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RESEARCH ARTICLE

OMEGA 3 AND OMEGA 6 IN CHILDHOOD DIET IN PEDIATRIC

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ABSTRACT

Objective: Review omega 3 and omega 6 in childhood diet.

Data Sources: From previous Literatures, reviews and studies as well as medical websites (PubMed, MD consult, Medscape) and Scientific Journals data- bases were searched from the start date of each data- base.

Study Selection: Selection was done by supervisors for studying new advancement in omega 3 and omega 6 in childhood diet in pediatric and studies that addressed the important of omega 3 and omega 6 in childhood diet.

Data Extraction: Data from published studies were manually extracted and summarized. Study quality assessment included whether ethical approval was gained, prospective design, eligibility criteria specified, appropriate controls used, adequate follow-up achieved and defined outcome measures.

Data synthesis: In this review the data found that several studies of omega 3 and omega 6 in childhood diet to know which omega 3 and omega 6 can used in several diseases

Findings: A total of 50 studies were included in the review as they were deemed eligible by fulfilling the inclusion criteria. Of these 50 articles, included in this review, 32 were Omega 3 and omega 6 in child diet and 18 were omega and diseases

Studies indicate that omega 3 and omega 6 can used in the treatment of some diseases.

Conclusion: Omega-3 and Omega-6 are essential fatty acids and are important for human health and diet must be balanced in the omega-6 and omega-3 fatty acids decreasing omega-6 and increasing omega-3 fatty acids.

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INTRODUCTION

Fatty acids can either be saturated fatty acids or unsaturated. Omega-3 fatty include eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and Alpha-linolenic acid (ALA) acid. Omega-6 and Omega-3 fatty acids are essential polyunsaturated fatty acids (PUFA) because they are required by our body to synthesize prostaglandins and other physiological regulators. Omega-3 fatty acids can be obtained from foods such as soybeans and salmon .Omega-6 can be obtained from vegetable oils such as soybeansoil, corn oil, sunflower oil and other oils (Gomez *et al.*, 2011). Health benefits of these fatty acids, especially Omega-3 include reducing inflammation as well as lowering the risk of chronic diseases such as cardiovascular disease, coronary heart disease, cancer, diabetes, high cholesterol and arthritis.

They are also important for cognitive and behavioral function (Swansson *et al.*, 2012). The omega-3 fatty acids (EPA and DHA) are essential for proper fetal development and supplementation during pregnancy has also been linked to decreased immune responses in infant including decreased incidence of allergies in infant (Gomez *et al.*, 2011). Polyunsaturated fatty acids (PUFA) constitute an important component of all cell membranes and influence membrane fluidity and the behavior of membrane-bound enzymes and receptors. PUFAs regulate a wide range of functions in the body, including blood pressure, blood clotting, and correct development and functioning of the brain and nervous systems and have a role in regulating inflammatory responses through the production of inflammatory mediators termed eicosanoids (Das, 2006).

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MATERIALS AND METHODS

Search strategy

We reviewed papers omega 3 and omega 6 in childhood diet from Medline databases (PubMed, Medscape, and Science Direct) and also materials available on the internet. We used omega 3 and omega 6 in the Treatment of several diseases searching terms. In addition, the search was performed in the electronic databases from 2003 to 2014.

Study selection

All the studies were independently assessed for inclusion criteria. They were included if they fulfilled the following criteria:

1. Published in English language.
2. Published in peer-reviewed journals.
3. Focused on omega 3 and omega 6 fatty acids.
4. Discussed the effectiveness of omega 3 and omega 6 in childhood diet
5. If a study had several publications on certain aspects, we used the latest publication giving the most relevant data.

Data extraction

Studies that did not fulfill the above criteria, such as studies on ordinary omega 3 treatment and studies not focused on topical use of omega 3 in skin lesions were excluded. The publications analyzed were evaluated according to evidence-based medicine (EBM) criteria using the classification of the US Preventive Services Task Force and UK National Health Service protocol for EBM in addition to the Evidence Pyramid.

US Preventive Services Task Force:

Level I: Evidence obtained from at least one properly designed randomized controlled trial.

Level II-1: Evidence obtained from well-designed controlled trials without randomization.

