RESEARCH ARTICLE

Editorial Process: Submission:03/23/2021 Acceptance:04/21/2022

Clinical Assessment of Efficacy of Omega 3 in Oral Submucous Fibrosis Patients - A Randomized Controlled Trial

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Abstract

Background: Oral submucous fibrosis (OSMF) is a chronic, potentially malignant condition affecting the oral cavity. Omega 3 has shown innumerable health benefits in yesteryears. So, the aim of the study was to evaluate the efficacy of Omega 3 in the medical management of this disease. **Methods:** A randomized controlled trial was designed and 48 clinically confirmed patients of OSMF (24 in each group) completed the study. Patients of both the groups were given biweekly intralesional injections of dexamethasone 1.5ml, hyaluronidase 1500 IU mixed with lignocaine for 6 weeks. Additionally, group A received a placebo (lactose capsule) for 3 months while group B received 1gm of omega 3 (flaxseed oil) three times daily continuously for 3 months. Patients were followed every month for 3 months and then, after 6 months and one year. **Results:** During the first two months, improvement was observed in both the groups independently but intergroup comparison showed no significant difference. However, after 3 months statistically significant ($p<0.05$) improvement among all three clinical parameters i.e. inter-incisal distance (mean improvement in group A = 3.79±1.07mm and group B = 6.58±1.24mm, p=0.019), tongue protrusion (mean improvement in group A = 1.87±1.54mm and group B = 4.62±1.78mm, p=0.044) and cheek flexibility (mean improvement in group A = 2.08±1.38mm and group B = 3.50±1.84mm, p=0.035) was observed in group B when compared to group A. In contrast, statistically significant improvement in burning sensation was observed after one month itself in group B when compared to group A (mean drop in group A = 2.5±0.78 points and group B = 6.0±1.144 points, $p<0.05$). **Conclusion:** Omega 3 in conjunction with intralesional injections is an effective therapy when compared to intralesional injections alone in treatment of patients with OSMF (grade II and III) with no side effects.

Keywords: OSMF- OSF- oral submucous fibrosis- Omega 3- treatment

Asian Pac J Cancer Prev, **23 (4)**, 1185-1192

Introduction

Oral submucous fibrosis (OSMF) is a potentially malignant condition which is complex, irreversible, chronic and inflammatory in nature affecting the patient's quality of life significantly (Chaudhry et al., 2020; Memon et al., 2021). With a reported prevalence rate of 0.2% to 2.01% worldwide, prevalence rates as high as 6.3%-7.85% are also reported in some parts of India (Nigam et al., 2014; Varghese et al., 1986). A recent study from Taiwan reported the increase in prevalence of OSMF from 8.3 (per 105) to 16.2 (per 105) over a period of seventeen years (Yang et al., 2018). The malignant transformation rate of OSMF ranges from 2.3% (Murti et al., 1985) to 30% (Bari et al., 2017). Chewing areca-nut is the main causative agent and its use is noticed more among wage earners, laborers and tea sellers when compared to other professionals like employed workers, managers and engineers (Tariq et al., 2020). Pathophysiology involves the release of alkaloids and flavonoids from the areca-nut that undergo metabolism and initiate the secretion of transforming growth factor – beta (TGF-β); in particular, with other cytokines. All this acts as a constant source of irritation to oral tissues resulting in juxta-epithelial inflammation (Rajalalitha and Vali et al., 2005; Sheshaprasad and Pai, 2018).

Medicinal treatment is favored over surgery and it can not only provide relief to these patients, but can also improve their oral health related quality of life (Memon et al, 2022). Many drugs have been tried till date like corticosteroids (Aara et al., 2012; Datarkar et al., 2020; James et al., 2015; Lanjekar et al., 2020), anti-oxidants (Lanjekar et al., 2020; Patil et al., 2015; Selvam and Dayanand AA, 2013), anti-fibrotic agents (Jain et al. 2016; Sheshaprasad and Pai, 2018), herbal medicines and nutritional supplements (Annigeri and Jadhav 2015; Jain et al. 2016; Lanjekar et al., 2020), which provide varying degrees of benefits, due to the defiant nature of this disease (Warnakulasuriya and Kerr, 2016). Moreover, some of them have definite adverse effects (Poljsak

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and Milisav, 2018; Sheshaprasad and Pai, 2018; Stacey and McEleney, 2021). This warrants the need for more studies on exploration of other agents, to provide more improvement when compared to current standards of treatment with minimal or no side effects.

