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Effects of omega-3 on thyroid function tests in healthy volunteers

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ABSTRACT

Supplements play a pivotal role in medicine especially fish consumption or supplementation with omega 3. Omega-3 and thyroid hormones are important in keeping some essential body functions working normally and alterations of thyroid hormones levels can result in many pathological states. Our study aimed to investigate whether omega-3 supplementation (1000 mg/day for 2 months given orally) would affect thyroid hormones and thyroid-stimulating hormone in healthy volunteers with normal thyroid status. Normal thyroid status of the experimental group was well defined by serum levels of triiodothyronine (T_3), thyroxine (T_4), and by thyroid-stimulating hormone. Thyroid hormones (T_3 and T_4) levels were increased insignificantly in treated volunteers compared to the same volunteers before consumption of omega-3 (2.20 ± 0.37 to 2.23 ± 0.39 and 89.87 ± 9.93 to 90.98 ± 11.85 nmol/L, respectively). On the other hand, thyroid-stimulating hormone significantly increased after 2 months of omega-3 consumption (1.46 ± 0.47 to 1.68 ± 0.39 µIu/L). In conclusion, supplementation of omega-3 in the present study did not significantly modify either T_3 or T_4 and bodyweight in healthy volunteers. These data reinforce recommendations that indicate consumption of omega-3 is considered safe as far as thyroid function is concerned in healthy human volunteers. These findings advocate continued investigation of omega-3 for more than 2 months and higher dose to confirm its safety.

Keywords: Omega-3, thyroid stimulating hormone, triiodothyronine, thyroxine

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INTRODUCTION

There is a growing body of evidence on the importance of dietary supplements. For example, in the United States, 52% of adults reported the use of a dietary supplement. [1] Among these, omega-3 fatty acids represent one of the strongest players in the food supplement market. This role was enhanced by the allowance of American Food and Drug Administration (FDA) in 2004 for omega-3 manufacturers to add to the labels that omega-3 can reduce the risk of coronary heart disease. [2]

Omega-3 is a type of polyunsaturated fatty acids. Fatty acids are carboxylic acids with a long hydrocarbon chain. When there are two or more double bonds in the hydrocarbon chain, the fatty acid is termed "polyunsaturated". If there are 3 carbon atoms between the terminal carbon in the hydrocarbon chain (furthest from the carboxyl group, the omega carbon or Cω) and the first double bond in the chain, the fatty acid is one of the omega-3 series. [3] Animals and plants can supply omega-3; fish is a rich source of eicosapentaenoic acid (20-carbon chain) and docosahexaenoic acid (20-carbon chain), while certain plants such as walnut and soybean supply α-linolenic acid (18-carbon chain). [4]

The health benefits of omega-3 fatty acids arise mainly from their role in lowering the risk of cardiovascular diseases. [4] In addition, it has been reported that omega-3 fatty acids have beneficial effects in certain chronic inflammatory conditions, neurological disorders and fetal development. [5] Examples of cardiovascular events that can benefit from omega-3 fatty acids include reduced risk of sudden cardiac death resulting from ventricular arrhythmias, [6] protection against atrial fibrillation especially in the elderly, [7] reduced risk of heart failure, [8] reduced risk of the formation of atherosclerotic plaque, [9] reduction of triglyceride concentration to the extent that can be used therapeutically when diet and lifestyle changes are not enough, [10] and reduction in blood pressure. [11] Inflammatory conditions that can benefit from omega-3 consumption include rheumatoid arthritis and psoriasis. [12] Depression and Alzheimer's disease are examples of neurological conditions where omega-3 might offer some benefit. [5]

Relying on a marine diet to supply omega-3 fatty acids in the amounts required to produce the above-mentioned benefits is possible but not practical in many parts of the world. Therefore, therapeutic supplementation is desirable. [13,14] According to the British National Formulary (BNF), omega-3 fatty acids are available from the pharmacies as 600-mg, 1,000-mg or 1,200-mg soft gelatine capsules containing a combination of eicosapentaenoic acid and docosahexaenoic acid.