Level II-2: Evidence obtained from a well-designed cohort or case-control analytic studies, preferably from more than one Center or research group.

Level II-3: Evidence obtained from multiple time series with or without intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.

Level III: Opinions of respected authorities, on the basis of clinical experience, descriptive studies or reports of expert committees.

Quality assessment

The quality of all the studies was assessed. Important factors included the study design, attainment of ethical approval, evidence of a power calculation, specified eligibility criteria, appropriate controls, adequate information and specified

assessment measures. It was expected that confounding factors would be reported and controlled for and appropriate data analyses made in addition to an explanation of missing data.

Data synthesis

A structured systematic review was performed.

Study selection and characteristics

In total, 170 potentially relevant publications were identified: 120 articles were excluded as they did not meet our inclusion criteria. A total of 50 studies were included in the review as they were deemed eligible by fulfilling the inclusion criteria. Of these 50 articles, included in this review, 32 were omega 3 and omega 6 in child diet and 18 were omega and diseases. A study to discuss efficacy and important of omega3 and omega6 and the use of these fatty acids in several diseases.

Importance of Fatty Acids to Human Body

Importance of ω 3FAs

Omega-3 (EPA and DHA) have the ability to influence cell membrane fluidity, permeability or membrane protein-mediated responses. By being precursors to lipid mediators (eicosanoids) these omega-3 PUFAs affect cell and tissue physiology and response to external signals (Burri *et al.*, 2012). The omega-3PUFAs, in particular EPA and DHA, have been implicated to have an inhibitory effect on pro-inflammatory cytokines, such as tumour necrosis factor- α (TNF- α), interleukin-1, and interleukin-6, with the replacement of ω 6 (AA) by ω 3 (EPA and DHA) causing altered production of eicosanoids towards less inflammatory products (Vaughan *et al.*, 2013). By these means, EPA and DHA support cardiovascular health as well as cognitive, visual, immune, and reproductive system functions. There are also indications that they confer health benefits regarding e.g. tumorigenesis, hypertriglyceridemia, atherosclerosis, mental illness, dementia, bone health, and attention-deficit hyperactivity disorder (ADHD) (Adrian *et al.*, 2015). Moreover, the competition that exists between omega-6 and omega-3 fatty acids applies to their balance being critical for brain development and structural integrity. DHA is essential for vision, brain neurons, and cell signaling. While DHA is clearly concentrated in the signaling systems of the brain, EPA is more likely to be involved in vascular blood flow and eicosanoid production where it can down-regulate the AA metabolites to maintain homeostasis (Burri *et al.*, 2012).

Brain Health and Neurological Function

Human brain growth starts around the 28th week of gestation and 15% of brain growth occurs during infancy and remaining brain growth is completed during pre-school years and depends on an adequate supply of omega3 fatty acid especially DHA (Barbara *et al.*, 2015). Once your baby is born and through the first two years of life his brain develops more rapidly than it ever will again. In fact, the brain grows 175% in the first year of life. That's why many experts believe it's important for babies to receive enough DHA during this critical time of brain development (Innis, 2008). Studies with

human newborns indicate that DHA is essential for the normal functional development of the retina and brain, particularly in premature infants. Because omega 3 fatty acids are essential in growth and development throughout the life cycle, they should be included in the diets of all humans (Calder and Yaqoob, 2009). Deficiencies of omega3 fatty acids especially EPA and DHA have been linked to decreased cognitive abilities, increased aggression and memory loss. Sufficient intake of omega3 fatty acid has been shown to be effective in promoting cognitive and emotional health (Makrides *et al.*, 2010).

Developmental Milestones and Intelligence Quotient

Children whose mothers had been supplement with fish oil and who had been breast fed at least 3 months after birth had better Intelligence Quotient (IQ) (Innis and friesen., 2008). Adequate maternal intake of sea foods during pregnancy improves verbal communication skills at 6 and 18 months, reduces the risk of preterm birth and low birth weight, improves the infant's problem solving capacity and eye and hand coordination (Barbara *et al.*, 2015). The highest levels of maternal fish consumption during pregnancy have been associated with improved cognitive development, social skills and earlier acquisition of language in infants throughout the world (Isabelle *et al.*, 2010). There are so many milestones to achieve during your baby's first year. As he grows, his cognitive, motor, communication and social skills are continually developing, too. From smiling and sitting up to standing and walking. Clinical studies show that DHA improves cognitive development (Isabelle *et al.*, 2014).

