



COMPARATIVE STUDY ON THE EFFICACY OF OMEGA 3, VITAMIN A AND VITAMIN E ON THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS – A NON OBSERVATIONAL STUDY

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Abstract:

Aim And Objectives: This study evaluated the efficacy of Omega 3, Vitamin A and Vitamin E on the management of Oral Submucous Fibrosis.

Materials And Methodology: A non observational study was designed and a total of 21 clinically confirmed adult patients of OSMF were included in the study. Group A was given Omega 3 once daily for 6 weeks. Group B was given Vitamin A once daily for 6 weeks. Group C was given Vitamin E once daily for 6 weeks. Follow up assessment for various symptoms was performed and the results were analyzed.

Results: After 6 weeks of follow up, statistically significant improvement among all four clinical parameters i.e. inter-incisal distance (mean improvement in group A = 4.86mm), tongue protrusion (mean improvement in group A = 4.14 mm) , cheek flexibility (mean improvement in group A= 0.37cm) and reduced burning sensation (VAS in group A = -5.29 score) was observed in group A when compared to group B and Group C.

Conclusion: Omega3 is found to be effective in improving Inter-incisal distance, Tongue protrusion, Cheek flexibility and Burning sensation in OSMF Grade 1 and Grade II patients compared to Vitamin A and Vitamin

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INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic progressive and irreversible disease affecting the oral, oropharyngeal and sometimes the esophageal mucous¹. The disease is characterized by blanching and stiffness of the oral mucosa, trismus, a burning sensation in the mouth, and hypo mobility of the soft palate and tongue with loss of gustatory sensation². It is described as a scarring disease of the oral mucosa associated with excess oxidants and insufficient antioxidants. It is known for its high rate of malignant transformation which is about 2.3 to 7.6%³. 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 engineers⁴. Omega 3 fatty acids are polyunsaturated essential fatty acids. Humans cannot synthesize them de novo and hence depend on the diet source⁵

Vitamin A must be obtained from the diet: green and yellow vegetables, dairy products, fruits and organ meats are some of the richest sources. Within the body, vitamin A can be found as retinol, retinal and retinoic acid. The antioxidant activity of vitamin A and carotenoids is conferred by the hydrophobic chain of polyene units that can quench singlet oxygen, neutralize thiyl radicals and combine with and stabilize peroxy radicals⁶

Vitamin E's antioxidant function, as a peroxy radical scavenger that terminates chain reactions, is well-known⁷. Vitamin E is the major lipid soluble antioxidant responsible for protecting the polyunsaturated fatty acids in membrane against lipid peroxidation⁸.

Clinical management of OSMF continues to be unsatisfactory. Signs and symptoms persist and progress despite attempted treatments. Several categories of drugs are used to treat debilitating fibrosis. But they are not effective in reversing the initiation and development of OSMF. They may be due to various reasons such as the progressive nature of the disease, the lack of complete knowledge of the pathogens is of the disease, and the limited routes of administration.

An attempt has been made to study the effect of omega 3, vitamin A and Vitamin E in the treatment for OSMF. The Objective of the study is to compare the efficacy of omega 3, Vitamin A and Vitamin E in the management of Oral Submucous Fibrosis, by observing the patients with following

clinical parameters:

1. Burning sensation
2. Mouth opening
3. Tongue protrusion
4. Cheek flexibility

MATERIALS AND METHODS:

A non observational study was carried out to compare efficacy of omega 3, Vitamin A and Vitamin E in the management of Oral Submucous Fibrosis, among 21 patients diagnosed with the disease. A total of 21 clinically confirmed patients of OSMF grade I and grade II (according to Khanna and Andrade) reporting to the Department of Oral Medicine and Radiology, Tagore Dental College and hospital were recruited.

The patients were selected, irrespective of age, sex, religion, and socio-economic status, from all those attending the outpatient Department of Oral Medicine and Radiology, Tagore Dental College and hospital. Patients with positive history of areca nut chewing or one of its commercial preparations, difficulty in chewing and swallowing, burning sensation on eating spicy food, restricted mouth opening and changes in oral mucosa including presence of palpable vertical fibrous bands, stiffness and blanching were included in the study.

