



Journal Homepage: - www.journalijar.com
**INTERNATIONAL JOURNAL OF
 ADVANCED RESEARCH (IJAR)**

Article DOI: 10.21474/IJAR01/1562
 DOI URL: <http://dx.doi.org/10.21474/IJAR01/1562>



RESEARCH ARTICLE

A REVIEW OF OMEGA 3 AND IT'S ROLE IN ORAL DISEASES.

Dr. Milanjeet Kaur, Dr. DM Sable, Dr. Asha Chowdhery and Dr. Mahesh Chavan.

Manuscript Info

Manuscript History

Received: 15 July 2016
 Final Accepted: 19 August 2016
 Published: September 2016

Key words:-

Omega 3, oral health, Periodontitis and oral ulcers.

Abstract

The very long chain polyunsaturated fatty acid and Omega 3 are apparently widely accepted as a part of modern nutrition because of their beneficial effects on metabolism. Unlike saturated fats, which have been shown to have negative health consequences, omega-3 fatty acids are polyunsaturated fatty acids that have been associated with many health benefits. Studies have shown Omega-3 fatty acids to be efficacious in a number of psychiatric and mood disorders, inflammatory disorders, cardiovascular disorders, diabetes and now in oral disorders as well. These reports led to PUFAs becoming one of the most accepted and consumed food supplements. Despite this weight of evidence and the considerable current use, there is still a need for studies, which will determine whether the n-3 omega fatty acids are in fact important functional supplements with no adverse effects. However, its role in dental health has not been reviewed so far. So, this review attempts to explore and present a gist of role of omega 3 in oral diseases.

Copy Right, IJAR, 2016., All rights reserved.

Introduction:-

Oral health touches every aspect of our lives but is often taken for granted. Our mouth is a window into the health of our body. It can show signs of nutritional deficiencies or general infection. Systemic diseases those that affect the entire body, may first become apparent because of mouth lesions or other oral problems.

Hippocrates stated 'Let food be thy medicine and medicine be thy food'. A similar saying is "eat your food as medicine or you will have to eat medicines as your food". The foundation of Ayurveda (natural Indian medicine) is also on diet. Omega 3 and omega 6 are essential fatty acids which are not endogenously synthesized in our body and must be obtained from the diet. Long chain omega-6 fatty acids include linoleic, gamma-linolenic, and arachidonic acids. Omega-3 fatty acids are the bioactive lipids which contains eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA). These polyunsaturated fatty acids are an important part of cell membranes where they modulate membrane protein function, cellular signaling, and gene expression.³

Sources of omega3:-

Common dietary sources of omega-3 fatty acid are cod liver oil, fish oil, and marine animals with a high amount of fat, such as, tuna, sardines, herring mackerel, salmon, and menhaden. Certain fish and microalgae contain high levels of this essential bioactive omega-3 products EPA and/or DHA. Plants also

contain various levels of omega-3 fatty acids as 'precursors' mainly in the form of alpha-linolenic acid (ALA).²⁶ Plant oils from walnuts, flaxseed, and canola contain the omega-3 fatty acid ALA (alpha linoleic acid), which is a metabolic precursor of the very-long-chain omega-3 fatty acids EPA and DHA.³

Dietary Recommendations:-

Dietary guidelines recommended by The American Heart Association (AHA) for healthy individuals include consumption of fatty fish at least two times a week, along with plant-derived omega-3 fatty acids, including ALA from soybean products, walnuts, flaxseed oil, and canola oil.¹⁵ The dose and duration of treatment to treat or prevent inflammatory conditions are not clear. American heart association has suggested that 0.5 to 1.8 gm/day of EPA/DHA is regarded as safe in healthy people. But consuming high doses of EPA/DHA (>3gm/day) requires monitoring because of potential complications of excessive bleeding.¹³