In general, omega-3 fatty acids are safe and well-tolerated in the doses given for dietary supplementation. [15] However, some adverse effects have been reported with the use of omega 3. Most important of these include impaired wound healing due to reduced platelet activation resulting from the less potent platelet activator thromboxane A3 that is produced in higher ratio following omega-3 intake. Omega-3 fatty acids can accumulate in cell membranes where that may be easily peroxidated with a consequent reduction in membrane stability. This effect can be avoided by co-administration of antioxidants which are free radical scavenger. [16–18] To further validate the safety of omega-3 as a dietary supplement, this work aims

to investigate the effect of these fatty acids on thyroid function in healthy adults. This was achieved by studying the correlation between omega-3 administration and the level of thyroid hormones and TSH. One of the reasons for choosing thyroid in particular is its being one of the basic elements, along with omega-3 fatty acids, for normal functions of vital organs such as the brain. [19]

MATERIALS AND METHODS

Study design

To achieve the aim of the present study, an open-label trial was adopted. This research was conducted on 40 healthy volunteers (they were 50 at the beginning but 10 subjects withdrew due to lack of desire to continue with the study) aged between 25 and 40 years. All participants have confirmed to be free from diseases and drug intake. This was ascertained to avoid any drug or disease interaction that may affect the results.

Ethical approval

The protocol of this study was approved by Nineveh Health Directorate, Training Centre and Human Development, by their certificate numbered 1050. All participants involved in this study were well informed of the approved study protocol and they signed informed consent before the study.

Blood sampling

Five to ten millilitres of venous blood were collected before and after the administration of tested agent from each volunteer. The participants were instructed to be fasting overnight before each blood sample collection. The blood samples were centrifuged after collection and the serum was separated and kept frozen at -20 °C to be tested later on.

Agent used

The volunteers selected for the study started to receive omega-3 soft gelatine capsule [eicosapentaenoic acid (EPA) 300 mg and docosahexaenoic acid (DHA) 200 mg] once daily for two months. Omega-3 capsules used were manufactured by ADRIEN GAGNON (Canada).

Thyroid function test

Thyroid function test was carried out by enzyme-linked fluorescent assay (mini VIDAS®- bioMérieux) according to the kit's manufacturer instructions.

Statistical analysis

Experiments were conducted >3 times. Student's paired *t*-test was used to determine statistical significance. The minimal level of significance ($p < 0.05$) was determined using Graph Pad Prism 8.0 software. All values were expressed as the mean ± standard deviation.

RESULTS

Body weight and Body mass index

Bodyweight and body mass index (BMI) were measured before and following 2 months exposure of participants to a single daily dose of omega 3. Time-dependent increases in bodyweight and BMI were not evident after 2 months of omega-3 use. At a single daily dose of the tested agent, the mean of weight and BMI were insignificantly increased from 71.12 ± 7.69 to 72.94 ± 8.98 kg, and from 24.10 ± 1.44 to 24.46 ± 2.27 kg/m2 respectively (Figure 1). The mean age of participants was 36.88 years.

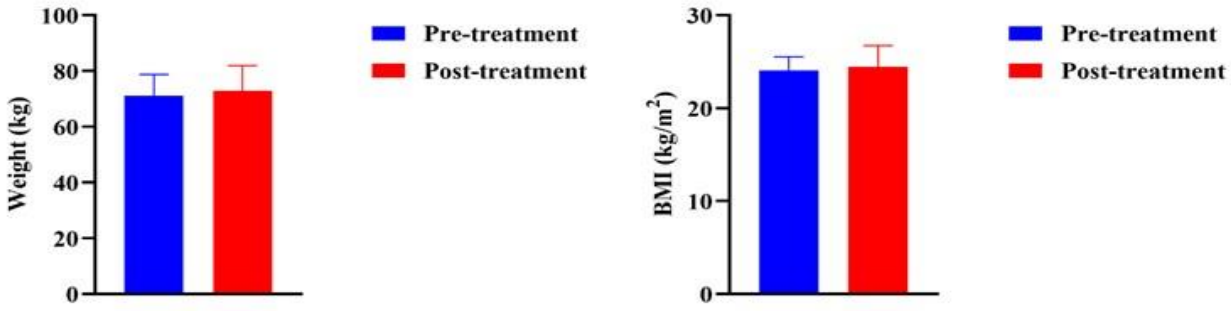

Figure 1: The effect of omega-3 on bodyweight and BMI after 2 months.