Patients with uncontrolled diabetes, compromised immunity, and chronic infection were excluded from this study. Also patients with oro-ulcerative lesions and patients with a known allergy or contraindications to study medications were excluded from the study.

The study protocol was reviewed and approved by the Institutional Ethical Committee. After diagnosis, each patient was informed about the condition, its precancerous potential. The treatment plan was explained to all the study participants, and their consent was obtained. Patients were actively discouraged from consuming the identified etiologic factors, such as pan masala, gutkha, betel quid, tobacco, and other chronic irritants such as hot and spicy food. Patients were graded according to the classification given by Khanna and Andrade. Grade I includes very early cases with common symptoms like burning sensation in the mouth, acute ulceration and recurrent stomatitis and not associated with mouth opening limitation. Grade II includes early cases where buccal mucosa appears mottled and marble like, widespread sheets of fibrosis palpable,

inter-incisal distance of 26 to 35mm²²

Patients with grade I and grade II OSMF are included in the study. Patients were divided into three groups. Group A were given Omega3, once daily for 6 weeks. Group B were given Vitamin A, once daily for 6 weeks. Group C were given Vitamin E, once daily for 6 weeks. Patients were followed every week for 6 weeks.

Patients were evaluated for Mouth opening based on interincisal separation, Tongue protrusion, Cheek flexibility and burning sensation.

MOUTH OPENING: Mouth opening was measured as distance between the upper and lower central incisors when maximally extended with a scale and divider.

Normal values were considered as 35-45 mm in males and 30-42 mm in females. **TONGUE PROTRUSION:**

Tongue protrusion was measured as the distance from the mesio-incisal edge of central incisor to the tip of the protruded tongue and normal values were taken as 5-6 cms in males and 4.5-5.5 cms in females.

CHEEK FLEXIBILITY: Cheek flexibility indicates the suppleness and elasticity of the buccal mucosa which was assessed based on the distance (in centimeters) between the tips of the ear lobes on maximal cheek blowing.

BURNING SENSATION: Burning sensation was determined by use of a 0-10 Visual Analogue Scale (VAS).

STATISTICAL ANALYSIS:

Data was entered in Microsoft excel sheet (version 2016) and analysed in SPSS software version 27.0. Normality of data was assessed by Shapiro-wilk test, which showed normal distribution of data. Repeated measures ANOVA was used to assess the mean difference within and between groups across the visits. Pair wise comparison was carried out by Tukey's HSD test with Bonferroni correction.

RESULTS:

A total of 21 participants were included in the study with the a range of 30-35 years.

The average age of the patient was 32.9. Out of 21 patients, 17 patients

were male and 4 patients were female. Thus the present study shows male predominance. All the

patients had the habit of chewing areca nut in one form or the other. Only grade I and grade II patients were included in the study.

INTER-INCISAL DISTANCE:

In table 1, Repeated measures ANOVA showed that Inter-incisal distance (mm) differed significantly between the visits [F (5, 90)= 174.701, p < 0.001], between the groups [F(2,18)= 8.167, p=0.003] and significant interaction was present between group and visits [F(10,90)= 6.776, p < 0.001]. Post hoc Tukey's test with Bonferroni correction revealed that Omega 3 significantly (p=0.007) increased the Inter-incisal distance by 4.86mm at 6th visit compared to vitamin A (2.57mm) and vitamin E (3mm). There exists no statistically significant difference between Vitamin A and Vitamin E group in improving inter-incisal distance in OSMF patients (p=1).

Graph 1 shows that Omega 3 group has significantly increased the Inter-incisal distance (mm) across the follow-up visits when compared to Vitamin A and E.

TONGUE PROTRUSION:

In table 2, Repeated measures ANOVA showed that Tongue protrusion (mm) differed significantly between the visits [F(5, 90)= 281.852, p < 0.001], between the groups [F(2,18)= 14.641, p<0.001] and significant interaction was present between group and visits [F(10,90)= 8.607, p < 0.001]. Post hoc Tukey's test with Bonferroni correction revealed that Omega 3 significantly (p=0.002, <0.001) improved the tongue protrusion by 4.14mm at 6th visit compared to vitamin A (2.14 mm) and vitamin E (2.71 mm). There exists no statistically significant difference between Vitamin A and Vitamin E group in improving tongue protrusion in OSMF patients (p=1).

