

ASSESSMENT OF QUALITY OF LIFE, PERFORMANCE STATUS AND CLINICAL OUTCOME IN ORAL SUBMUCOUS FIBROSIS

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ABSTRACT:

Aim: The aim of this study was to evaluate the efficacy of spirulina in patients with oral submucous fibrosis; and to assess one to three months effects of disease and treatment on patient's performance and functional status, report of symptoms, and quality of life.

Materials and Methods: Hundred patients with oral submucous fibrosis were randomly divided into 2 groups. Group A and Group B. Group A (number 100) received oral Spirulina capsule 500 mg twice daily. Group B (number 100) received oral Spirulina capsule 500 mg twice daily along with topical triamcinolone acetonide 0.1%. Clinical follow up and review of all the patients was carried out at 1 month intervals for the whole trial period of 3 months.

Results: Group A showed 80% increase in mouth opening and group B showed 89% increase in mouth opening. Burning sensation of oral mucosa was decreased by 73% in group A and 81% in group B. ($Z > 1.96$, $P < 0.05$). On the quality of life head and neck 35 (QLQ-H&N35) questionnaire, all symptom scales of the quality of life were affected negatively. On the performance status scale, all the functional measures of eating demonstrated significant linear increases over time, indicating an improvement in function.

Conclusion: Spirulina is a safe and reliable modality in the management of oral submucous fibrosis.

Keywords: oral submucous fibrosis, spirulina, triamcinolone acetonide, quality of life

INTRODUCTION:

Oral submucous fibrosis (OSMF) is a potentially malignant disorder that primarily affects any part of the oral cavity and sometimes the pharynx. The disease is chronic, insidious and progressive in nature. This generalized condition of the mouth eventually becomes a debilitating disease with mucosal rigidity causing discomfort, burning and limitation of opening of the mouth. It is predominantly seen in people in southern Asian countries or southern Asian immigrants to other

parts of the world.^[1] The prevalence rates of OSMF in India range from 0.2% to 1.2%.^[2,3] The condition carries a high relative risk for malignant transformation (7.5%).^[4]

A variety of etiologic factors including betel nut alkaloids, capsaicin, autoimmunity, genetic predisposition and malnutrition have been suggested. The most common of which is chewing areca nut.^[5] Treatment of OSMF is a challenge, especially as the disease

progresses. To aid in treatment planning, a classification system of OSMF based on interincisal opening (MIO) was followed (Khanna et al, 1995).^[6] Group 1 - Early OSMF 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 of OSMF is multimodal and 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. All available treatments (vitamins, steroids, oral iron preparations, local submucosal injections of steroids, hyaluranidase and surgical excision of the fibrous bands, etc) give the patient only symptomatic relief, which is short lived. Hence a new treatment modality like spirulina was tried in this study. Spirulina is a blue-green alga (cyanobacterium) that has been consumed as food in many countries since ancient times. It is presently marketed as a food supplement due to its high contents of proteins, g-linolenic acid, vitamins and minerals.^[7] Spirulina is listed by the US Food and Drug Administration under the category Generally Recognized as Safe (GRAS).^[8] Spirulina and many other Cyanobacteria had been found to exhibit many immune-stimulating and antiviral activities not only in-vitro but also in animals and human volunteers. It had been found to activate macrophages, NK

cells, T cells, B cells, and to stimulate the production of antibodies and cytokines. It enhances Interferon gamma (IFN-g) production in an interleukin12, 18 (IL-12/IL-18)- dependent fashion.^[9-11] In addition, Spirulina is a source of b-carotene, a-tocopherol, and phycocyanin, molecules with antioxidant properties.^[12]

Oral submucous fibrosis remains a considerable challenge to both patients and health care providers. Evaluation of OSMF must also include QOL and functional end points as well as disease control. OSMF patients have significant and extensive impairment, including trismus, speech disorder, dry mouth, stiffening/constriction of local tissues, chewing and swallowing dysfunction. None of the interventions reported so far have examined any improvement in oral health-related quality of life (QOL) among patients treated for OSMF. Both burning and trismus can affect oral function, oro-facial appearance and social interaction. Hence there is a need to evaluate how well those treated for OSMF can perform common functions. Therefore, this study was undertaken to evaluate the efficacy of spirulina along with tiamcinolone acetonide in the management of oral sub mucous fibrosis; to evaluate the effect of OSMF on patient's quality of life (QOL) and performance status; and to assess one to three months effects of disease and treatment on patients performance and functional status, report of symptoms, and QOL.