Essential fatty acids in maternal and child health

Polyunsaturated fatty acids are vitally important structural elements of cell membranes and essential for formation of new tissues, as occurs during pregnancy and fetal development (Buckley and Howe, 2009). High intakes of long chain omega-3 fatty acids from seafood or fish oil supplements have been shown to increase gestational length and infant birth weight. Birth weight and gestational age are important determinants of neonatal morbidity and mortality, subsequent neurocognitive development and risk for infant and childhood obesity. Therefore, promotion of optimal prenatal intake of seafood or DHA is important to pregnancy outcome (Makrides *et al.*, 2010). The protective effect of breastfeeding on obesity in children has been recently reviewed. Breastfeeding is consistently found to be protective against development of obesity in childhood which is at least partially attributable to the DHA contribution of breast milk compared to formula. A recent study determined that at three years of age, (Muhlhausler *et al.*, 2010). Fetus and infant are unable to convert enough α Linolenic acid to docosahexaenoic acid due to immature de-saturation enzyme systems in human liver. The capacity of the placenta to synthesize long chain polyunsaturated fatty acids from essential fatty acids is very limited, but there is an active transport of long chain polyunsaturated fatty acids across the placenta by a maternal-fetal concentration gradient (Makrides *et al.*, 2010). Pregnant woman should take at least 200 mg/day from DHA (2 portions of oily fish /week) plus taking a multi-nutrient fish in

antioxidants especially vitamin E (Koletzo and Berthold, 2007).

There is association between high fish consumption and lower risk of pre-eclampsia. EPA and DHA has been shown to modulate inflammatory and vascular effects. It has been postulated that omega-3 fatty acid may benefit this condition (Koletzo and Berthold, 2007).

Digestive tract, Bone and Joint Health

Omega3 fatty acids support also colonization of the digestive tract with healthy bacteria or pro- biotics. It was found that supplementation with fish oil inhibits the proliferation of abnormal cells (a precursor to polyps) in patient at risk for colon cancer (Kenmogne *et al.*, 2014). Omega3 fatty acids support healthy level of calcium, improves calcium absorption and promote calcium deposition in the bone tissue and therefore strengthen the bone (Reza *et al.*, 2015)

Eye Health

Docosahexaenoic acid normally accounts for greater than one third of the total fatty acid of brain and retina specifically in the disk membranes of the outer segments of photoreceptors cells. DHA is incorporated into phospholipids in neuronal and photoreceptors membranes where it proper visual and neural activity (McNamara *et al.*, 2013) Biochemical properties of DHA may affect photoreceptor membrane function by altering their permeability, fluidity and thickness. In the retina, n-3 fatty acids are especially important. N-3 fatty acid deficiency has resulted in decreased vision and abnormalities of the electroretinogram. (McNamara *et al.*, 2013)

Cardiovascular Health

Omega3 fatty acids have direct effects on endothelial vasomotor function through uptake and incorporation into endothelial and smooth muscle cells. Omega3 supplementation change membrane fluidity of endothelial cells, promoting increased synthesis and release of nitric oxide which considered one of the potential mechanism for the restoration of endothelial function (Nigam *et al.*, 2014). Release of nitric oxide produces a cascade of physiological effects as vasodilatation, decrease platelet aggregation and smooth muscle cells proliferation that inhibit the development of early CHD and atherosclerosis (Asenath *et al.*, 2015). Omega-3 fatty acids increase bleeding time; decrease platelet aggregation, blood viscosity, and fibrinogen; and increase erythrocyte deformability, thus decreasing the tendency to thrombus formation (Simopoulos, 2008). EPA and DHA and their use with regard to major coronary events and their use after myocardial infarction. EPA+DHA has been associated with a reduced risk of recurrent coronary artery events and sudden cardiac death after an acute myocardial infarction (Simopoulos, 2008). Dietary fish oil prevents atherosclerosis through lowering plasma cholesterol concentrations. The effect of fish oil on hyperlipidemia. Fish oil especially lowers plasma cholesterol and triacylglycerol concentrations through inhibition of the synthesis of triacylglycerol and very low-density lipoprotein (VLDL) in the liver Apolipoprotein B

production is reduced by consumption of fish oil in comparison with vegetable oils such as safflower or olive oil (Asenath *et al.*, 2015).

