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A protocol for Comparative Evaluation of Efficacy of Ksheerabala Oil and Steroid mouthwash In Management of Oral Submucous Fibrosis- an in vivo study

DR. SURBHI JUNEJA,

Post graduate student, Oral Medicine and Radiology, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha. India.

Email- surbhijuneja2211@gmail.com

DR. SUWARNA DANGORE- KHASBAGE

Professor, Oral Medicine and Radiology, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha. India.

Email – dangore_suwarna@rediffmail.com,

Abstract: Background: OSMF, apre-malignant condition is a very common and chronic condition occurring mostly due to habit of tobacco consumption and various other factors which affects the oral cavity characterized by mucosal burning on consuming hot & spicy food, oral ulcerations, fibrosis leading to difficulty in mouth opening. There are vast treatment options for this condition including pharmacotherapy, physiotherapy, surgical approaches but in our study we used an ayurvedic preparation called ksheerabala oil which has least side effects and is having holistic approach for treatment. It will also be compared with effectiveness of steroid mouthwash in the treatment of OSMF.

Objectives: To evaluate efficacy of steroid mouthwash, ksheerabala oil and the combination of ksheerabala oil and steroid mouthwash in improvement and management of mouth opening, burning sensation of the mouth and cheek flexibility.

Method: This study targets 90 patients clinically diagnosed to have OSMF which will be divided in three groups: Group A, B & C with 30 subjects in each group. Group A will be instructed to gargle with 10 ml of 0.1% Dexamethasone for 10 min. three times daily for 1 month. Group B will be instructed to to gargle initially with 10 ml of 0.1% Dexamethasone for 10 min& then with 10 ml of ksheerabala oil for 10 min three times daily for 1 month & Group C to gargle with 10 ml of ksheerabala oil for 10min three times daily for 1 month. Patients will be recalled after every 7 days for a period of 1 month and on each visit, mouth opening, burning sensation and cheek flexibility will be recorded.

Results: The primary outcome of the study will be increase in degree of mouth opening and secondary outcome will be decrease in burning sensation and improvement in cheek flexibility after treatment in OSMF patients. The severity of burning sensation will reduce after using ksheerabala oil and steroid mouthwash both while combination of both may or may not be effective but ksheerabala oil will be more effective in improvement of mouth opening and cheek flexibility compared to steroid.

***Conclusion:* An attempt to determine the effectiveness of ksheerabala oil compared to steroid mouthwash in treatment of OSMF is taken as an holistic approach. Also, motivating and empowering the patient to cease the habit of tobacco and making them aware with its complications is utmost important. Also, being an ayurvedic preparation, ksheerabala oil will have more holistic approach and better outcome in the management of OSMF.**

Keywords: Ksheerabala oil, Steroid mouthwash, OSMF treatment

INTRODUCTION:

Oral submucous fibrosis (OSMF) is a well known chronic, insidious, premalignant condition that affects mucosa of mouth, as well as the pharynx and the upper two-thirds of the esophagus, that characteristically shows epithelial and sub-epithelial inflammation, succeeding by fibro-elastic alterations in sub-mucosa that results in difficulty to open mouth due to marked rigidity.[1,2] The burning sensation and difficulty to eat hot, spicy food occurs due to epithelial atrophy. The disease occurs mostly in India with prevalence in Kerala of around 0.4 percent, Andhra Pradesh- 0.04 percent and Gujarat- 0.2 percent.[3] It also occurs in South East Asia and there are cases which were reported in Kenya, China, United Kingdom, and Saudi Arab.[4]

The OSMF prevalence has increased over the past four decades ranging from 0.03 to 6.42 with 5 million cases just in India. OSMF causes detrimental health-related impacts such as functional limitations and psychosocial impairment with significant worsening of QoL in advanced stages[5]. Pathogenesis of OSMF is multifactorial. The exact etiology of OSMF is not known but is in close relation to the areca nut chewing. Areca nut contains primarily arecoline alkaloid which has the capacity to modulate matrix metalloproteinases, lysyl oxidases and collagenases, affecting collagen metabolism leading to an increased fibrosis.[6]

The etiological factors considered to trigger this disease process includes chewing of areca nut, deficiency of nutrients, predisposition of genes and various immunological processes.[7,8] Nutritional deficiency, primarily of iron and vitamins, over consumption of chilies and spicy food, genetic predisposition and smoking is also implicated in the etiology of OSMF. Histopathologically, OSMF is characterised initially by hyperplasia of epithelium, followed by epithelial atrophy due to loss of rete pegs, increased collagen deposition, sub-epithelial chronic inflammatory cell infiltrate, decreased vascularity, and hyalinization of tissue of submucosa and there is flat epithelium and connective tissue interface.[9,10]