Graph 2 shows Omega 3 group has significantly improved the tongue protrusion (mm) across the follow-up visits when compared to Vitamin A and Vitamin E

CHEEK FLEXIBILITY:

In Table 3, Repeated measures ANOVA showed that cheek flexibility (cm) differed significantly between the visits [F (2.946, 53.022) = 103.49, p < 0.001], between the groups [F(2,18) = 13.878, p<0.001] and significant interaction was present between group and visits [F(5.891, 53.022)= 9.049, p<0.001]. Post hoc Tukey's test with Bonferroni correction revealed

that Omega 3 significantly ($p=0.001$, <0.001) improved the cheek flexibility by 0.371 cm at 6th visit compared to vitamin A (0.171 cm) and vitamin E (0.157 cm). There exists no statistically significant difference between Vitamin A and Vitamin E group in improving cheek flexibility in OSMF patients ($p=1$).

Graph 3 shows Omega 3 group has significantly improved the cheek flexibility (cm) across the follow-up visits when compared to Vitamin A and Vitamin E.

BURNING SENSATION:

Table 4. Repeated measures ANOVA showed that burning sensation assessed by visual analogue scale differed significantly between the visits [$F(5,90) = 369.442$, $p < 0.001$], between the groups [$F(2,18) = 7.317$, $p < 0.001$] and significant interaction was present between group and visits [$F(10, 90) = 8.221$, $p < 0.001$]. Post hoc Tukey's test with Bonferroni correction revealed that Omega 3 significantly ($p=0.032$, 0.006) reduced the burning sensation by -5.29 score at 6th visit compared to vitamin A (-3.85 score) and vitamin E (-3.57 score). There exists no statistically significant difference between Vitamin A and Vitamin E group in reducing burning sensation in OSMF patients ($p=1$).

Graph 4 shows omega 3 group has significantly reduced the burning sensation (VAS score) across the follow-up visits when compared to Vitamin A and Vitamin E

DISCUSSION:

Oral submucous fibrosis is a premalignant condition. The habit of chewing betel quid containing areca nut will cause chronic irritation leading to a series of chronic inflammatory response. The average age of patients in our study was 32.9, with most of the patients falling in the range of 30 - 35, similar to other studies, (Singh et al., 2016), although average range between 21 - 30 years is also reported (Annigeri and Jadhav, 2015; Jain et al., 2016; Aara et al., 2012). In this study, majority of patients were male compared to females, which is similar to other studies done earlier (Singh et al., 2016; Jain et al., 2016).

The management of OSMF includes nutritional support, immunomodulatory drugs, local drug delivery and even surgical management. According to Khanna and Andrade, this condition was staged into four categories. Patients with an early stage of OSMF can be treated with medications and those with advanced stage of

OSMF requires surgical treatment¹⁰.

Omega 3 supplementation has shown significant improvements in lipid profiles and indices of lipid peroxidation in many diseases¹⁵. Several studies have reported anti-inflammatory effects of fish oil in patients with RA, due to decreased production of LTB₄, PGE₂, IL-1, and decreased plasma IL-1 β concentrations, serum C-reactive protein concentrations and normalisation of the neutrophil chemotactic response¹⁷.

To our knowledge, there is no documentary evidence on the efficacy of vitamin A and Vitamin E in the management of OSMF patients. So a comparative analysis was not possible. Hence, a comparative analysis of the results of Vitamin A and E with other related treatment modalities was done.

The Interincisal distance in group A - Omega 3 increased by 4.86 mm at 6th visit compared to group B - Vitamin A (2.57mm) and group C - Vitamin E (3mm). This is less than the mean mouth opening improvement (6.3mm) found by Milanjeet Kaur Raizada. But it is found to be more compared to the study conducted by Yadav et al on the effectiveness of curcumin (1.25mm). The study conducted by Patil et al 2015 on effectiveness of aloe vera showed a mean mouth opening improvement of 4.3mm.

The tongue protrusion was found to be improved by 4.14mm in group A - Omega 3 compared to group B - Vitamin A (2.14 mm) and group C - Vitamin E (2.71mm). This is less than the tongue protrusion improvement found by Jain et al 2016 with garlic pearls and pentoxifylline was 4.5mm. But it is found to be better than the study conducted by Yadav et al on the effectiveness of curcumin (0.38mm) and Milanjeet Kaur Raizada on effectiveness of omega 3 (2.3mm).