Immune and Inflammatory Responses

Experimental studies have provided evidence that incorporation of omega3 modifies the inflammatory and immune reactions. Their effects are brought about by the type and amount of eicosanoids and cytokines and by altering gene expression (Sorensen *et al.*, 2014). Omega3 fatty acids (especially EPA and DHA) as immunomodulators. They assist in lymphocyte proliferation and activation macrophage function, natural killer cell function and neutrophil function. These actions are mediated by modulation of the eicosanoid pathways (Howe and Buckley, 2014). The two most potent omega-3 fatty acids are known as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). These fatty acids are essential nutrients and enter every cell membrane in the human body, serving as a cell lubricant, improving flexibility and communication between cells, and aiding cell metabolism and gene expression (Lattka *et al.*, 2010). According to (Milan, 2015) the possible mechanisms of anti carcinogenic effect of omega-3 FAs are: They suppress the synthesis of pro-inflammatory eicosanoids from ω 6-arachidonic acid and thus have anti inflammatory effect. They suppress excessive production of nitrogen oxide during chronic inflammation and prevent DNA damage and impaired DNA repair. They decrease estrogen production through their effect on membrane (lipid)-bound enzymes such as cytochrome P450 that regulate estrogen metabolism and thus reduce the estrogen stimulated growth of hormone dependent cancer cells. Omega-3 fatty acids deficiency lead to structural and functional changes of cell membranes resulting in alterations of hormone and growth factor receptors.

Importance of omega-6 FAs

Linoleic acid, an omega-6, is the parent molecule of arachidonic acid, another omega-6 fatty acid. This essential fatty acid is involved in many signaling pathways involving both inflammation and the central nervous system (Challem 2009). Omega-6 fatty acids are important in the diet but should be consumed in equal or lesser proportions as omega-3. The pro-inflammatory properties of omega-6 fatty acids are favored in the human body since they play a role in a robust immune system. Omega-3 and omega-6 fatty acids follow parallel, competitive biochemical pathways. imbalance in the diet leads to a pro-inflammatory response (Gomez *et al.*, 2011).

Omega and diseases

Childhood asthma

Fish oil consumption has a beneficial effect on lung function, promotes respiratory Health and lessens the effect of stress and prevalence of asthma (Tsaroucha *et al.*, 2013). Study found that there is improvement in cough and wheezes with higher dietary intake of omega-3 fatty acids rich foods (Tabak *et al.*, 2005). Dietary fatty acids play a critical role in modulation of airway inflammation in asthma. Higher intake of omega-3 fatty

acids and lower levels of inflammatory factors in the healthy one compared to asthmatic one may explain the protective role of essential fatty acids in asthma (Haidari *et al.*, 2014).

Gastro intestinal disease

Fish oil supplementation in patients with inflammatory bowel diseases (IBD) have shown to modulate levels of pro-inflammatory mediators and may be beneficial for the induction and maintenance of remission in ulcerative colitis. (De Ley *et al.*, 2007)

Eye diseases

Retinopathy of prematurity (ROP) may resolve spontaneously and sometimes can progress to a severe form, which may lead to permanent blindness especially in childhood (Cask *et al.*, 2006). Omega-3 fatty acids create bioactive mediators which protect against the growth of abnormal blood vessels. these mediators suppress tumor necrosis factor(TNF- α) which is closely associated with abnormal growth of retinal blood vessels (Purslow, 2014).

Omega3 fatty acids and cancer

Epidemiological studies have shown a reduced incidence of cancer in population consuming high levels of dietary fish.omega-3 fatty acids have regulatory effects on cell proliferation and apoptosis. they may help sensitizing tumors to different chemotherapeutics (Calviello *et al.*, 2007). Improving quality of life and reducing post surgical morbidity in cancer patients (Colomer *et al.*, 2007). The literature suggests that marine PUFAs have potential as an effective adjuvant to chemotherapy treatment, may have direct anticancer effects, and may help ameliorate some of the secondary complications associated with cancer. Although a range of doses have been trialled, It would appear that supplementation of fish oil (43 g per day) or EPA/DHA (41 g EPA and 40.8 g DHA per day) is associated with positive clinical outcomes (Vaughan *et al.*, 2013).