Functional foods are described as foods that not only provide basic nutritional requirements, but also have additional known health-promoting benefits (Alkhatib et al., 2017; Niva, 2007). Flax, in the form of seeds or seed-derived oil, is a "functional food" recognized for its exceptional nutritional value due to its high concentration of fiber-based lignans and large amounts of polyunsaturated fatty acids (Oomah and Mazza, 1999; Parikh et al., 2019) especially omega 3. Omega 3 has beneficial effects in managing chronic inflammatory diseases including chronic periodontitis (Castro Dos Santos et al., 2020; Kujur et al., 2020) and recurrent apthous stomatitis (Khouli and Gendy, 2014). It is also shown to prevent cardiac fibrosis and cardiac dysfunction by blocking TGF-β1 (Chen et al., 2011).

However, the effectiveness of omega 3 in treatment of OSMF is still unknown. In our pilot study omega 3 has shown promising results in alleviating subjective symptoms (Raizada et al., 2017). It improved other clinical parameters as well but results were statistically not significant. Therefore, a study with larger sample size and duration was conducted for definitive results.

Materials and Methods

Methodology

An open labelled randomized controlled trial was designed according to ethical principles and declaration of Helsinki. Study was conducted in Dr. D. Y. Patil Dental College and Hospital, Pimpri, Pune after obtaining clearance from the institutional ethical committee. Clinically confirmed adult patients of OSMF (grade II and III) (Khanna and Andrade, 1995) were included in the study. Informed consent was taken in English/local language from all subjects. A detailed case history including habit history with details of duration, in years, frequency of chews per day and kind of areca nut used was recorded. OSMF patients who were >18 years of age, physically healthy and well oriented in time, space and not on any treatment for the same were included in the study. In case they were, then such treatment was stopped and a wash out period of 2 weeks was given. Patients suffering from any other systemic diseases like diabetes, hypertension, cardiovascular diseases, bleeding disorders, renal dysfunction, liver disorders, mucosal disease or any other skin lesions, patients on any drug therapy or with a known allergy or contraindication to study medications were excluded from the study.

Dexamethasone was purchased from the market while hyaluronidase was sponsored by Shreya life sciences (Mumbai, Maharashtra, India). Alvel omega 3 oil was purchased from Real world nutrition laboratory and every 2ml of this oil had 1gm of omega 3. Vitamin E in small amount (500ppm alfa-tocopherol) was also added as a stabilizer and antioxidant to prevent the oxidation of the oil. It also contained omega 9 (0.2gms per ml) and omega 6 (0.15gms per ml). Certificate of analysis of alvel omega 3 flax seed oil, and certificate of registration of the company is included for reference (supplementary material no.1 and 2).

Lactose capsules were used as placebo which were arranged from AISSMS (All India Shri Shivaji Memorial Society) college of pharmacy, Pune. Weight of lactose per capsule was 0.95gms. Placebo was given just to rule out the psychological aspect of the patient. The study was registered under clinical trials registry – India, with registration number CTRI/2017/09/009953.

A pilot study was conducted initially (Raizada et al., 2017) and accordingly sample size was calculated by Winpepi which came out as 8 patients in each group at significance 5% and power of 80%. However, 80 patients were selected taking attrition into consideration owing to the limited compliance of OSMF patients, and as expected only 48 out of them completed the study. Patients were randomly assigned to two groups A and B. Group A was given biweekly intralesional injections of dexamethasone 1.5 ml and hyaluronidase 1500 IU mixed with lignocaine for 6 weeks and the placebo for 3 months. Patients were asked to open their mouth and wherever palpable bands were present in buccal mucosa, injections were given at that site bilaterally.

Group B was also given biweekly intralesional injections of dexamethasone 1.5 ml and hyaluronidase 1500 IU mixed with lignocaine along with 3 gm of omega 3 per day. Every 2 ml of flax seed oil contained 1gm of omega 3. So, patients were advised to take 2ml of flaxseed oil orally by medicine dropper three times a day continuously for 3 months. Patients were followed every month for 3 months, then after 6 months and then after one year.