MATERIALS AND METHODS

Two hundred patients presenting with signs and symptoms suggestive of oral sub mucous fibrosis were selected from the department of oral medicine and radiology, Bhabha College of dental sciences, Bhopal, India. The following parameters were used in the establishment of diagnosis; a positive history of chewing of areca nut or one of its preparations, difficulty in swallowing and chewing, burning sensation on eating spicy food; and restricted mouth opening and changes in the oral mucous membrane, including the presence of palpable fibrous bands, stiffness and blanching. A detailed case history of all patients was recorded and diagnosis of OSMF was made by clinical examination. The patients with OSMF group 1, 2 and 3 according to classification by Khanna et al^[6] were included in this trial. Patients with OSMF group 4a and 4b were not included in this trial and were referred for surgical therapy. All the patients had habit of betel nut chewing since 1 to 15 years. Patients with any systemic disorder were not included in this trial.

After the diagnosis, each patient was informed about the condition and its premalignant potential and was advised to discontinue the use of areca nut in all preparations. Written consent letter was obtained from each patient.

100 oral sub mucous fibrosis patients were divided into two groups, Group A and Group B. Group A (number 50) received oral Spirulina capsule 500 mg twice daily. Group B (number 50)

received oral Spirulina capsule 500 mg twice daily along with topical triamcinolone acetonide 0.1%.

The patients were comfortably seated in dental chair and an elaborated history was noted which included chewing habits, type, form, brand used, frequency and duration of chewing, site of keeping the quid and duration. A thorough clinical examination was performed and recorded in the proforma. The objective and subjective variables namely, burning sensation and measurement of maximum mouth opening were recorded.

Mouth opening was assessed by measuring the interincisal distance from the mesioincisal edge of the upper left central incisor tooth to the mesioincisal edge of the lower left central incisor tooth. The measurement was done by using a geometric divider and scale and is recorded in millimetres. The intensity of burning sensation was determined using a Visual Analogue Scale (VAS) of 0-10 with 1 mm division, where 0 is no burning sensation and 10 is the worst possible burning sensation. The patients were asked to mark the VAS at a point which best represented the burning sensation at that visit.

Quality of life and performance status were evaluated by self-administered questionnaire which was given to the patients. Patients were assessed before treatment (baseline) and 1, 2 and 3 months after completion of treatment.

The following assessment tools were used:

1. European organization for research and treatment of cancer (EORTC) QLQ– Head and Neck 35. The head & neck cancer module is meant for use among a wide range of patients with head & neck cancer, varying in disease stage and treatment modality.^[13,14] The module comprises 35 questions assessing symptoms and side effects of treatment, social function and body image/sexuality. The head & neck cancer module incorporates seven multi-item scales that assess pain, swallowing, senses (taste and smell), speech, social eating, social contact and sexuality. There are also eleven single items. For all items and scales, high scores indicate more problems.
2. The Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) consists of three subscales: Normalcy of Diet, Understandability of Speech, and Eating in Public. The interviewer will rate the patient on each subscale based on the patient's responses to targeted questions. Scores on each subscale range from 0 to 100, with higher scores indicating better performance.^[15]

Post treatment follow-up involved the evaluation of the patient once in one month over a period of three months.

RESULTS:

Among the 100 OSMF patients, 96 (96%) cases were detected in males and 4 (4%)

in females. The age range of patients was between 16 to 44 years. The most commonly affected age group was 21-30 year followed by 14-20 years, 31-40 years and 41-50 years. The buccal mucosa was the site most affected, followed by retromolar region, labial mucosa, palate, floor of the mouth. Burning sensation in oral mucosa was the most frequent symptom present in 87%, while recurrent ulcerations were present in 26% patients. Group A showed 80% increase in mouth opening and group B showed 89% increase in mouth opening. Burning sensation of oral mucosa was decreased by 73% in group A and 81% in group B. ($Z > 1.96$, $P < 0.05$) (Table 1). No reportable complications or side effects were recorded from any of the patients included in the study.