Omega-3: Omega-6 ratio has become a model for gauging the proper balance of these fats in oils and the diet. Diets with greater than a 1:10 ratio of omega-3 to omega-6 are not recommended, whereas a 1:1 ratio is considered perfect. Very unhealthy ratios of 1:25 and 1:50 are common, especially with the consumption of 'fast food', high amounts of fried food, and low intake of fresh whole foods.²⁶

Mechanism of Action:-

According to various researches Omega-3 or EPA and DHA has the ability to alter cellular functions of polymorphonuclear leukocytes (by regulating the flow of inflammatory cells to the sites of inflammation and blocking proinflammatory cytokine production), modulate lymphocyte proliferation, and significantly increase the activities and mRNA expression of endogenous host antioxidant enzymes including glutathione peroxidase, superoxide dismutase, and catalase, thus enhancing clearance of inflammation within the lesion to promote tissue regeneration.^{12,23,25,29}

Furthermore, EPA and DHA plays a role in limiting tissue damage by competitively inhibiting the production of arachidonic acid metabolites via the cyclooxygenase and lipoxygenase pathways.^{1,20} In addition, metabolism of omega-3 polyunsaturated fatty acids was found to result in the production of the proresolving lipid mediators, resolvins and protectins, with anti-inflammatory and immunoregulatory actions that can enhance resolution of inflammation and aid in wound healing.²⁴

Role of omega 3 in various medical conditions:-

Consumption of n-3 polyunsaturated fatty acids (PUFAs) found in fish oil suppresses inflammatory processes making these fatty acids attractive candidates for both the prevention and amelioration of several organ-specific and systemic autoimmune diseases.²²

Omega-3 supplementation decreased heart rate variability in patients after myocardial infarction, which correlated with a lower risk of mortality and malignant arrhythmia⁷. Omega-3s may be significant co therapeutic treatments for lowering triglyceride levels in pre-diabetic and type 2 diabetic patient's also⁹. However, omega-3 supplements may not directly affect glucose homeostasis, yet these essential fatty acids are protective against lipid oxidative stress in diabetic patients. It is critical for brain, eye and central nervous system development and functioning.²⁶

In a prospective, double-blind, randomized study of dietary supplementation with 2 different dosages of fish oil and 1 dosage of olive oil, forty-nine patients with active rheumatoid arthritis completed a 24-week treatment plan. Twenty patients consumed daily dietary supplements of omega 3 fatty acids containing 27 mg/kg eicosapentaenoic acid (EPA) and 18 mg/kg docosahexaenoic acid (DHA) (low dose), 17 patients ingested 54 mg/kg EPA and 36 mg/kg DHA (high dose), and 12 patients ingested olive oil capsules containing 6.8 gm of oleic acid. They found that the clinical benefits of dietary supplementation with omega-3 fatty acids are more commonly observed in patients consuming higher dosages of fish oil for time intervals that are longer than those previously studied.¹⁴

A meta-analysis that included data from nine trials published between 1985 and 1992 inclusive and from one unpublished trial has concluded that 'dietary fish oil supplementation for three months significantly reduced tender joint count and morning stiffness in patients with rheumatoid arthritis.⁵

Role of omega 3 in oral Squamous cell carcinoma:-

According to a study by Nikolakopoulou Z et al (2013) both DHA and EPA leads to cell death and growth arrest in human normal and neoplastic keratinocytes from the epidermis and oral cavity. They found that EPA, at a lower dose, inhibited the growth of premalignant and malignant keratinocytes more than the growth of normal keratinocytes, whereas DHA was less selective. The growth inhibition at the selective low doses of EPA required occupancy of the epidermal growth factor receptor (EGFR) and was associated with a sustained activation of ERK1/2, which did not occur in non-neoplastic keratinocytes at the same dose. PI3 kinase was not activated in parallel. Their results suggest that n-3 PUFAs may exert some of their anticancer effects by inducing over-stimulation of ERK1/2 or a signalling imbalance downstream of the EGFR pathway. They also suggested that n-3 PUFAs or their derivatives may have potential in the prevention or reduction of aerodigestive tract and epidermal Squamous cell carcinoma.¹⁹