Interincisal distance (IID) was recorded as the distance between the upper and lower central incisors when maximally extended with mouth wide open by Vernier calipers. Tongue protrusion (TP) was measured as the distance from the mesio-incisal edge of maxillary central incisor to the tip of the protruded tongue. Cheek flexibility (CF) was recorded by measuring tape based on the distance between specified points on the cheek skin, where V2 was marked at one third the distance from the angle of the mouth to the tragus of the ear. Subject was then asked to blow his cheeks fully and the distance V1 was measured between the two points marked on the cheek. CF was calculated as the difference between the two (V1-V2). Three readings were taken for all the parameters and the mean of all three readings was recorded. Burning sensation was determined by use of a visual analogue scale (VAS -0-10). All patients were advised to do mouth exercises 2-3 times a day for whole one year so as to prevent any relapses.

Statistical analysis used- Age distribution in both the groups, baseline comparison and intergroup comparison for quantitative data was done by t test. Patient distribution in both the groups based on staging was compared by chi square test. Mean, standard deviation and p value was calculated by repeated measures ANOVA test. For qualitative data i.e. visual analogue scale, Friedman test was used for within group comparison while

Mann-Whitney U test was used for intergroup comparison.

Results

A total of 48 patients were included in the study, 24 in each group. The study sample included the patients with age groups of 19 to 52 with maximum no. of patients in the age group of 21–30 years. The average age of patients was 30.79. Out of 48 patients, 2 patients were in age range of 18-20, 21 in age range of 21-30, 19 in age range of 31-40, 5 in age range of 41-50 and 1 in age range of 51-60. Mean age in control group was 31.67±8.781 while in intervention group it was 29.92±6.086. t test was used to compare age in both the groups and p value was 0.426 > 0.05 suggesting that age was not significant and has no effect on the outcome. Out of 48 patients, 44 patients were males and 4 patients were females. So male-to-female ratio was 11:1. No. of females was too small for any further comparison.

All the patients consumed areca-nut in one or the other form. 41 patients were gutkha chewers (areca-nut is one of the major constituent of gutkha-the smokeless tobacco), 4 patients consumed areca-nut with misri, 2 patients were panmasala chewers and 1 consumed areca-nut in form of paan with scented tobacco. Out of 48 patients 42 were also alcoholic and 4 patients use to smoke also. All 48 patients had a mixed diet.

Only grade II and grade III patients were included in the study. Out of 48, 27 patients had grade II OSMF (12 in group A and 15 in group B) while 21 patients had grade III OSMF (12 in group A and 9 in group B). Chi square test was used for intergroup comparison and p value came out as 0.281>0.05 suggesting that both the groups were comparable based on grading and difference seen in both the groups based on grading was not significant. Moreover, grading is dependent on interincisal distance which was taken as a continuous variable. So, considering grading as a cofactor was not required.

Baseline comparison of all the parameters is shown in Table 1. t test was used and p value was >0.05 for all the parameters in both the groups indicating that they were comparable at baseline. The mean clinical improvement in both the groups irrespective of grading is shown in Figure 1.

The mean improvement of mouth opening of grade II patients was 3.91±0.903mm and grade III patients was 3.66±1.15 mm in group A. While the mean improvement in grade II patients was 7.13±1.06 mm and grade III patients was 5.66±1.0 mm in group B. The mean improvement of TP in grade II patients was 2.33±1.49mm and grade III patients was 1.41±1.5 mm in group A and 4.93±1.83 mm and 4.11±1.69 mm respectively in group B. The mean improvement of CF in grade II patients was 2.58±1.54 mm and grade III patients was 1.58±1.37 mm in group A while the mean improvement in grade II patients was 3.8±2.14 mm and grade III patients was 3±1.11 mm in group B. The mean decrease in burning sensation in grade II patients was 5.41±1.44 and 6.5±1.0 in grade III patients in group A. While the mean decrease in burning sensation in grade II patients was 8.06±1.66 and 9.22±0.83 in grade