The cheek flexibility which was measured as ear lobe distance was found to be improved by 0.371 cm in group A - Omega 3 compared to group B - Vitamin A (0.171cm) and group C - Vitamin E (0.157 cm). In a study conducted by Sarwar Alam et al on efficacy of aloe vera, the mean ear lobe distance increased from 27.36 cm to 27.8 cm within first 3 weeks of treatment. This indicated the suppleness and elasticity of the buccal mucosa in the initial phase of medicinal treatment.

Omega 3 reduced the burning sensation by -5.29 score at 6th visit compared to vitamin A (-3.85 score) and vitamin E (-3.57 score). This is similar to the improvement in burning sensation as found in other studies (Jain et al., 2016; 2012; Singh et al., 2016; Lanjekaretal., 2020)

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 lipoxygenase pathways which in turn limits tissue damage²¹ The effect of Omega3, Vitamin A and Vitamin E was not studied histopathologically and immuno histochemically as they can lead to trauma and thus more fibrosis. Hence the study groups were not subjected to preoperative and post operative biopsy. This study is conducted on a small sample size in a short duration of only 6 weeks follow up. So a larger sample size and duration of the study is needed for further studies. These can be considered as the limitations of the study.

In conclusion, the results of our study suggest that, Omega3 is found to be effective in improving Interincisal distance, Tongue protrusion, Cheek flexibility and Burning sensation in OSMF Grade 1 and Grade II patients compared to Vitamin A and Vitamin E. Further studies with larger sample size and long follow up periods should be planned to assess the role of Omega 3 , Vitamin A and Vitamin E as a mainstream therapeutic regimen.

REFERENCES:

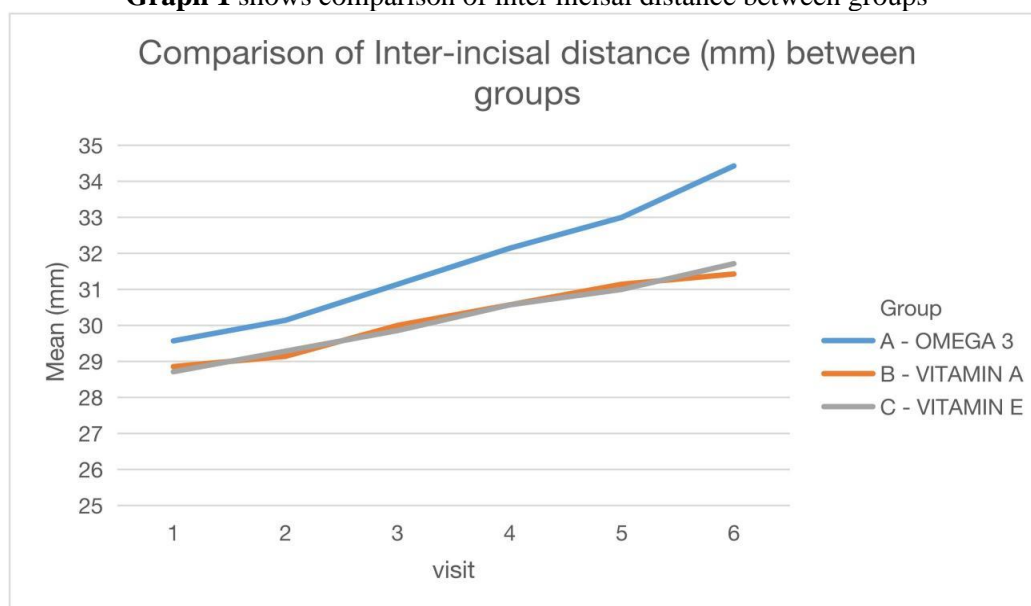
1. Afroz, N., Hasan, S.M., & Naseem, S. (2006). Oral Submucous Fibrosis a Distressing Disease with Malignant Potential. *Indian Journal of Community Medicine*, 31, 270.
2. Alam, S., Ali, I., Giri, K. Y., Gokkulakrishnan, S., Natu, S. S., Faisal, M., Agarwal, A., & Sharma, H. (2013). Efficacy of aloe vera gel as an adjuvant treatment of oral submucous fibrosis. *Oral surgery, oral medicine, oral pathology and oral radiology*, 116(6), 717–724.
3. Raizada, M.K., Sable, D.M., Chowdhery, A., Chavan, M.S., & Rajpurohit, L.S. (2017). Omega 3: a novel treatment agent in oral submucous fibrosis: a pilot study. *Journal of oral pathology & medicine : official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology*, 46(6), 439–442. <https://doi.org/10.1111/jop.12542>
4. Raizada, M. K., & Sable, D. M. (2022). Clinical Assessment of Efficacy of Omega 3 in Oral Submucous Fibrosis Patients - A Randomized Controlled Trial. *Asian Pacific journal of cancer prevention : APJCP*, 23(4), 1185–1192. <https://doi.org/10.31557/APJCP.2022.23.4.1185>
5. Chandran, Kana Veetil Aiswarya; Abhinethra, Mariyappa Shanthali; Deepak, Timmasandra