In one more study Omega 3 enhanced formulas with different omega3/omega6 ratios were given in post surgical head and neck cancer patients. They were asked to consume two cans per day of either a specially designed omega 3 fatty acid enhanced supplement with a high ratio of omega3/omega6 (I) or an omega 3 fatty acid enhanced supplement with a low ratio of omega3/omega6 (II). Their results suggested improved serum protein concentrations in ambulatory postoperative head and neck cancer patients with good tolerance in both the groups.¹⁶

Role of omega 3 in Treating oral ulcers:-

Several clinical trials have been conducted that used omega-3 acids for a variety of wounds. An omega-3 dressing has been used in the treatment of wounds with varied etiology, such as burns, diabetic ulcers, and tropical ulcers.^{17,27,28} So, in a study by Hashemipour MA et al (2012) effect of locally and systemically applied n-3 fatty acids on oral ulcer recovery process was studied in rats. They found that Omega-3 fatty acid (L and S) increases fibroblast counts and decreases PMN cell counts. Moreover, this compound causes an increase in reepithelialization and epithelial thickness.¹⁰

In a recent clinical trial, daily omega-3 treatment achieved a significant reduction in number of ulcers, duration of ulcers, and level of pain in patients with recurrent aphthous stomatitis. Patients were advised to take 1gm of omega 3 three times daily. Their results suggested that a daily omega-3 regimen showed promising results as therapy for treatment and management of patients with recurrent aphthous stomatitis.¹³

Role of omega 3 in Periodontitis:-

Role of omega 3 in periodontal health is a well known fact. Periodontitis is a chronic inflammatory irreversible condition, with progressive loss of both soft and hard tissues. Periodontal disease is a major public health concern, as it is among the most prevalent human diseases. The host inflammatory response to predominantly gram-negative bacteria causes alveolar bone loss, which characterizes periodontitis. Omega-3 Poly Unsaturated Fatty Acids has well-recognized anti-inflammatory properties due to which it has shown positive results in patients with this disease in many studies.²¹ Omega 3 intake, particularly DHA and EPA, are inversely associated with periodontitis in the US population.¹⁸

In a recent trial the efficacy of systemic administration of omega-3 polyunsaturated fatty acids plus low-dose aspirin was evaluated as an adjunctive treatment to regenerative therapy of furcation defects. The experimental group received decalcified freeze-dried bone allograft (DFDBA) + omega-3 polyunsaturated fatty acids combined with low-dose aspirin; and control group received DFDBA + placebo. Their findings suggested that the combination therapy demonstrated successful reduction of gingival inflammation, reduction of pocket depth and attachment level gain⁸ but at the same time clinical intervention studies to date have been on small sample sizes, and this indicates there is need for larger and more robust clinical trials to verify these initial findings.⁶

To date, the treatment of periodontitis has primarily involved mechanical cleaning and local antibiotic application. Thus, a dietary therapy, if effective, might be a less expensive and safer method for the prevention and treatment of periodontitis.¹⁸

In one more study the longitudinal relation between dietary ω -3 fatty acids (FAs), docosahexaenoic acid (DHA), and eicosapentaenoic acid (EPA) to periodontal disease in community-dwelling elderly was studied. They found that low DHA intake was significantly associated with more periodontal disease events. The mean number of periodontal disease events for participants who consumed the lowest tertile of DHA was approximately 1.5 times larger than the reference group, after simultaneously adjusting for possible confounders. Their findings suggested that there may be an inverse, independent relation of dietary DHA intake to the progression of periodontal disease in older people.¹¹

Relation between consumption of omega 3 and risk of prostate cancer:-

One recent study reported an increased risk of prostate cancer among men with high blood concentrations of long chain poly unsaturated fatty acids.⁴ But a critical analysis of the study by Dr. Harris (2013) said that Brasky et al. (2013) provided no data on fish intake or supplement use. So the question of whether fish oil supplements or an intake of more oily fish increases prostate cancer risk was not tested. Moreover with the Japanese intake of omega-3 fatty acids at about eight-fold that of Americans and with their blood levels twice as high, one would expect a higher risk in them. However, the Japanese prostate cancer rate of 22.7 per 100,000 in 2008 was dramatically lower than the U.S. rates of 83.8 per 100,000. He explained in an interview:

“I specialize in fatty acid levels, and I was surprised at how small the omega-3 fatty acid differences are, especially for EPA, and DHA. In our lab, we would not consider these small differences to be biologically significant. Because of the large number of subjects in the SELECT trial, it turned out to be statistically significant, though.”²

So, any correlation between omega 3 and prostate cancer is still not clear.