Table 1. Baseline Comparison of All Four Parameters

Parameter	Group A(Mean and standard deviation)	Group B (Mean and Standard deviation)	p value/Sig. – t test
IID0	24.46±5.429	25.46±4.293	0.483
TP0	34.63±10.008	39±12.827	0.194
CF0	5.29±1.6	5.54±2.187	0.657
VAS0	8.54±1.53	8.58±1.5	0.925

IID0, Inter-incisal distance at baseline; TP0, Tongue protrusion at baseline; CF0, Cheek flexibility at baseline; VAS0, Visual analogue scale value at baseline; (Values of IID, TP, CF recorded in mms and VAS in points)

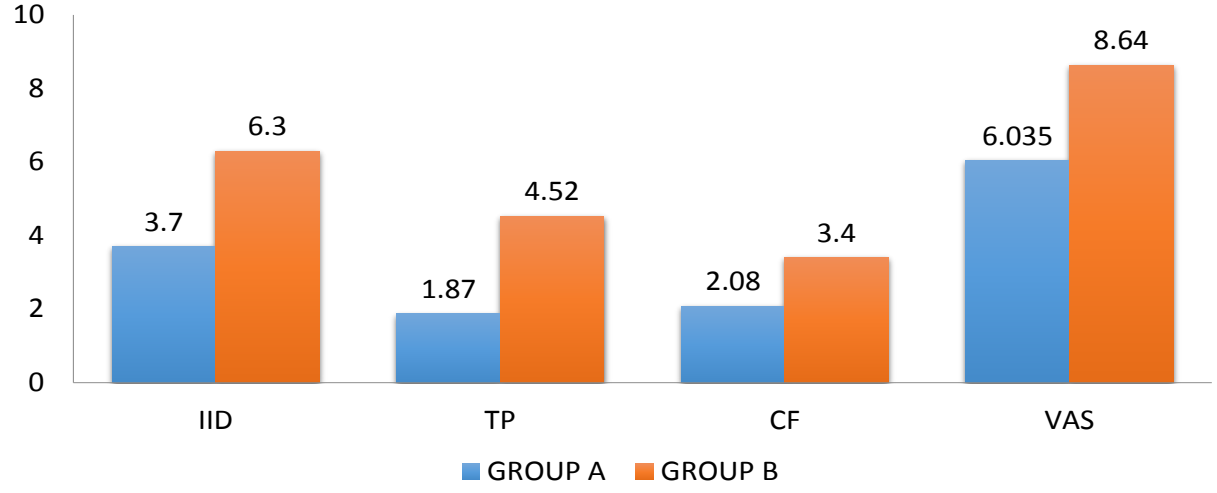

Figure 1. Improvements in the Clinical Parameters Assessed in Both the Groups. IID, Inter-incisal distance; TP, Tongue protrusion; CF, Cheek flexibility; VAS, Visual analogue scale value. (Values of IID, TP, CF recorded in mms and VAS in points)

Table 2. Intergroup Comparison based on IID, TP and CF

Parameter	Group A (Mean and std. Deviation)	Group B (Mean and std. Deviation)	Intergroup comparison – Sig. by ANOVA
IID0	24.46± 5.429	25.46 ±4.293	0.483
IID1	26.37± 5.686	28.17 ±4.430	0.23
IID2	28.25 ±5.720	30.58 ±4.836	0.134
IID3	28.25± 5.720	32.04 ±5.034	0.019<0.05
IID 6	28.16±5.64	32.04±5.03	0.02
IID12	28.08±5.58	31.91±5.02	0.03
TP0	34.63± 10.0	39.0± 12.8	0.194
TP1	35.67± 10.42	41.00± 12.98	0.123
TP2	36.5± 10.6	42.54± 13.19	0.087
TP3	36.5± 10.6	43.6± 13.12	0.044<0.05
TP6	36.41±10.54	43.54±13.13	0.045
TP12	36.29±10.43	43.4±13.18	0.046
CF0	5.29±1.6	5.54±2.1	0.657
CF1	6.42±1.9	7.17±2.3	0.238
CF2	7.38±2.2	8.33±2.6	0.19
CF3	7.38±2.2	9.04±3.0	0.035<0.05
CF6	7.29±2.23	9.04±2.99	0.036
CF12	7.20±2.16	8.87±3.19	0.037