- Ashwathappa1; Choudary, Amirneni Sailaja1; Upasana, Lingaiah1. Effectiveness of Omega-3 Fatty Acids and Spirulina as an Adjuvant Antioxidant to Corticosteroid in the Treatment of Oral Submucous Fibrosis – A Comparative Study. *Journal of Indian Academy of Oral Medicine and Radiology* 34(2):p150-155, Apr–Jun 2022. |DOI:10.4103/jiaomr.jiaomr_212_21
6. Palace, V. P., Khaper, N., Qin, Q., & Singal, P. K. (1999). Antioxidant potentials of vitamin A and carotenoids and their relevance to heart disease. *Free radical biology & medicine*, 26(5-6), 746–761. [https://doi.org/10.1016/s0891-5849\(98\)00266-4](https://doi.org/10.1016/s0891-5849(98)00266-4)
7. Traber, M.G., & Atkinson, J. (2007). Vitamin E, antioxidant and nothing more. *Free radical biology & medicine*, 43(1), 4–15. <https://doi.org/10.1016/j.freeradbiomed.2007.03.024>
8. Di Mascio, P., Murphy, M. E., & Sies, H. (1991). Antioxidant defense systems: the role of carotenoids, tocopherols, and thiols. *The American journal of clinical nutrition*, 53 (1 Suppl), 194S–200S.
9. Bose, K. S., Vyas, P., & Singh, M. (2012). Plasma non-enzymatic antioxidants-vitamin C, E, beta-carotenes, reduced glutathione levels and total antioxidant activity in oral submucous fibrosis. *European review for medical and pharmacological sciences*, 16(4), 530–532.
10. Khanna, J. N., & Andrade, N. N. (1995). Oral submucous fibrosis: a new concept in surgical management. Report of 100 cases. *International journal of oral and maxillofacial surgery*, 24(6), 433–439. [https://doi.org/10.1016/s0901-5027\(05\)80473-4](https://doi.org/10.1016/s0901-5027(05)80473-4)
11. Singh, N., Hebbale, M., Mhapuskar, A., Ul Nisa, S., Thopte, S., & Singh, S. (2016). Effectiveness of Aloe Vera and Antioxidant along with Physiotherapy in the Management of Oral Submucous Fibrosis. *The journal of contemporary dental practice*, 17(1), 78–84. <https://doi.org/10.5005/jp-journals-10-024-1806>
12. Annigeri R G, Jadhav M (2015). A double blind, randomized, comparative evaluation of efficacy of prak-20 and garlic in oral submucous fibrosis – a preliminary study. *Int J Oral Health Med Res*, 2, 67-72.
13. Aara, A., Gp, S., Vani, C., Venkat Reddy, M., Sreekanth, K., & Ibrahim, M. (2012). Comparative Study of Intralesional Dexamethasone, Hyaluronidase and Oral Pentoxifylline in Patients with Oral Submucous Fibrosis. *The Journal of medical research*, 12.
14. Jain, N., Annigeri, R.G., & Pipalia, P.R. (2016).