***Left**: The effect of daily use of 1000 mg of omega-3 on the weight of healthy individuals.*

***Right**: The effect of daily use of 1000 mg of omega-3 on BMI of healthy volunteers. Student's paired t-test was used to represent a statistically insignificant difference, in the bodyweight and BMI, between pre- and post-treatment. Data represented as the mean ± standard deviation*

Thyroid function tests

Thyroid function tests revealed insignificant changes in the triiodothyronine (T_3) and thyroxine (T_4) levels after a single daily dose of omega-3 for 2 months (Figure 2). However, profound thyroid stimulating hormone (TSH) elevation was observed from 1.46 ± 0.47 to 1.68 ± 0.39 µIu/L ($P < 0.05$) following 2 months of exposure to omega-3 (Figure 2).

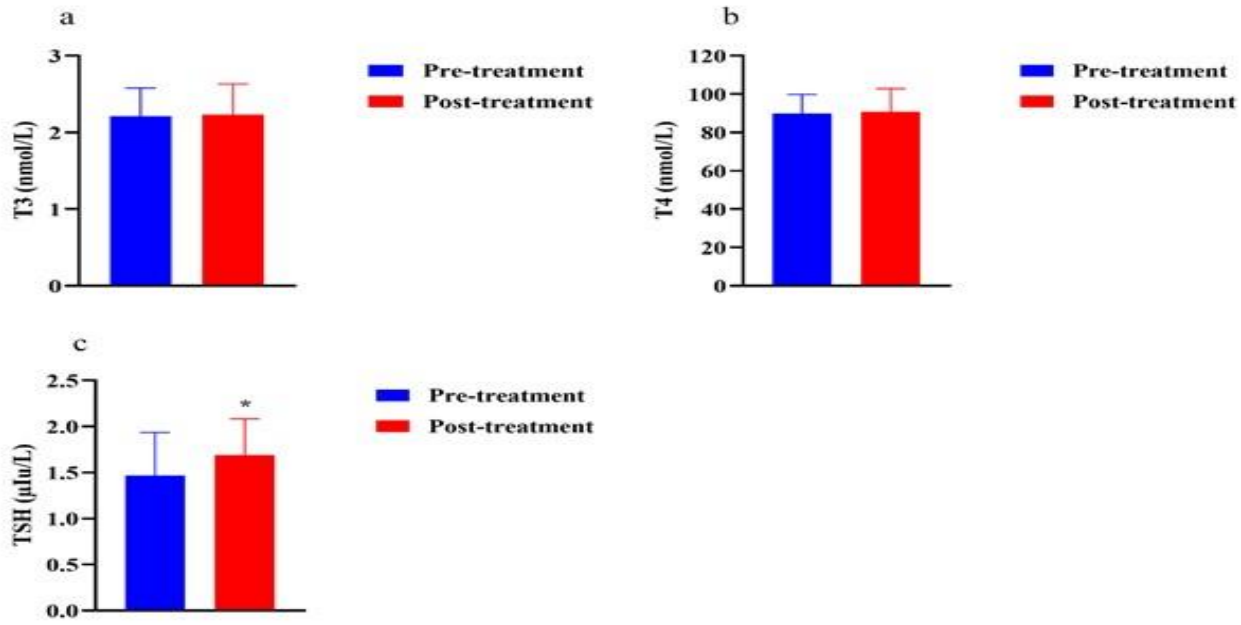

Figure 2: The effect of omega-3 on T_3, T_4 and TSH after 2 months of administration of omega-3.