The QLQ-H&N35 questionnaire was applied before starting the treatment, and subsequently at 1, 2 and 3 months later. After one, two and three month after the treatment, compared to before starting the treatment, all symptom scales of the quality of life were affected negatively. After the 3rd month after the treatment, there was a decrease in the pain, in swallowing problems, in speech problems, in problems with eating in a social environment, in problems with socializing with other people, in feeling sick, in loss of sexual desire and in opening mouth.

Compared with Group A, Group B had better outcome in mouth opening, burning sensation, pain, swallowing,

senses (taste/smell), speech, social eating, social contact, teeth, dry mouth, sticky saliva, and feeling ill, but with statistically significant difference in pain, senses (taste/smell), speech, social eating, social contact, teeth and opening mouth.

Functional measures related to eating improved over time with normalcy of diet, public eating, and understandability of speech, all increasing between 1, 2 and 3 months post treatment. Linear regression coefficients were calculated for each measure across the 100 subjects. All the functional measures of eating (PSSD, PSSE and PSSS) demonstrated significant linear increases over time, indicating an improvement in function. PSSD had a mean regression coefficient of 4.47 ($p < 0.005$), PSSE had a mean regression coefficient of 2.51 ($p < 0.005$), and PSSS had a mean regression coefficient of 5.23 ($p < 0.005$).

DISCUSSION:

Spirulina is a microscopic and filamentous cyanobacterium that derives its name from the spiral or helical nature of its filaments. It has a long history of use as food and it has been reported that it has been used during the Aztec civilization.^[16] Spirulina refers to the dried biomass of *Arthrospira platensis*, an oxygenic photosynthetic bacterium found worldwide in fresh and marine waters. This alga represents an important staple diet in humans and has been used as a source of protein and vitamin supplement in humans without any significant side-effects. Apart from

the high (up to 70%) content of protein, it also contains vitamins, especially B12 and provitamin A (β -carotenes), and minerals, especially iron. It is also rich in phenolic acids, tocopherols and γ -linolenic acid. Spirulina lacks cellulose cell walls and therefore it can be easily digested.^[16]

In our study spirulina significantly reduced the signs and symptoms of OSMF ($Z > 1.96$, $P < 0.05$). Our results were similar to one study performed on fifty-eight patients with oral submucous fibrosis in which patients were randomly divided into 3 groups, evaluated weekly over a 2-month period. Patients of group A ($n = 21$) received 16 mg of lycopene, those of group B ($n = 19$) received 16 mg of lycopene along with biweekly intralesional steroid injections, and those of group C ($n = 18$) were given a placebo. Mouth-opening values for the patients showed an average increase of 3.4 mm, 4.6 mm, and 0.0 mm for patients in groups A, B, and C, respectively.^[17]

Corticosteroids are also commonly used in the treatment of oral submucous fibrosis. In one study 96 patients with oral submucous fibrosis received four regimens of treatment - local dexamethasone, local hyaluronidase, local combination of dexamethasone and hyaluronidase, and local placental extract. The patients were followed up for a period varying from 3 months to 2 years. The group of patients receiving hyaluronidase alone showed quicker improvement in symptoms although its

combination with dexamethasone gave somewhat better longer-term results. Thus they recommended a new regimen for the treatment of submucous fibrosis.^[18] Another study divided three hundred twenty-six untreated patients suffering from oral submucous fibrosis, into two groups. Group 1 patients were given biweekly submucosal injections of triamcinolone 10 mg/mL in 1 ml of lidocaine 2% and hyaluronidase 1,500 IU. Group 2 patients were given topical vitamin A 50,000 IU in the form of chewable tablets once daily, oral ferrous fumarate tablets in a dose of 200 mg once daily, and topical betamethasone drops (0.5 mg/mL) four times a day for 3 weeks. The patients were followed up for a period of one year. The conventional treatment with injections was found to be hazardous, whereas the conservative treatment was found to be safe. Both treatments were purely palliative.^[19]