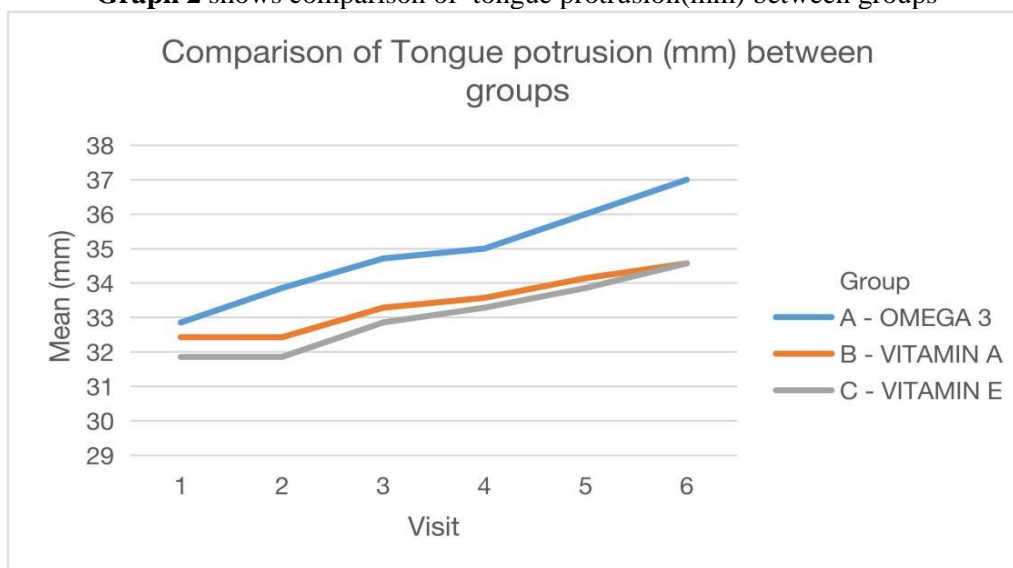
EFFICACY OF GARLIC INCONJUNCTION WITH PENTOXIFYLLINE IN THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS– A PRELIMINARY STUDY.

15. Yates, A., Norwig, J., Maroon, J. C., Bost, J., Bradley, J. P., Duca, M., Wecht, D.A., Grove, R., Iso, A., Cobb, I., Ross, N., & Borden, M. (2009). Evaluation of lipid profiles and the use of omega-3 essential Fatty Acid in professional football players. *Sportshealth*, 1(1), 21–30. <https://doi.org/10.1177/1941738108326978>
16. Tayebi khosroshahi, H., Mousavi Toomatari, S.E., Akhavan Salamat, S., Davar Moin, G., & Najafi Khosroshahi, S. (2013). Effectiveness of Omega-3 Supplement on Lipid Profile and Lipid Peroxidation in Kidney All organ Recipients. *Nephro-urology Monthly*, 5, 822 – 826.
17. Calder P. C. (2008). Session 3: Joint Nutrition Society and Irish Nutrition and Dietetic Institute Symposium on 'Nutrition and autoimmune disease' PUFA, in inflammatory processes and rheumatoid arthritis. *The Proceedings of the Nutrition Society*, 67(4), 409–418. <https://doi.org/10.1017/S0029665108008690>
18. Yadav, M., Aravinda, K., Saxena, V. S., Srinivas, K., Ratnakar, P., Gupta, J., Sachdev, A. S., & Shivhare, P. (2014). Comparison of curcumin with intralesional steroid injections in Oral Submucous Fibrosis - A randomized, open-label interventional study. *Journal of oral biology and craniofacial research*, 4(3), 169–173. <https://doi.org/10.1016/j.jobcr.2014.11.003>
19. Patil, S., Al-Zarea, B. K., Maheshwari, S., & Sahu, R. (2015). Comparative evaluation of natural antioxidants spirulina and aloe vera for the treatment of oral submucous fibrosis. *Journal of oral biology and craniofacial research*, 5(1), 11–15. <https://doi.org/10.1016/j.jobcr.2014.12.005>
20. Lanjekar, A. B., Bhowate, R. R., Bakhle, S., Narayane, A., Pawar, V., & Gandagule, R. (2020). Comparison of Efficacy of Topical Curcumin Gel with Triamcinolone-hyaluronidase Gel Individually and in Combination in the Treatment of Oral Submucous Fibrosis. *The journal of contemporary dental practice*, 21(1), 83–90.
21. El Khouli, A.M., & El-Gendy, E.A. (2014). Efficacy of omega-3 in treatment of recurrent aphthous stomatitis and improvement of quality of life: a randomized, double-blind, placebo-controlled study. *Oral surgery, oral medicine, oral pathology and oral radiology*, 117(2), 191–196. <https://doi.org/10.1016/j.oooo.2013.09.003>
22. More, C.B., Gupta, S., Joshi, J., Verma, S., & Kailasam, S. (2012). Classification system for oral submucous fibrosis. *Journal of Indian Academy of Oral Medicine and Radiology*, 24, 24–29.