IID0,1,2,3, 6, 12 - Interincisal distance at baseline, after 1,2,3,6,12 months; TP0,1,2,3, 6, 12 – Tongue protrusion at baseline, after 1,2,3,6,12 months; CF0, 1,2,3,6,12- Cheek flexibility at baseline, after 1,2,3,6,12 months; (Values of IID, TP, CF recorded in mms)

III in group B. Intergroup comparison of IID, TP and CF is shown in Table 2, and VAS is shown in Table 3

Both the groups have shown statistically significant improvement in mouth opening, TP, CF and VAS from baseline to post treatment ($p<0.05$) but by the end of three months' group B has shown statistically significant improvement when compared to Group A in all the parameters. As the response to treatment might differ in different grades of OSMF, all the four parameters were also assessed based on grading (Table 4 and 5). So, in both the grades, group B has shown statistically significant improvement when compared to group A except for cheek flexibility in grade II patients where results were not significant ($p=0.094$).

All patients complained of pain after taking intralesional injections for 1–2 days which subsided by itself after that. No other adverse effects were reported during the treatment period. Patients were followed up till 1 year, and no episode of bleeding or any significant change in clinical data was noted.

Discussion

The average age of patients in our study was 30.79, with most of the patients falling in the age range of 21-30 similar to other studies, (Annigeri and Jadhav, 2015; Jain et al., 2016; Aara et al., 2012) although average range between 30-35 years is also reported (Singh et al., 2016). In the present study, majority of the participants enrolled were males in comparison to females which is similar to all the studies done earlier showing a male preponderance of the disease (Annigeri and Jadhav, 2015; Jain et al., 2016; Singh et al., 2016). The use of areca-nut in different forms like tobacco, paan masala etc. is definitely the whole and sole reason for this disease (Annigeri and Jadhav, 2015).

To the best of our knowledge no documentary evidence in English literature is present till date on the role of omega 3 in OSMF patients. So, a comparative analysis was not possible. However, a comparative analysis of results of omega 3 with other related treatment modalities was done.

We noted a mean improvement of 6.3 mm in interincisal distance in our study group which is more than

Table 3. Intergroup Comparison based on Visual Analogue Scale

Parameter	Group A (Mean and std. Deviation)	Group B (Mean and std. Deviation)	Mann-Whitney U Test Intergroup comparison Sig.
VAS0	8.54±1.5	8.58±1.5	0.957
VAS1	6.04±1.4	2.58±1.41	<0.05
VAS2	4.13±1.32	0.67±0.91	<0.05
VAS3	2.58±1.38	0.08±0.28	<0.05
VAS6	2.54±1.44	0.083±0.28	<0.05
VAS12	2.41±1.44	0.083±0.28	<0.05

Footnotes- VAS 0,1,2,3, 6, 12 – Visual analogue scale at baseline, after 1,2,3,6,12 months recorded in points

Table 4. Mean Improvement in IID, TP and CF in both the Groups in Grade II and Grade III OSMF at Various Time Intervals and Its Comparative Analysis by ANOVA Test (Diff means improvement seen in that parameter from baseline)

Parameter	Grade II			Grade III		
	Group A (Mean and standard deviation)	Group B (Mean and standard deviation)	Sig. /p value-ANOVA	Group A (Mean and standard deviation)	Group B (Mean and standard deviation)	Sig. /p value-ANOVA
Diff _IID1	2.08±0.66	2.73±1.16	0.098	1.75±0.75	2.66±1.0	0.027
Diff _IID2	3.91±0.90	5.6±0.9	0	3.66±1.15	4.33±0.66	0.163
Diff _IID3	3.91±0.90	7.13±1.06	0	3.66±1.15	5.66±1.00	0.001
Diff _IID6	3.83±0.80	7.13±1.06	0	3.58±1.08	5.66±1.00	0
Diff _IID12	3.75±1.00	7±1.19	0	3.49±1.15	5.55±1.13	0.001
Diff _TP1	1.41±0.90	2.13±1.3	0.118	0.666±0.98	1.77±0.66	0.009
Diff _TP2	2.33±1.49	3.80±1.69	0.027	1.41±1.50	3.11±1.16	0.011
Diff _TP3	2.33±1.49	4.93±1.83	0.001	1.41±1.50	4.11±1.69	0.001
Diff _TP6	2.24±1.32	4.80±1.89	0.001	1.33±1.46	4.11±1.69	0.001
Diff _TP12	2.08±1.25	4.74±1.94	0.002	1.25±1.38	4.00±1.73	0.002
Diff _CF1	1.33±0.98	1.6±1.12	0.523	0.916±0.99	1.66±1.22	0.138
Diff _CF2	2.58±1.24	3.0±1.6	0.467	1.58±1.37	2.44±1.13	0.144
Diff _CF3	2.58±1.24	3.8±2.14	0.094	1.58±1.37	3.00±1.11	0.021
Diff _CF6	2.41±1.38	3.80±2.14	0.081	1.58±1.37	3.00±1.11	0.021
Diff _CF12	2.33±1.27	3.73±2.21	0.106	1.50±1.44	2.89±1.06	0.018