The rate of malignant transformation in OSMF ranges from 7%-13% [11] and dysplastic changes is seen in 26% of OSMF lesions that is consistent with the high rate of transformation into malignancy.[12] Treatment of OSMF consists of nutritional supplements and antioxidants, physiotherapy, immunomodulatory drugs, steroids injection intra-lesionally, hyaluronidase, human placental extracts either single or in combination at initial stages of disease and surgical measures need to be taken in advanced stage.[13]

Therapeutic effects of corticosteroids are mainly anti inflammatory and direct healing action. Steroids are immunosuppressive agents that prevents or suppresses the inflammation present in oral submucous fibrosis, thus heals this condition.[14] Various forms like pastes, ointments and lotions have been used in different studies but due to better access in posterior region of oral cavity, mouthwashes are more useful than topical forms.[15] Corticosteroid mouthwashes also help in management of painful ulcers. Due to very limited success of medical and

surgical interventions because of adverse effects and recurrence.[16] Due to limitations of the present treatment options available, there is a necessity to find an effective & reliable remedy.

Life style changes along with ayurvedic treatment can provide relief to the patient without causing any side effects.[17] Various ayurvedic preparations has been used in previous studies like turmeric(curcumin), aloe-vera and tulsi for management of OSMF. The name Ksheerabalataila was first mentioned in sahasra yoga, an authentic Ayurvedic formulary of kerala. Ksheera(cow milk), Bala(sidacordifolia Linn) and Tila taila(sesame oil) are the main ingredients of this preparation. Cow milk, as we know, has all the minerals which are required for growth & development of bones, nerves and muscles, it also improves immunity and accelerates wound healing.

Sidacordifolia(Bala) is a herb from the *Malvaceae* family that is used widely in ayurvedic medicine and contains alkaloids to extent of 0.085%. Studies have reported that S. cordifolia has analgesic, anti-inflammatory & hepato-protective activities.[18,19,20]

Sesame oil is rich in antioxidants and also contains linoleic acid that gives both antibacterial and anti inflammatory properties. Hence, aim of the parallel group trial study is being conducted in department of Oral medicine & Radiology to determine **whether in Oral Submucous Fibrosis patients Ksheerabala Oil is more effective compared to steroid mouthwash in mouth opening, burning sensation & cheek flexibility**

Objectives:

In management of mouth opening, burning sensation of mouth and cheek flexibility,

- To evaluate efficacy of steroid mouthwash
- To evaluate efficacy of ksheerabala oil
- To evaluate efficacy of combination of ksheerabala oil and steroid mouthwash
- To compare efficacy of ksheerabala oil, steroid mouthwash and combination of ksheerabala oil & steroid mouthwash

Material and methods:

Research ethics approval: The research protocol is approved by the Institutional Ethics Committee (IEC) with the reference number- DMIMS(DU)/IEC/2018-19/7524.

After taking approval from Institutional Ethics Committee, the present in vivo study will be conducted in department of Oral Medicine &Radiology, Sharad Pawar Dental College and Hospital ,Sawangi(Meghe), Wardha. The sample size of 90 patients clinically diagnosed to have OSMF will be divided into three groups: Group A, B & C with 30 subjects in each group. Patients from all groups will be examined thoroughly.

Tablet Dexona 0.5mg (company name Zydus Alidac) will be purchased from the pharmacy & dispensed to the patient to use as gargle. Patient will be asked to dissolve 2 tablets each of 0.5 mg (dexamethasone IP, brand name Dexona) in 10ml of water to prepare 0.1% conc. Of **dexamethasone mouthwash** and the **Ksheerabala oil** will be prepared at the Dattatray

Ayurved Rasashala, Department of Rasa shastra and Bhaishajya Kalpana, Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod(H) Wardha. The method of preparation of ksheerabala oil is according to Ashtang Hridaya.[21] As bala i.e; Sida cordifolia is not available or rare so instead of Sida cordifolia, Abutilon indicum will be used as a bala. The useful part of bala (Abutilon indicum) is whole plant, for the preparation of oil.

Ayurvedic Formulation of ksheerabala oil:

Ingredients: 1. Bala Kashaya(decoction) – 16 parts

- Bala Kalka(paste) – 1 part
- Tila taila(sesame oil) – 4 parts
- Godugdha(cow milk) – 4 parts

Method of preparation: 1. Take all the ingredients in steel vessel and mix together and boil on moderate fire.

2. Heating is continued till all the water contents are evaporated completely.

3. On cooling, taila is filtered through doubled muslin cloth and stored in 200ml of amber colored air-tight bottle& bottle will be labelled with date of manufacturing and expiry.

Inclusion criteria:

Patients above the age of 18 years diagnosed clinically with oral submucous fibrosis will be included in study.

