Then we ask the subject to blow air in the cheeks or blow the cheeks fully and now the distance is measured between the same points. This is V1. So CF=V2-V1.

4. Tongue protrusion was recorded by asking the patient to completely extend the tongue with fully open mouth then the distance from mesio-incisal angle of upper central incisor to the tip of the tongue was recorded.

INCLUSION CRITERIA:

- Patients between the age group of 18-60 years.
- Patients with clinically diagnosed OSMF.

EXCLUSION CRITERIA:

- Individuals with known history of hypersensitivity to Aloe Vera.
- Individuals with any known systemic disorders.
- Individuals under any drugs like anti-cholinergic, diuretics, antihistamines, anti-hypertensive, & psychoactive substance
- Pregnant females, lactating mothers.
- Individuals with the positive history of head and face surgery, ear and oral and maxillofacial surgery.
- Patients who had received prior treatment for OSMF were excluded.

All the patients' demographic characteristics, habit history with clinical parameters were recorded in a pre-determined proforma and was subjected to statistical analysis.

OBSERVATIONS AND RESULT

STATISTICAL ANALYSIS

Data were summarized as Mean $\pm$ SD (standard deviation). Groups (periods) were compared by one factor repeated measure (RM) analysis of variance (ANOVA) and the significance of mean difference between (inter periods) the groups was done by Tukey's HSD (honestly significant difference) post hoc test after ascertaining normality by Shapiro-Wilk's test and homogeneity of variance between groups by Levene's test.

The age of patients ranged from 23-60 years. Among patients, there were 17 (34.0%) females and 33 (66.0%) males. The study population was thus, predominately young and male predominance with 1:1.9 female to male ratio (Table 1)

Table 1: Demographic characteristics of OSMF patients at presentation

Demographic characteristics	Total OSMF patients (n=50) (%)
Age (yrs):	
≤40	30 (60.0)
>40	20 (40.0)
Sex:	
Female	17 (34.0)
Male	33 (66.0)

Data were summarized as Mean $\pm$ SD (standard deviation). Groups (periods) were compared by one factor repeated measure (RM) analysis of variance (ANOVA) and the significance of mean difference between (inter periods) the groups was done by Tukey's HSD (honestly significant difference) post hoc test after ascertaining normality by Shapiro-Wilk's test and homogeneity of variance between groups by Levene's test. A two-tailed ($\alpha=2$) $P < 0.05$ was considered statistically significant. Analysis was performed on SPSS software (Windows version 22.0).

The VAS score at baseline, 1st, 2nd, 3rd, 4th, 5th and 6th month ranged from 6-9, 4-7, 4-6, 3-4, 1-3, 1-3 and 1-2 respectively with mean ($\pm$ SD) 8.06 $\pm$ 0.87, 5.64 $\pm$ 0.60, 4.62 $\pm$ 0.57, 3.52 $\pm$ 0.50, 2.48 $\pm$ 0.54, 2.36 $\pm$ 0.63 and 1.54 $\pm$ 0.50 respectively and median 8, 6, 5, 4, 3, 2 and 2 respectively. The mean VAS score decreased (i.e. improvement in burning sensation) gradually after the treatment (Table 2)

Table 2: Pre and post VAS score of OSMF patients over the periods

Time period	VAS (score) (Mean $\pm$ SD, n=50)	F value	P value
Baseline	8.06 $\pm$ 0.87	715.96	< 0.001
1 st month	5.64 $\pm$ 0.60		
2 nd month	4.62 $\pm$ 0.57		
3 rd month	3.52 $\pm$ 0.50		
4 th month	2.48 $\pm$ 0.54		
5 th month	2.36 $\pm$ 0.63		
6 th month	1.54 $\pm$ 0.50		

net mean decrease/improvement in burning sensation (i.e. mean decrease in VAS score from baseline to 6 months) of OSMF patients

was found to be 80.9% (Fig: 1).

Burning sensation (VAS scale)

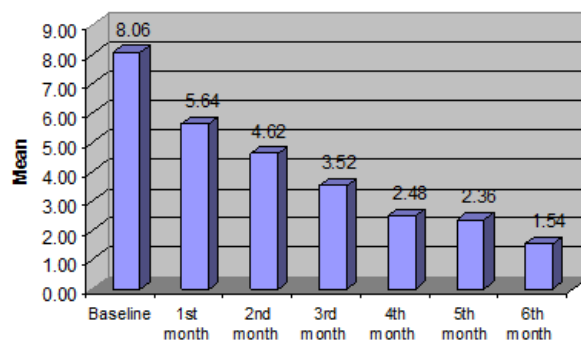


Fig. 1. Bar graphs showing pre and post mean VAS score of OSMF patients over the periods.