Diff _IID1,2,3,6,12, Difference in Interincisal distance from baseline, after 1,2,3,6,12 months; Diff_TP1,2,3, 6, 12 – Difference in Tongue protrusion from baseline, after 1,2,3,6,12 months; Diff_CF1,2,3,6,12- Difference in Cheek flexibility from baseline, after 1,2,3,6,12 months; (Values of IID, TP, CF recorded in mms)

studies on intralesional injections alone (3.4 mm) (Selvam and Dayanand, 2013), curcumin (1.25 mm) (Yadav et al., 2014), combination therapy of mucoadhesive semisolid gel of curcumin 1%, a combination of triamcinolone acetonide 0.1% and hyaluronidase 1% mucoadhesive semisolid gel (4.05 mm) (Lanjekar et al., 2020), curcumin gel (5.45mm), curcumin mucoadhesive patches (5.9 mm) (Chandrashekahr et al., 2020), pentoxyphylline (5.9mm) (Patil et al., 2015), aloevera (4.3 mm) (Patil et al., 2015), garlic along with pentoxyphylline (5 mm) (Jain et al., 2016), lycopene/multivitamin A-Z capsules with intralesional injections(4.3-4.9mm) (Selvam and Dayanand, 2013), and is similar to spirulina(6 mm) (James et al., 2015) but less than study on prednisolone mouthwash and antioxidant capsule (10.46 mm) (Datarkar et al., 2020).

Similarly, improvements seen in our study group in respect to tongue protrusion and cheek flexibility is better than pentoxyphylline alone (1.7 mm, 2.7 mm) (Aara et al., 2012), with curcumin (0.38 mm) (Yadav et al., 2014) or with intralesional injections (2.3 mm,3.7 mm) (Selvam and Dayanand, 2013) and is similar to garlic pearls with pentoxifylline (4.5 mm, 2 mm) (Jain et al., 2016).

However, absolute improvement in burning sensation was noticed in most of the studies which is similar to our study group (Jain et al., 2016; Aara et al., 2012; Singh et al., 2016; Lanjekar et al., 2020). Complete relapse of treatment was not noted in our study also, like other studies (Goel and Ahmed, 2015). Some difference was noted in clinical parameters in few patients after one year of treatment which was statistically non-significant.

Corticosteroids decrease inflammation, decrease fibroblastic proliferation and collagen formation thereby preventing fibrosis (Tsai et al., 1999). Hyaluronidase (Ghom et al., 2013) is given to OSMF patients as it breaks down hyaluronic acid which lowers the viscosity of intercellular substance and also makes way for diffusion of other drugs.

Table 5. Mean Improvement in VAS in Both the Groups in Grade II and Grade III OSMF at Various Time Intervals and Its Comparative Analysis

Parameter	Grade II			Grade III		
	Group A (Mean and standard deviation)	Group B (Mean and standard deviation)	Sig. /p value– MANN whitney U test	Group A (Mean and standard deviation)	Group B (Mean and standard deviation)	Sig. /p value – Mann- Whitney U test
Diff _VAS1	2.5±0.79	5.8±1.14	0	2.50±0.79	6.33±1.11	0
Diff _VAS2	4.16±1.19	7.6±1.59	0	4.66±0.98	8.44±1.13	0
Diff _VAS3	5.41±1.44	8.06±1.66	0.001	6.50±1.00	9.22±0.833	0
Diff _VAS6	5.41±1.44	8.06±1.66	0.001	6.58±1.16	9.22±0.833	0
Diff _VAS12	5.50±1.38	8.08±1.78	0.001	6.75±1.21	9.44±0.52	0