Exclusion criteria:

1. Subjects who are undergoing treatment for oral submucous fibrosis for last 6 months

2. Patients with TMJ problems, Pericoronitis of lower third molars etc. which may cause reduced mouth opening.

3. Subjects with past history of TB, Diabetes Mellitus & endocrinal disorders.

4. Pregnant or lactating female patients.

5. Patients with other local or systemic conditions which are known to cause burning of oral mucosa.

Total 90 subjects are divided into three groups as:

Group A : 30 patients having OSMF will be instructed to **gargle with 10 ml of 0.1% Dexamethasone for 10 min**& then spit it out, **three times daily for 1 month.**

Group B : 30 patients having OSMF will be instructed to to **gargle with 10 ml of 0.1% Dexamethasone for 10 min**& then spit it out **and** after 5 min, **gargle with 10 ml of ksheerabala oil for 10 min** & then spit out the oil, **three times daily for 1 month.**

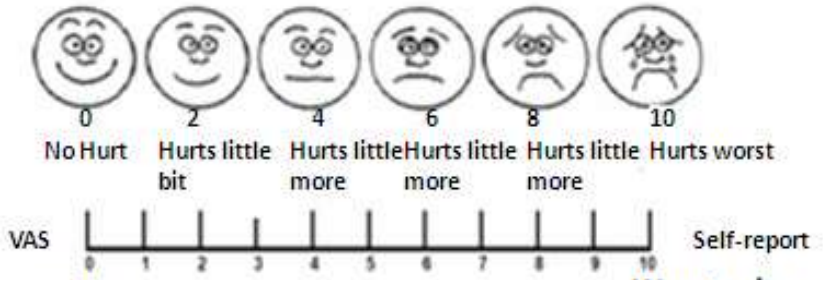
Group C : 30 patients having OSMF will be instructed to **gargle with 10 ml of ksheerabala oil for 10min** & then spit out the oil, **three times daily for 1 month.** Patients will be instructed not to consume anything for next 15 minutes and will be recalled after every 7 days

for a period of 1 month (total 4 visits for each patient). On each visit; mouth opening, burning sensation and cheek flexibility will be recorded.

1. Mouth opening:

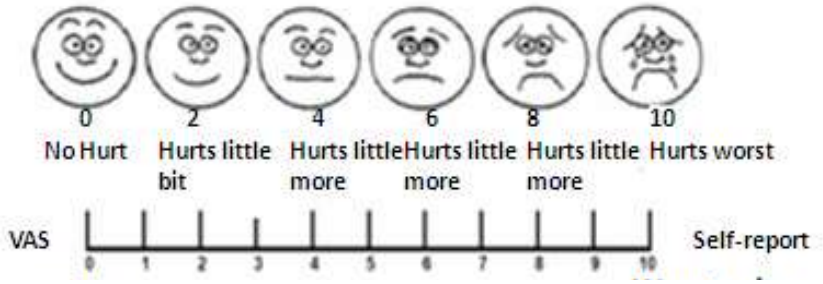
Objective: It is the distance at maximum opened mouth between the centre of incisal edges of upper central incisors and lower central incisors . In edentulous patients, the inter ridge (alveolar) distance along the midline will be measured . The inter-incisal distance will be measured on Verniercalipre (in millimetres).

Subjective: It should be evaluated by asking the patient, extent of mouth opening before and after treatment and whether he/she is satisfied with it, by scoring according to VAS scale.



2. Burning sensation:

Objective: Burning sensation will be evaluated using VAS (VISUAL ANALOGUE SCALE) before and after treatment.



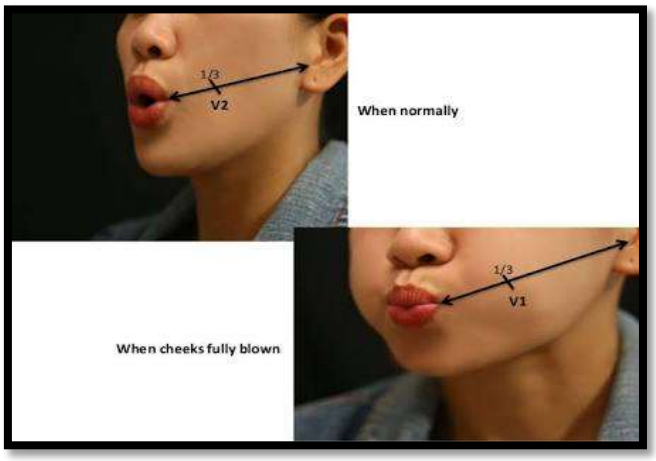
3. Cheek flexibility:

Objective: 1) Cheek blow method:

A line will be drawn from the tragus of ear to the angle of mouth. An imaginary perpendicular line from the outer canthus of ipsilateral eye will be extended downwards to intersect the ala tragus line using a protractor at 90 degree.