The pre and post VAS score of OSMF patients over the periods were summarised in Mean $\pm$ SD and compared by RM ANOVA.

The mean inter incisal distance increased gradually (i.e. improvement in inter incisal distance) after the treatment (Fig. 3). Comparing the mean inter incisal distance among periods, ANOVA showed significantly different inter incisal distance among the periods ($F=628.33$, $P < 0.001$). Furthermore, at all post periods, it was also found significantly ($P < 0.001$) different and higher at successive periods as compared to predecessor periods. The net mean increase/improvement in inter incisal distance (i.e. mean decrease in inter incisal distance from baseline to 6 months) of OSMF patients was found to be 33.3% (Fig 2).

Inter incisal distance (mm)

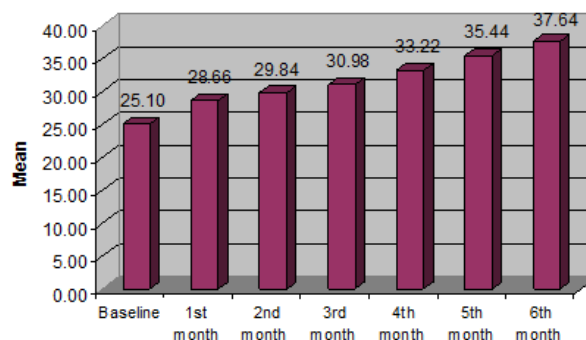


Fig. 2. Bar graphs showing pre and post mean inter incisal distance of OSMF patients over the periods.

The cheek flexibility at baseline, 1st, 2nd, 3rd, 4th, 5th and 6th month ranged from 0.2-0.4, 0.2-0.5, 0.3-0.5, 0.4-0.5, 0.4-0.6, 0.5-0.7 and 0.6-0.8 cm respectively with mean ($\pm$ SD) 0.22 $\pm$ 0.06, 0.25 $\pm$ 0.07, 0.35 $\pm$ 0.05, 0.45 $\pm$ 0.05, 0.50 $\pm$ 0.06, 0.57 $\pm$ 0.05 and 0.69 $\pm$ 0.06 cm respectively and median 0.2, 0.2, 0.4, 0.5, 0.5, 0.6 and 0.7 cm respectively. The mean cheek flexibility increased gradually (i.e. improvement in cheek flexibility) after the treatment. the net mean increase/improvement in cheek flexibility (i.e. mean decrease in cheek flexibility from baseline to 6 months) of OSMF patients was found to be 68.6% (Fig: 3)

Cheek flexibility (cm)

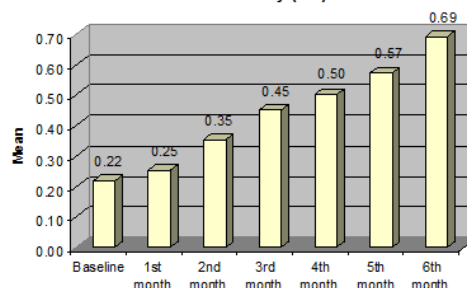


Fig. 3. Bar graphs showing pre and post mean cheek flexibility of

OSMF patients over the periods.

The tongue protrusion at baseline, 1st, 2nd, 3rd, 4th, 5th and 6th month ranged from 2.4-3.4, 2.6-3.5, 2.9-3.7, 3.1-3.7, 3.3-4.0, 3.5-4.0 and 3.6-4.0 cm respectively with mean ($\pm$ SD) 2.85 ± 0.27 , 3.08 ± 0.22 , 3.35 ± 0.20 , 3.45 ± 0.15 , 3.63 ± 0.15 , 3.81 ± 0.14 and 3.84 ± 0.12 cm respectively and median 2.9, 3.1, 3.4, 3.5, 3.6, 3.8 and 3.9 cm respectively. The mean tongue protrusion increased gradually (i.e. improvement in tongue protrusion) after the treatment. Comparing the mean tongue protrusion among periods, ANOVA showed significantly different tongue protrusion among the periods ($F=551.97$, $P<0.001$). the net mean increase/improvement in tongue protrusion (i.e. mean decrease in tongue protrusion from baseline to 6 months) of OSMF patients was found to be 25.8% (fig. 4)