Omega-3 PUFAs and cardiovascular disease

Dietary intake of ω 3 PUFAs, particularly fish oil, has been clearly shown to have a beneficial effect on the cardiovascular system. So a coordinated effort is needed to make ω 3PUFAs more amenable for use in prevention and treatment of cardiovascular Disease (Vaughan *et al.*, 2013). Omega-3long chain PUFA intake in the primary prevention of coronary heart disease (CHD) assessing the efficacy of omega-3 long chain PUFA for the prevention of atrial fibrillation (AF)., the highest blood level of DHA plus EPA and DPA was associated with a 50% lower risk of developing AF (Rizos *et al.*, 2012). Many of the cardiovascular effects of ω 3 PUFAs have been linked to their anti-thrombotic, antioxidant / anti-inflammatory, anti-arrhythmic, and vasorelaxing activities (Vaughan *et al.*, 2013).

Diabetes mellitus

Experimental studies found that there is impairment in essential fatty acids metabolism in diabetic patients by

decreasing activities of de-saturase enzymes that convert dietary ω 6 linoleic acid and ω 3 α linolenic acid to long chain polyunsaturated fatty acids leading to fatty acid imbalance which contributes to reduction in peripheral nerve conduction velocity (Patricia *et al.*, 2015). Dietary intake of omega-3 fatty acids reduced the risk of islet autoimmunity (IA) in children with augmented genetic risk of type 1 diabetes. The beneficial activities of omega-3 PUFA on T cell functions in type 1 diabetes could be attributed to their suppressive effect and modulation of cytokine secretion, and improvement of intracellular oxidative status. Higher consumption of LCFAs and fish reduces the risk of type 2 diabetes mellitus. (Abdulrashedand Sharada, 2014)

Chronic renal failure (CRF)

(Friedman and Moe, 2006) found that Supplementation of patients with renal failure with omega-3 has many important effects on body systems as:

- Reduction of arterial blood pressure which is associated with CRF.
- Omega-3 may be effective in improving patency of dialysis shunt by their anti-thrombotic, anti aggregatory and anti proliferative actions.
- Omega-3 fatty acids improve uremic pruritus symptoms which is associated especially with dialysis

Atopic dermatitis and eczema

According to (Hwang *et al.*, 2007) who examined the levels of omega-3 fatty acids in red blood cells membrane in normal children and children with atopy (as atopic dermatitis), red blood cells fatty acid composition showed that total omega-6 and ω -6/ ω -3 ratio were greater in children with atopy. Eczema often results from excessive levels of PGE2 and LTs. Reducing ω 6 arachidonic acid levels by using high dose marine oil inhibit the production of leukotrienes. Various studies have indicated that high dose marine oil, without the use of corticosteroid, can contribute to some improvement in eczema (Koch, 2008).

Psoriasis

Omega-3s inhibit proliferation of skin cells which cause psoriasis, and Fish oil suppress the formation of leuktriene B4 and increase leuktriene B5 in psoriatic plaque within 4-7 days of starting treatment. Topical use of Fish oil may improve symptoms of psoriasis as reducing scaling and erythema (Robinson and Mazurak, 2013). Fish oil used in combination with anti- psoriasis therapy to reduce the hyperlipidemia caused by anti- psoriasis drug, and decrease the nephrotoxicity of cyclosporin in patients with psoriasis (Koch, 2008).

IgA Nephropathy

Patient with IgA Nephropathy have an abnormal essential fatty acids profile and supplementation with fish oil can correct this abnormality. This is also effective in slowing the progression of IgA Nephropathy with marked improvement in glomerular filtration rate (Elmesery *et al.*, 2009). Omega-3

supplementation in IgA Nephropathy alter several biologic systems including eicosanoid and cytokines production, membrane fluidity and TXA2 dependent platelet aggregation. The net effect could reduce glomerular injury (Robinson and Mazurak, 2013).