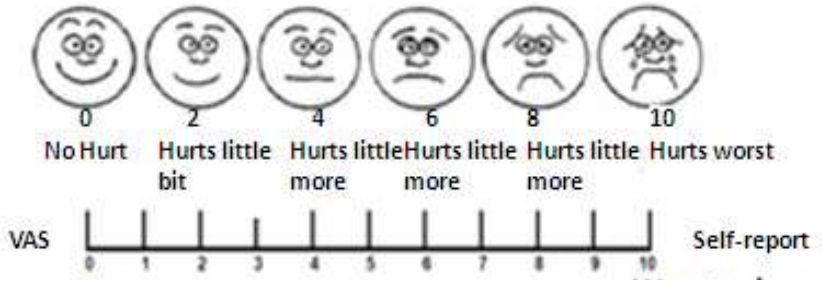
The point of intersection will be marked as a reference point. This will be done on both right and left side.The distance between two reference points will be recorded at normal centric occlusion as C1.The subject will be then asked to blow cheek fully with lips closed and the distance between the reference points will be recorded as C2.

The difference between two points (values) C2-C1, will be used as a measure of cheek flexibility.

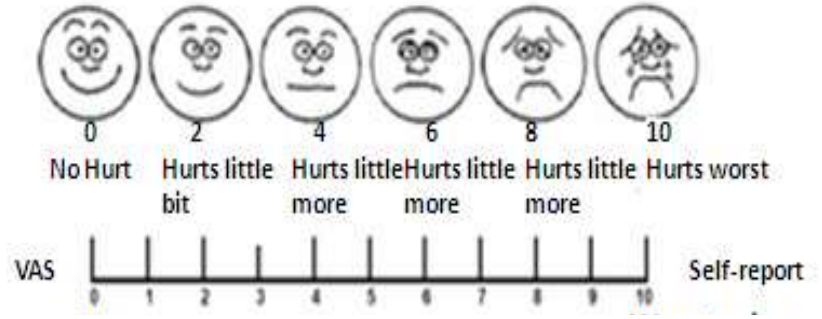


2. Palpation of fibrous bands: The fibrous bands are palpated over right buccal mucosa, left buccal mucosa, floor of the mouth, retromolar region, upper & lower labial mucosa to determine the taughtness and whether it has reduced after treatment.

After palpation of bands, staging is given



Subjective: It can be evaluated by asking patients percentage of his satisfaction with the reduced stiffness of buccal mucosa and ability to blow cheeks, before and after treatment by scoring according to VAS scale.



The grading of OSMF is done according to clinical & functional staging of Haider SM, Merchant AT, Fikree FF, Rahbar MH (1999):

Clinical and functional staging:

Clinical stage-

1- Faucial bands only
2- Faucial and buccal bands
3- Faucial, buccal and labial bands.

Functional stage-

A- Mouth opening > or equal to 20mm

B- Mouth opening 11-19mm

C- Mouth opening < or equal to 10mm

Data entry: All the obtained data will be entered in the structured tabular format

Statistical analysis: Total 90 sample size having OSMF will be divided into 3 groups and 30 sample in each group will be taken. Participants will be compared for mouth opening, burning sensation and cheek flexibility using ksheerabala oil, steroid mouthwash& combination. Mean and standard deviation will be calculated. One way anova test will be used for analysis.

Expected Results: The **primary outcome** of the study is to check mouth opening using ksheerabala oil and steroid mouthwash in OSMF patients

Secondary outcome is to check burning sensation and cheek flexibility using ksheerabala oil and steroid mouthwash in OSMF patients

Discussion:
This is an attempt to investigate the effectiveness of ksheerabala oil compared to steroid mouthwash in treatment of OSMF. Although there are various modalities available for its treatment but have some form of side- effects. Being an ayurvedic holistic formulation with minimal side-effects, ksheerabala oil can be a useful alternative. It contains sida cordifolia, sesame oil and cow milk having analgesic, anti-inflammatory & hepato-protective properties. Sesame oil is rich in antioxidants and also contains linoleic acid that gives both antibacterial and anti inflammatory properties. Even compared to steroids, ksheerabala oil can be an appropriate alternative to potentially harmful steroids. So, ksheerabala oil can be used for the treatment of OSMF. A number of articles on oral submucous fibrosis were reported [21-23]. Gondivkar et al reported on quality of life in cases of Oral submucous fibrosis [24-26]. Hande et al reported on role of hypoxia in malignant transformation of oral submucous fibrosis[27]. Balogun, S et al Effects of Separate and Combined Chronic Ingestion of Codeine and Tramadol on Feeding Behaviour of Female Albino Rats[28].Sarode et al studied the dysplastic features relevant to malignant transformation in OSMF [29]. Panchbhai reported the effect of oral submucous fibrosis on jaw dimensions[30].

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