*(a) the effect of a single daily dose of omega-3 on T_3 in healthy participants. (b) the effect of a single daily dose of omega-3 on T_4 in healthy participants. (c) the effect of a single daily dose of omega-3 on TSH in healthy participants. *P < 0.05 represents a statistically significant difference (Student's paired t-test) between pre- and post-treatment. Data represented as the mean ± standard deviation.*

DISCUSSION

Thyroid hormones have an essential role in the growth, development and function of vital body organs such as central nervous system (CNS). They control neuron communication across a synapse, regulate the production and turnover of neurotransmitters and change the sensitivity of their receptors. [20,21] They modify signal transduction pathways in the CNS through Ca^{2+} channels that play vital roles in the release of neurotransmitters and gene regulation. [20,21] The present study showed that omega-3 treated healthy volunteers had an insignificant change in T3 level, T4 level and bodyweight with a significant increase in TSH level as compared to the normal levels of these hormones. Omega-3 (polyunsaturated fatty acid (PUFA), including EPA) regulates the thyroid cell function via two main pathways: regulation of signal transduction pathway by manipulating the composition of membrane fatty acid; and rapid, direct modulation of gene transcription. [22] Several studies have confirmed these mechanisms via providing evidence demonstrating that the modulation in plasma membrane lipids in thyroid glands could modulate the TSH receptor and its sensitivity to binding TSH. [22] Furthermore, an essential role for phospholipids has been demonstrated in the TSH- responsive adenylate cyclase system. [22] In addition to that, arachidonic acid and EPA, constituents of the plasma membrane, are metabolized via the epoxygenase or lipoxygenase pathways to produce eicosanoids. These eicosanoids may affect thyroid hormone biosynthesis or release via affecting TSH receptor and signal transduction. [22] In related, several experiments, in animals, it has been shown that administration of eicosapentaenoic acid was responsible for inhibiting the decrease in plasma T3 and T4 concentrations and increase in plasma TSH concentration in the hypothyroid state.

Although these findings suggest that eicosapentaenoic acid may affect the level of thyroid hormones in hypothyroid patients, our finding ruled out that omega 3, including eicosapentaenoic acid has the same effect on T3 and T4 in healthy people. It will be interesting to determine whether other PUFAs, such as docosapentaenoic acid, would produce the same consequence. Although the significant increase in the level of TSH agreed with Makino et al, T3 and T4 were not significantly changed. Makino et al suggested that omega-3 could modulate the TSH receptor and affect the binding affinity of these receptors to TSH. [22] Even though thyroid hormones continued the same in healthy volunteers who used omega-3, the epidemiological data have afforded clear evidence that EPA administration is concomitant with a decrease in the risk of atherosclerosis, cardiovascular diseases and hyperlipidemia. [23–25] Several studies have confirmed that consuming diets deficient in EPA may contribute to several disease processes. [26] Omega-3, which contains unsaturated fatty acid including EPA and DHA, have an effective stimulatory effect on fatty acid oxidation with a potent suppressive effect on the synthesis of triglyceride and hepatic lipogenesis resulting in a decrease in the level of plasma triglycerides and modification in the hepatic metabolism of cholesterol, leading to a decline in cholesterol level. [26–28] These effects may be attributed to the ability of EPA to enhance thyroid hormone action in the liver without affecting the level of thyroid hormones. [26] EPA modulates thyroid hormone action via higher protein expression of liver thyroid expression receptor (TR) β1. [26] The activity of the hepatic mitochondrial glycerophosphate dehydrogenase, an enzyme that plays a role in thermogenesis stimulated by T3 via TRβ1 receptor, was found to be higher in the presence of EPA, leading to boost of thyroid hormone action. [26,29]

CONCLUSION

Taken together, we found that there are no statistically significant changes after 2 months consumption of omega-3 at a single daily dose on thyroid hormones. These data reinforce recommendations of the safety of omega-3 supplementation in healthy people while suggesting the same useful therapeutic effects in treatment, or decrease in the risk of atherosclerosis, cardiovascular diseases and hyperlipidemia via enhancing thyroid hormones action in the liver without affecting on the level of these hormones. However, we recommend future researches using higher dose and longer time of consumption of omega-3 to confirm these data.

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