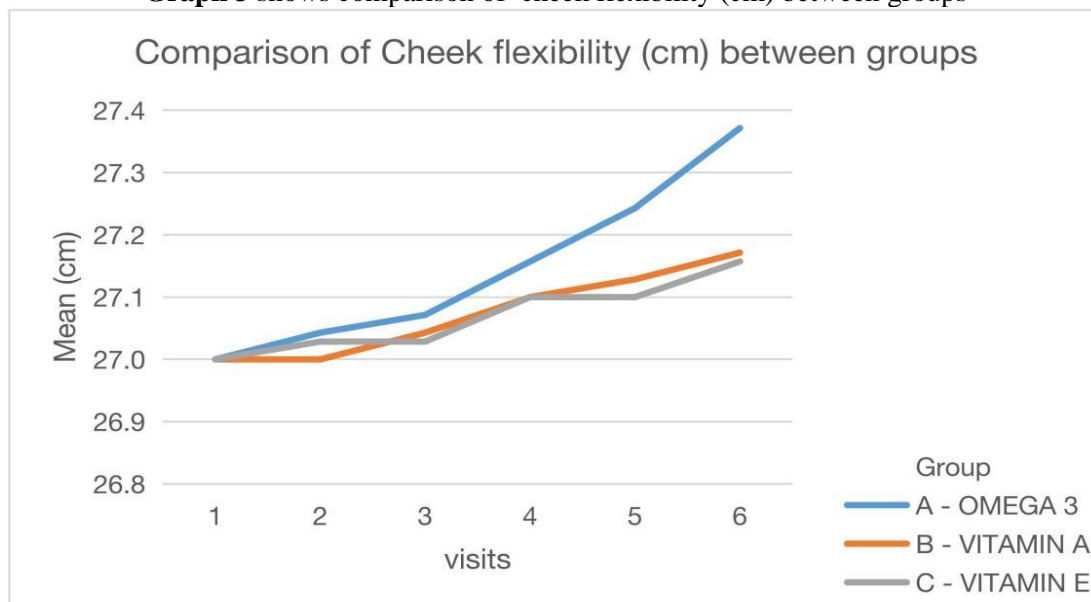
Graph 1 shows comparison of inter incisal distance between groups