Turmeric extract and turmeric oil have shown chemoprotective effect against chemically-induced malignancies in experimental animals. They can reverse precancerous changes in oral submucous fibrosis in humans. The use of turmeric or *Curcuma longa* Linn as a spice and household remedy has been known to be safe for centuries. In one study it was observed that turmeric oil decreased the number of micronucleated cells both in exfoliated oral mucosal cells and in circulating lymphocytes in patients with OSMF. Turmeric oleoresin was found to be more effective in reducing the

number of micronucleated cells in oral mucosal cells ($P < 0.001$).^[20]

The QLQ-H&N35 questionnaire was applied before starting the treatment, and subsequently at 1, 2 and 3 months later. After one, two and three month after the treatment, compared to before starting the treatment, all symptom scales of the quality of life were affected negatively. After the 3rd month after the treatment, there was a decrease in the pain, in swallowing problems, in speech problems, in problems with eating in a social environment, in problems with socializing with other people, in feeling sick, in loss of sexual desire and in opening mouth. Compared with Group A, Group B had better outcome in mouth opening, burning sensation, pain, swallowing, senses (taste/smell), speech, social eating, social contact, teeth, dry mouth, sticky saliva, and feeling ill, but with statistically significant difference in pain, senses (taste/smell), speech, social eating, social contact, teeth and opening mouth. Gunsoy B et al reported that EORTC QLQ-C30 questionnaire parameters on social functioning and financial difficulties, and EORTC QLQ-H&N35 questionnaire parameters on speech problems, reduced sexuality, and nutritional support revealed statistically meaningful results ($p < 0.001$).^[21] Chaukar DA et al suggested that the EORTC QLO-C30 and the QLQ-H&N 35 are reliable and valid questionnaires when applied to a sample of head and neck cancer patients in India.^[22] Bjordal K et al stated that the QLQ-H&N35, in conjunction with the QLQ-C30, provides a valuable

tool for the assessment of health-related quality of life in clinical studies of H&N cancer patients before, during, and after treatment with radiotherapy, surgery, or chemotherapy.^[14]

Functional measures related to eating improved over time with normalcy of diet, public eating, and understandability of speech, all increasing between 1, 2 and 3 months post treatment. Linear regression coefficients were calculated for each measure across the 60 subjects. All the functional measures of eating (PSSD, PSSE and PSSS) demonstrated significant linear increases over time, indicating an improvement in function. PSSD had a mean regression coefficient of 4.47 ($p < 0.005$), PSSE had a mean regression coefficient of 2.51 ($p < 0.005$), and PSSS had a mean regression coefficient of 5.23 ($p < 0.005$). List MA et al.^[15] showed that the pattern of correlations between FACT-H&N and PSS-HN subscales supported the scales' construct validity. The strongest and most significant associations were observed between PSS-HN Normalcy of Diet and Eating in Public, and the head and neck subscale (HNS) of FACT-H&N, both of which were designed to measure the unique problems of head and neck cancer patients. More modest associations were observed between subscales measuring physical and functional areas of performance, social functioning, and emotional well-being. The PSS-HN provides unique information, independent of that

provided by the Karnofsky or the FACT-H&N. This study supported the multidimensional nature of QL for head and neck cancer patients, and thus the importance of assessing disease specific concerns in addition to general health status when assessing functional and QL outcome. Since ours was the first study assessing quality of life and performance status in OSMF, it was not possible to compare the results with other studies on head and neck cancer in a significant manner. The data presented here have a number of clinical applications. First, they can be used by clinicians to educate and prepare patients for the effects of their treatment, the acute declines as well as possible patterns of recovery. Second, the data point to a number of areas for possible intervention. Areas in which patients show no or minimum recovery might reasonably be selected as targets for intervention.

In our study there were no reported instances of side effects or intolerance to lycopene, triamcinolone acetonide and spirulina. There was significant improvement in mouth opening and relief from fibrotic bands. Subjective symptoms of intolerance to spices and burning sensation of mouth were also recorded significant improvement at the end of three months. Thus from this study it can be concluded that spirulina is a safe and reliable modality in the management of oral submucous fibrosis.

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TABLES:

Table 1: Mode of management in oral submucous fibrosis

Mode of management	No. of patients	Relief of symptoms/signs		
		Mouth opening	Burning sensation	
Spirulina 500 mg BD	50	80%	73%	Z > 1.96 P < 0.05
Spirulina + Triamcinolone acetone 0.1 %	50	89%	81%	