Conclusion:-

Proper nutrition plays a vital role in the well-being of a person. Presently, there is an important amount of scientific data as related to the beneficial and protective effects of omega 3 Poly Unsaturated Fatty Acids and their effects against inflammation, cancer and heart diseases. More studies with larger sample size and at various sites should be conducted to highlight its effect in oral ulcers, oral cancer and chronic periodontitis. Due to its anti-inflammatory properties can it be used in treatment of other oral inflammatory disorders like OSMF, Oral Lichen Planus etc? is an important question to brood over and can be answered by conducting clinical trials in these diseases as well.

References:-

1. Alam SQ, Bergens BM and Alam BS. (1991): Arachidonic acid, prostaglandin E2 and leukotriene C4 levels in gingival and submandibular salivary glands of rats fed diets containing n-3 fatty acids. *Lipids*, 26: 895-900.
2. Alexander W. (2013): Prostate cancer risk and omega 3 fatty acid intake from fish oil-A closer look at media messages versus research findings. *Controversies in Practice*, 38(9):561-64.
3. Bradberry JC and Hilleman DE. Overview of Omega-3 Fatty Acid Therapies (2013): *P&T*, 38 (11): 681-691.
4. Brasky TM, Darke AK, Song X, et al. (2013): Plasma phospholipid fatty acids and prostate cancer risk in the SELECT Trial. *JNCI J Natl Cancer Inst*, 105:1132-1141.
5. Calder PC. (2008): Joint Nutrition Society and Irish Nutrition and Dietetic Institute Symposium on ‘Nutrition and autoimmune disease’ PUFA, inflammatory processes and rheumatoid arthritis. *Proceedings of the Nutrition Society*, 67:409–418.
6. Chee B, Park B, Fitzsimmons T, Coates AM and Bartold PM. (2016): Omega-3 fatty acids as an adjunct for periodontal therapy-a review. *Clin Oral Investig*, 20(5): 879-94.
7. Christensen JH, Gustenhoff P, Korup E et al. (1996): Effect of fish oil on heart rate variability in survivors of myocardial infarction: a double blind randomized controlled trial. *Bio Med J*, 312: 677-8.
8. Elkhoul AM. (2011): The efficacy of host response modulation therapy (omega-3 plus low-dose aspirin) as an adjunctive treatment of chronic periodontitis (clinical and biochemical study): a randomized, double-blind, placebo-controlled study. *J Periodont Res*, 46: 261-268.