Attention Deficit Hyperactivity Disorder (ADHD)

Several clinical studies have noted that ADHD have deficiency of Omega-3 fatty acids with a very high arachidonic acid/eicosapentaenoic acid (Gomes *et al.*, 2011). In another Study, Children were given polyunsaturated fatty acids capsules for 15 weeks then evaluated for ADHD symptoms. There was significant improvement in attention, hyperactivity, behavior and in social problem. This improvement is equivalent to or slightly better than that observed with medical treatment (Johnson *et al.*, 2011).

Autism

Autistic children also had a significantly higher ratio of omega-6/omega -3 deficiency of DHA observed in Autistic children may be due to poorer ability to form DHA and/or enhanced break down of polyunsaturated fatty acids in phospholipid membrane (Mostafaand. AL-Ayadhi, 2015).

Rheumatoid arthritis

Omega-3 help in reducing symptoms of rheumatoid arthritis. Some preliminary evidence suggests evening may Omega-3 reduce pain, swelling, and morning stiffness; but other studies have found no effect. When using GLA for symptoms of arthritis, it may take 1-3 months for benefits to appear (Robinson and Mazurak, 2013).

DISCUSSION

In the omega family, there are omega-3, omega-6, and omega-9 fatty acids. The most common omega-3 fatty acids, are α -linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and Stearidonic acid (SDA), The most common omega-6 fatty acid is linoleic acid. The ratio of omega-6: omega-3 may play a role in health (Kelly and Kathleen, 2010). In Egypt, the major edible vegetable oil sources are cottonseed, sunflower and corn oils, palm, soybean. Palm oil rich in saturated fatty acids and very low in ω 3 FAs represents more than 70% of the total oil consumption. This was behind the increase of the cardiovascular diseases (CVD) and blood cholesterol between male and female in Egypt (Attia, 2013). In omega fatty acids metabolism both n-6 linoleic and n-3 linolenic acids interact with liver enzymes and converted to long chain fatty acids through a process of desaturation and elongation, respectively and the new produced fatty acids build hormone like eicosanoids that regulate immune and inflammatory responses. Such hormones include prostaglandins, leukotrienes and thromboxanes (Attia, 2013). There are many recent studies explain the benefits of using marine-derived ω 3 PUFAs in cancer prevention, cancer therapy, and the prevention and treatment of cancer cachexia (Vaughan *et al.*, 2013). Investigate the association of fish and ω 3 PUFA consumption and hepatocellular carcinoma and

found that consumption of ω 3PUFA-rich fish and supplements was inversely associated with hepatocellular carcinoma in a dose-dependent manner (Scorletti and Byrne, 2013).

Conclusion

Omega-3 and omega-6 are polyunsaturated essential fatty acids which can't be constructed by the body and must be obtained through diet. Sources of omega-3 (linolenic acid, eicosapentaenoic acid and docosahexaenoic acid) include fish and flax (eg. Fish oil) and sources of omega-6 (Linoleic acid) account for majority of polyunsaturated fats in the food (eg. Corn oil). Polyunsaturated fatty acids are vitally important structural elements of cell membranes and essential for formation of new tissues. Fetus and infants are unable to convert enough α -linolenic acid and are dependent on maternal supply. The human milk provides all dietary essential fatty acids. Docosahexaenoic acid is a predominant structural fatty acid in the retina and brain and is critical for optimal brain health and function at all ages. Omega-3 is important for brain and emotional health, neurological function, better developmental milestones and intelligence quotient. Eicosapentaenoic acid and docosahexaenoic acid have powerful modulating and stabilizing qualities and help to overcome many psychiatric disorders as schizophrenia, childhood autism. Omega-3 fatty acids have cardio protective effect, important for digestive tract health, bone and joint health, eye health, and play an important role in immune system maturation. Omega-3 supplementations can improve many symptoms of cystic fibrosis, promotes respiratory health and function and decreases the prevalence of asthma. Also, it is helpful in treatment of acute respiratory distress syndrome, ocular diseases, irritable bowel disease, IgA nephropathy, nephrotic syndrome, chronic renal failure and type 1 diabetes mellitus. Topical omega-3 application can benefit many dermal diseases as psoriasis, eczema and atopic dermatitis. Epidemiological studies have shown a reduced incidence of cancer in populations consuming high levels of dietary fish.

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