Graph 2 shows comparison of tongue protrusion(mm) between groups



Graph 3 shows comparison of cheek flexibility (cm) between groups



Graph 4 shows comparison of burning sensation (VAS) between groups

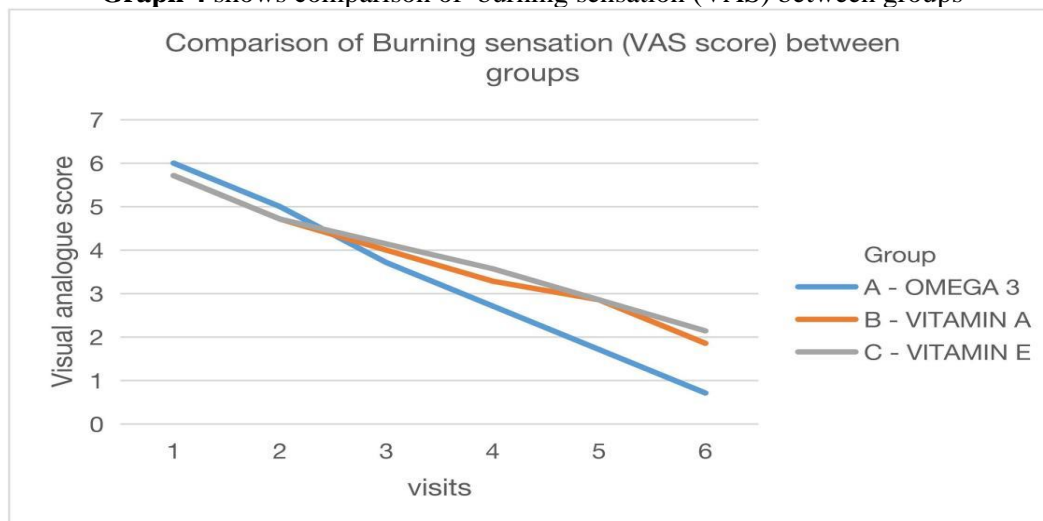


Table1 -Comparison of Inter-incisal distance (mm) between group

Group	Follow-up visits (Mean±SD)						Repeated measures ANOVA					Tukey's Posthoc test		
	Visit 1	Visit 2	Visit3	Visit4	Visit 5	Visit 6	Parameter	Type III Sum of Squares	df	F	error	p-value	Comparison group	p-value
Omega 3	29.57±0.976	30.14±0.9	31.14±0.690	32.14±0.690	33±0.577	34.43±0.787	Visit (Within group)	183.944	5	174.701	90	<0.001	Omega 3 vs vitamin A	0.007
Vitamin A	28.86±0.690	29.14±0.9	30±0.816	30.57±0.535	31.14±0.690	31.43±0.535	Group (Between group)	67.063	2	8.167	18	0.003	Omega 3 vs vitamin E	0.007

Table2 -Comparison of Tongue protrusion (mm) between groups

Group	Follow-up visits (Mean±SD)						Repeated measures ANOVA					Tukey's posthoc test		
	Visit 1	Visit 2	Visit3	Visit 4	Visit5	Visit 6	Parameter	Type III Sum of Squares	df	F	error	p-value	comparison group	p-value
Omega 3	32.86±0.690	33.86±0.690	34.71±0.951	35±0.816	36±0.816	37±0.816	Visit (Within group)	136.452	5	281.852	90	<0.001	Omega3 vs vitamin A	0.002
Vitamin A	32.43±0.535	32.43±0.535	33.29±0.488	33.57±0.535	34.14±0.378	34.57±0.535	Group (Between group)	81.571	2	14.641	18	<0.001	Omega 3 vs vitamin E	<0.001
Vitamin E	31.86±0.900	31.86±0.900	32.86±0.900	33.29±0.951	33.86±0.900	34.57±0.535	Visit*Group	8.333	10	8.607	90	<0.001	Vitamin A vs Vitamin E	1

Table3 -Comparison of Cheek flexibility (cm)between groups

Group	Follow-up visits (Mean±SD)						Repeated measures ANOVA						Tukey's posthoc test	
	Visit1	Visit2	Visit 3	Visit 4	Visit 5	Visit 6	Parameter	Type III Sum of Squares	df	F	error	p-value	comparison group	p-value
Omega 3	27±0	27.043±0.535	27.071±0.0488	27.157±0.535	27.243±0.0787	27.371±0.1113	Visit(Within group)	0.838	2.946	103.49	53.022	<0.001	Omega 3 vs vitamin A	0.001
Vitamin A	27±0	27±0	27.043±0.0535	27.1±0	27.129±0.0488	27.171±0.0488	Group (Between group)	0.163	2	13.878	18	<0.001	Omega 3 vs vitamin E	<0.001
Vitamin E	27±0	27.029±0.0488	27.029±0.0488	27.1±0	27.100±0.000	27.157±0.0535	Visit*Group	0.147	5.891	9.049	53.022	<0.001	Vitamin A vs Vitamin E	1

Table4 -Comparison of burning sensation between groups

Group	Follow-up visits (mean±SD)						Repeated measures ANOVA						Tukey's posthoc test	
	VISIT1	VISIT2	VISIT3	VISIT4	VISIT5	VISIT6	Parameter	Type III Sum of Squares	df	F	error	p-value	Comparison group	p-value
Omega3	6±0	5±0	3.71±0.488	2.71±0.488	1.71±0.756	0.71±0.488	Visit(Within group)	252.159	5	369.442	90	<0.001	Omega3 vs vitamin A	0.032
Vitamin A	5.71±0.488	4.71±0.488	4±0	3.29±0.488	2.86±0.378	1.86±0.378	Group(Between group)	6.968	2	7.317	18	<0.001	Omega 3 vs vitamin E	0.006