9. Friedberg CE, Janssen MJ, Heine RJ et al. (1998) Fish oil and glycemic control in diabetes. A meta-analysis. *Diabetes Care*, 21: 494-500.
10. Hashemipour MA, Ghasemi AR, Dogaheh MA and Torabi M. (2012): Effects of Locally and Systemically Applied n-3 Fatty Acid on Oral Ulcer Recovery Process in Rats. *WOUNDS*, 24(9):258–266.
11. Iwasaki M, Yoshihara A, Moynihan P, Watanabe R, Taylor GW and Miyazaki H. (2010): Longitudinal relationship between dietary ω -3 fatty acids and periodontal disease. *Nutrition*, 26(11-12): 1105-9.
12. Kesavalu L, Bakthavatchalu V, Rahman MM, et al. (2007): Omega-3 fatty acid regulates inflammatory cytokine/mediator messenger RNA expression in *Porphyromonas gingivalis* induced experimental periodontal disease. *Oral Microbiol Immunol*, 22: 232-239.
13. Khouli AE and Gendy EA. (2014): Efficacy of omega-3 in treatment of recurrent aphthous stomatitis and improvement of quality of life: a randomized, double-blind, placebo-controlled study. *OOOOE*, 117 (2):191-196.
14. Kremer JM, Lawrence DA, Jubiz W, et al. (1990): Dietary fish oil and olive oil supplementation in patients with rheumatoid arthritis. *Arthritis Rheumatol*, 33:810-820.
15. Kris-Etherton PM, Harris WS and Appel LJ. (2003): Omega-3 fatty acids and cardiovascular disease: New recommendations from the American Heart Association. *Arterioscler Thromb Vasc Biol*, 23: 151–152.
16. Luis DD, Izaola O, Aller R, Cuellar L, Terroba Mc And Martin T. (2008): A randomized clinical trial with two omega 3 fatty acid enhanced oral supplements in head and neck cancer ambulatory patients. *European Review for Medical and Pharmacological Sciences*, 12: 177-181.
17. Mooney MA, Vaughn DM, Reinhart GA, et al. (1998): Evaluation of the effects of omega-3 fatty acid-containing diets on the inflammatory stage of wound healing in dogs. *Am J Vet Res*, 59: 859-863.
18. Naqvi AZ, Buettner C, Phillips RS, Davis RB and Mukamal KJ. (2010): Omega 3 fatty acids and periodontitis in U.S. adults *J Am Diet Assoc*, 110(11): 1669–1675.
19. Nikolakopoulou Z, Nteliopoulos G, Michael-Titus AT and Parkinson EK. (2013): Omega-3 polyunsaturated fatty acids selectively inhibit growth in neoplastic oral keratinocytes by differentially activating ERK1/2. *Carcinogenesis*, 34(12):2716–2725.
20. Offenbacher S, Odle BM and Green MD. (1990): Inhibition of periodontal PGE2 synthesis with selected agents. *Agents Actions*, 29: 232-238.
21. Peeran SW, Mugrabi MHE, Bashir Al-Taher O, Grain A, Alsaïd FM and Kumar N. (2014): Therapeutic role of dietary omega-3 fatty acids in periodontal disease. *URJD*, 4(2): 82-86.
22. Pestka JJ. (2010): N-3 Polyunsaturated Fatty Acids and Autoimmune-Mediated Glomerulo nephritis. *Prostaglandins Leukot Essent Fatty Acids*, 82(4-6): 251–258.
23. Schwab JM, Chiang N, Arita M and Serhan CN. (2007): Resolvin E1 and protectin D1 activate inflammation-resolution programmes. *Nature*, 14: 869-874.
24. Serhan CN. (2006): Novel chemical mediators in the resolution of inflammation: resolvins and protectins. *Anesthesiol Clin*, 24: 341-364.
25. Serhan CN. (2008): Controlling the resolution of acute inflammation: a new genus of dual anti-inflammatory and proresolving mediators. *J Periodontol*, 79: 1520-1526.
26. Shukla G, Kumar S and Kumar CJS. Safe vegetarian source of omega-3 fatty acid. (2011): *IJRPC*, 1(3): 418-431.
27. Takada H, Takahashi M, Soma, R and Kuwayama H. (2004): Polyunsaturated fatty acid and ulcer healing. *J Med Sci*, 31: 217-223.
28. Terkelsen LH, Eskild-Jensen A, Kjeldsen H, Barker JH and Hjortdal VE. (2000): Topical application of cod liver oil ointment accelerates wound healing: an experimental study in wounds in the ears of hairless mice. *Scand J Plast Reconstr Surg Hand Surg*, 34(1):15-20.
29. Venkatraman JT, Chandrasekar B, Kim JD and Fernandes G. (1994): Effects of n-3 and n-6 fatty acids on the activities and expression of hepatic antioxidant enzymes in autoimmune-prone NZB x NZW F1 mice. *Lipids*, 29: 561-568.