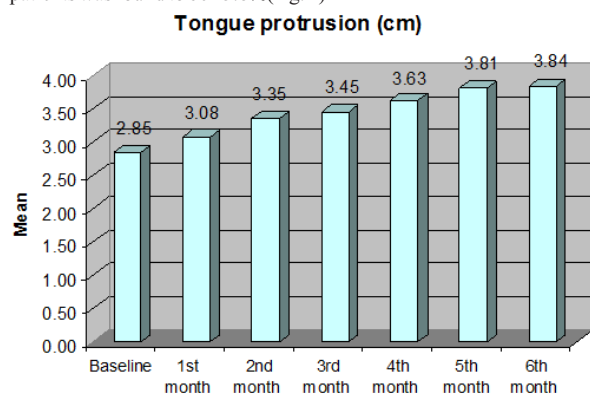


Fig. 4. Bar graphs showing pre and post mean tongue protrusion of OSMF patients over the periods.

DISCUSSION

The oral mucous membrane is quite a unique tissue which is over and over again exposed and experiences various kind of stresses for example like heat, cold, mechanical and chemical irritants, microorganism in the process of food intake. In response to such kind of stresses, both epithelium and connective tissue layers of the mucosa exhibit both acute and chronic reactive changes.^[6] OSMF is currently accepted globally as an Indian Disease which tends to show a highest malignant potential as compared to other oral pre-malignant lesions.^[7] Ever since the condition, OSMF was mentioned it has always been a puzzle to treat and cure it.

The conundrum surrounding OSMF is imperishable. The etiology along with its management always has been the question of discussion and none can come to a single conclusion. Day by day there is an increment in number of cases in OSMF as no fixed conclusive and effective treatment method is known. Thus people negligence towards the seriousness of the disease is aiding in rise of the number of people consuming the major causative factor i.e. areca nut or betel nut products with or without tobacco. The magnitude of the situation can be calibrated by the facts stated in a 2004 review that India ranks the highest among all the registries in the world for incidence of oral cancer with 75,000-80,000 cases reported each year.^[8]

Oral cancer is the most common cancer in India amongst men (16.1 % of all cancers). According to the **Globocan 2018 data the New cases registered are 92,011** in a year. Oral cancer is the second most common cancer in India amongst women (10.4 % of all cancers), **New cases registered in a year are 1,19,992** in females.^[9] Epidemiological studies have reported the prevalence of OSMF to be 6.42 per 1000, the male to female ratio, 4.9:1 and the malignant transformation of OSMF as 2.3-7.6% in the Indian context^[10]

The most common features that we come across in OSMF are:

- Burning sensation and discomfort in the oral cavity during mastication.
- Gradually various parts of the mouth lose their natural suppleness and related disabilities develop.
- With involvement of the tongue, speech and associated functions are affected. Extension of fibrosis to other areas in the oral cavity results in difficulty in mastication, reduced salivation, dysphasia, pain in the ears, and loss of auditory acuity due to stenosis of the pharyngeal end of the eustachian tubes.

Recently, aloe vera has been introduced as a natural herbal alternative

for the management of OSF. Aloe vera is an ancient plant that has several pharmacological benefits and has long been used as a remedy for numerous medical conditions without any reported side effects. Aloe vera is considered as an adaptogen. An adaptogen is a substance that invigorates or strengthens the system. Primarily, the medical benefits of aloe vera are attributed to its analgesic, anti-inflammatory, immune-modulatory, antioxidant, anti-neoplastic, and wound-healing properties. A number of clinical trials have assessed the efficacy of aloe vera in the management of OSF patients^[11].

Burning sensation is the most common representation among the patients of OSMF and is caused by epithelial atrophy preceded by juxtaepithelial inflammation.

In our study the Mean percentage improvement in burning sensation of OSMF patients was found to be 80.9%. Almost same results were observed in a study conducted by Ardra Anuradha et al who also administered aloe vera both topically and systemically observed drastic improvement in burning sensation with a significant result of 79.5% respectively^[5]. Similarly another study conducted by Santosh Patil et al in which he did comparative study between aloe vera and spirulina where he administered topical application of aloe vera gel in patients with OSMF. He observed that both the medicament showed equal amount of improvement in burning sensation. Other than that study also showed reduction in pain due to vesicles or ulcers observed in patients due to OSMF^[12].