Footnotes- Diff _VAS1,2,3,6,12 – Difference in Visual analogue scale from baseline, after 1,2,3,6,12 months recorded in points

Omega 3 helps in reducing inflammation by altering cellular functions of polymorphonuclear leukocytes. Additionally, it competitively inhibits the production of arachidonic acid metabolites by cyclo-oxygenase and lipooxygenase pathways which in turn limits tissue damage (Khouli and Gendy, 2014). Many studies have substantiated the inhibitory effect of omega 3 on pro-fibrotic TGFβ1 and MMP 9 secretion particularly in conditions like pulmonary fibrosis induced by silica (Abd Elhameed AG, 2021), cystic fibrosis (Gomaa and El-Aziz, 2016), cardiac and kidney fibrosis (Sharma et al., 2016). It also improves endogenous fibrinolysis by improving the endothelial vasomotor function (Vasilev et al., 2009) and even acts as a rheological modifier to improve microcirculation (Din et al., 2013). Thus it can enhance vasodilatation and improve the hampered mucosal vascularity evident in OSMF due to fibrosis.

So, we suggest that the improvement noticed in our study in all four parameters might be due to the synergistic effects of all these drugs. Improvement in tongue protrusion seen in the control group of our study even without any systemic treatment might be relative due to the improvement in mouth opening. At very high doses (e.g. 15 grams per day), omega-3 fatty acids increase bleeding time (Khouli and Gendy, 2014). But our dosage of omega 3 was quite less i.e. 3gm/day and therefore we have not noticed any complication related to bleeding in our study.

Omega 9 is a non-essential fatty acid while omega 6 is in very less quantity when compared to omega 3 (0.5gms/ml) in flax seed oil. Omega 6 is already high in our diets and it increases inflammation (Oomah and Mazza, 1999). So, we can say that the improvement seen in our study is because of Omega 3.

The effect of omega 3 histopathologically, immunohistochemically and at molecular level was not studied as trauma can lead to even more fibrosis in these patients. So, pre and post-operative biopsy of the patients was not performed. Also, blinding was not done due to manpower constraint. These can be considered as the limitations of the study. OSMF is a disease with poor compliance due to which, we had to drop the 42 participants initially enrolled. Some of them resumed their habit back, some went back to their native place while some did not respond to reminder/follow up calls. So, the reason why they left the treatment in between is unknown.

In conclusion, the results of our study suggest that intralesional injections alone or in conjunction with Omega 3, both are effective in improving IID, TP, CF and VAS in OSMF grade II and grade III patients. However, omega 3 in conjunction with intralesional injections has shown better clinical results than intralesional injections alone with no side effects. Further studies should be planned to assess the individual effect of omega 3 and its role in improving lipid profiles of OSMF patients, in preventing the conversion of premalignant lesions into malignancy and in different supplementation doses to find out the exact dosage with minimum side effects.

Author Contribution Statement

1. Author 1- conceptualization, methodology, conducting research, data curation, writing- original draft preparation.

2. Author 2- guiding the whole research-conceptualization and methodology, data collection, reviewing and editing

Acknowledgements

We would like to express our gratitude to Shreya life sciences (Mumbai, Maharashtra, India) for sponsoring hyaluronidase drug and AISSMS (All India Shri Shivaji Memorial Society) college of pharmacy, Pune for providing lactose capsules.

Approvals

A PhD thesis topic approved by series of committees namely institutional scientific/doctoral/research and review and ethical committee.

Ethical clearance

Approved by Institutional Ethical committee (Dr. D.Y.Patil Dental College and Hospital, Pimpri, Pune).

Availability of Data

Data is not present on any web portal but master chart provided as supplementary File 3.

Study is registered under Clinical Trials Registry – India, http://ctri.nic.in/ with registration number-CTRI/2017/09/009953

Conflicts of interest

None.

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