The reduction in burning sensation can be accredited to the anti-inflammatory properties of aloe vera. The probable mechanisms for the anti-inflammatory action of the aloe vera has been stated by various authors through various documented data for instance:

- Carboxypeptidase's in aloe inactivate bradykinin which is a principle participant of inflammation^[13]
- Magnesium lactate present in aloe vera inhibits histidine decarboxylase, thereby preventing the formation of histamine from histidine in mast cells
- Salicylates are by-products of aloe vera, aloe-emodin, and aloin
- Peptidase bradykinin isolated from aloe vera breaks down bradykinin, an inflammatory substance that induces pain
- Reduction in leukocyte adhesion and TNF- α level result in inhibition of inflammatory process^[5]

Reduced mouth opening can be considered to be the most pathognomic feature of OSMF, which is attributed to increase collagen production and decreased breakdown of collagen. Increased fibrosis is due to increased cross-linking of collagen through up-regulation of lysyl oxidase activity. In our study improvement in inter-incisal mouth opening was observed to be 33.3%. A study conducted by Sarwar Alam et al, a double-blind, placebo-controlled, parallel-group randomized controlled trial wherein He concluded that there was not significant improvement in mouth opening in both the groups with or without application of aloe vera gel^[14]. Another study conducted by Ramachandran Sudarshan et al on 20 subjects where he topically applied aloe vera gel it was observed that there was improvement in burning sensation and significant improvement in mouth opening^[15]

The net mean increase/improvement in cheek flexibility of OSMF patients was found to be 68.6%. A study conducted by Nisha Singh et al on effectiveness of aloe vera and antioxidant along with physiotherapy in the management of OSMF. 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. In a study conducted by Sudarshan et al it showed a reduction in the burning sensation by 65% on VAS, 7 mm improvement in mouth opening, 3 mm increase in tongue protrusion, and 0.05 cm in cheek flexibility, whereas the eight moderate cases in group A showed 55% reduction of burning sensation on VAS, 4.3 mm increase in mouth opening, 3 mm improvement in tongue protrusion, and 0.07 cm improvement in cheek flexibility. Improvement was more with the individuals receiving Aloe vera gel in both the studies^[15].

Due to fibrosis there is reduction in mouth opening resulting in loss of elasticity due to which tongue protrusion is hampered. So the last considering parameter in our study at final evaluation showed, the net mean increase/improvement in tongue protrusion of OSMF patients was found to be 25.8%. we can compare the results of our study with another study conducted by Ramachandran Sudarshan et al improvement in aloe vera group was 8.8%.

No serious side effects were noted among the patients administered with aloe vera juice. Thus one thing that we can conclude from the above mentioned various studies that aloe vera even though was medicament of choice in all the studies the mode of administration of it in most of the studies was in form of gel, topical application. As aloe vera has innumerable benefits on human body so it can be a considerable factor for its implementation in this chronic insidious disease. So our study also comprised of aloe vera juice and we evaluated how effective it is in OSMF patients. It was accompanied by certain parameters to evaluate efficacy of this magical treatment was significant improvement in all the parameters recorded by us which were burning sensation, inter incisal distance, cheek flexibility and tongue protrusion thus depicting how effective aloe vera is.

LIMITATIONS & FUTURE PROSPECTS

Aloe vera can be considered as an effective method for treating OSMF. As aloe vera has multiple properties that reduce or aid in reducing the symptoms of OSMF it can be attributed to be one of the emerging treatment modalities in treating OSMF. Thus, it is an effective mode of treatment. Though more studies need to be conducted on aloe vera to prove or study the effectiveness of it, more researches are necessary to be performed to add on the fact that aloe vera can be used in OSMF.

CONCLUSION

Thus we can conclude from our study that OSMF a crippling, debilitating, enfeebling disease is burdensome and strenuous to treat. But consecutive efforts are still made till date to alleviate it. Among so many alternative therapies, we chose aloe vera as the choice of treatment because of its properties as there is very less documented data on its use in Oral Submucous Fibrosis and to some extent it was capable to prove its worth on the criteria we judged it. Aloe vera was tremendously effective in alleviating burning sensation, significantly positive in increasing inter incisal distance, tongue protrusion and cheek flexibility. But the compulsory requirement is patient due compliance, regular follow up, timely consumption of the juice and that it takes time to show result. But more studies and researches still need to be conducted for its significance to be validated.

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