The Effect of Fish Oil Supplement on Serum Antioxidant Level in Patient with Rheumatoid Arthritis

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Abstract: *Purpose*: Rheumatoid arthritis (RA) is a common autoimmune disease characterized by inflammation and over-growth of the synovium. RA is accompanied with increased levels of free radical and stress oxidative. In recent years, there has been an increasing interest in nutritional factors on disease and autoimmune system. More recently literatures have emerged that offers contradictory findings about fish oil on antioxidant levels. So far however, there has been little discussion about fish oil as antioxidant on Rheumatoid arthritis. This paper will focus on effect of fish oil over serum antioxidant levels and activity disease of RA.

Methods: A randomized double blinded control trial 90 patients from a population of Rheumatoid Arthritis who were selected. Forty five patients received Fish oil (FO) (1gr /day) in addition of conventional therapy for RA versus 45 patients received placebo. And serum levels of plasma antioxidant capacity (TAC) and the activity of superoxide dismutase (SOD) and Glutathione peroxides (GPX) were measured.

Results: There was no statistically difference between groups in plasma antioxidant capacity and the activity of superoxide dismutase, Glutathione peroxides. There weren't any correlation among DAS and antioxidant serum levels.

Conclusion: The findings emerging from the present inquiry suggested that FO with 1 gram daily dose didn't have effect on serum antioxidant level and activity of disease in RA.

Keyword: Rheumatoid arthritis, omega3, Fish oil, antioxidant.

INTRODUCTION

Rheumatoid arthritis (RA) is one of the most important diseases in rheumatology medicine because of its prevalence, chronic course and treatment costs. RA characterized with the breakdown of cartilage, juxta-articular bone, and generalized bone loss with reduced bone mass. The consequences of this intense bone loss are painful joint deformities, progressive functional disability, and increased risk of bone fractures and increased mortality rates [1]. Alteration in the oxidant-antioxidant profile is known to occur in rheumatic diseases and oxidative stress is increased in RA, it contributes to immune system dysregulation, autoantibody production, free radical production and abnormal activation and processing of cell-death signals [2]. It has been shown that, under inflammatory or infectious conditions free radicals (FR) / reactive oxygen species (ROS) productions exceed the eliminating capacity of the body antioxidant mechanisms, causing oxidation injury by attacking macromolecules like lipids, carbohydrates, proteins and nucleic acids. On the other hand the auto-immune mediated inflammation observed in RA patients contributes to increased endothelial dysfunction, oxidative stress and activation and vascular migration of leukocytes [3].

Recent studies have emphasis that, diet and nutrition have played an important role in maintaining physiological homeostasis. Nutritional compounds which display anti-inflammatory and antioxidant effects have specific applications in preventing oxidative stress induced injury which characterizes their pathogenesis [4].

Many treatments introduced for RA, The common aspect of all RA treatments is anti-inflammatory effects on the inflammatory and immunologic system [5]. In recent years, there has been an increasing interest in about the effect nutritional factors on inflammation and immunity system [6]. Fish oil is an antioxidant and which has anti-inflammatory effects [7]. More recently literatures have emerged that offers contradictory findings about omega3 effect on antioxidant levels. Some study show severity of disease is low in patient with high serum antioxidant level [8, 9]. Attention to prevalence of RA in Iran (0.3 %) [10] And its important effects on all aspects of patient's life, we promise to focus on effect of antioxidants such as fish oil levels on activity of RA.

MATERIALS AND METHODS

The present study was conducted at Rheumatology Clinic of Tabriz University of Medical Sciences

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(RCTUMS) where patients registered and selected for study. The participants in this study included 90 patients from a population with Rheumatoid Arthritis who were selected based on American college of Rheumatology criteria (ACR) [11]. The exclusion criteria were: patients with BMI > 30 kg/m^2, history of smoking or alcoholism, coronary heart diseases, uncontrolled hypertension (systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg), diabetes mellitus, thyroid dysfunctions, or other metabolic diseases and patients who received micronutrient supplements, lipid-lowering drugs, and hormone replacement therapy. The patients with changed drug schedule in previous 2 months and during the study period were also excluded. Drug schedule was kept constant throughout the experimental period for all of the patients. The participants were grouped into two experimental and control groups based on Opaque packet selection. Forty five patients received fish oil (1gr /day) in addition of conventional therapy for RA versus 45 patients received conventional treatment and placebo. Each 1 gram capsule of fish oil (provided by Zahravi Co) composed of 180 mg eicosapentaenoic acid (EPA) and 120 mg docosahexaenoic acid (DHA). The appearance of placebo capsules were similar to the fish oil capsules but without ω-3 substance. The capsules were taken as a single dose daily in fasting time. To measure activity of disease, Disease Activity Score 28 (DAS28) questionnaire was utilized including the numbers of swollen and tender joints, high-sensitivity C-reactive protein (hs-CRP) and patient general health by the patient using visual analog scale (VAS) [online at www.das-score.nl] [12] To measure effect of supplement, two test were performed, one at the onset of study, another one after a 90 day after intervention.

The effect of supplement on total Antioxidant level (TA), superoxide desmotas (SOD), Glutation peroxides (GPX) were measured before and after intervention. Blood samples were obtained after overnight fasting at the beginning and the end of treatment with fish oil or placebo, respectively. The separated serums were collected and stored in -70 °C. Serum TA concentration was determined by commercially Enzyme-Linked Immunosorbent Assay (ELISA) kits; GPx by RANSEL

Table 1: Laboratory Findings of the Patients at Baseline and after 3 Months Treatment with Fish Oil vs. Placebo

Variable	fish oil group (n=40)	Placebo group (n=43)
hs-CRP (mg/dl)		
Baseline	5.8 (0.3 - 14.1)	4.8 (0.1- 14.0)
3 months	3.9 (0.1 - 14.8)	6.1 (0.1-16.5)
	(p = 0.1) [(1)]	(p = 0.5) [(1)]
Serum SOD (pg/ml)		
Baseline	233.83 ± 46.93	240.81± 49.26
3 months	226±39.94	240.85±53.89
	(p < 0.09) [(1)]	(p = 0.77) [(1)]
Serum GPX (pg/ml)		
Baseline	5190.58± 446.15	4980.21± 525.72
3 months	5484.95+517.73	5128.65 ± 537.15
	(p < 0.07) [(1)]	(p = 0.08) [(1)]
Serum MDA		
Baseline	3.46 ± 1.33	3.39 ± 1.05
3 months	3.48± 1.48	3.21± 1.24
	(p < 0.77) [(1)]	(p = 0.08) [(1)]
Serum TA (pg/ml)		
Baseline	0.83 ± 0.09	0.88 ± 0.14
3 months	0.92± 0.19	0.9 + 0.18
	(p = 0.08) [(1)]	(p = 0.08) [(1)]

SOD, superoxide desmotas; GPX, Glutation peroxides; MDA, Malandial deid; TA,Antioxidant; hs-CRP, high-sensitivity C-reactive protein; (1) Before treatment vs. after treatment with fish oil or Placebo.

kit (Lot. No.: RD-1839 hs-CRP was determined by immune turbidometry assay (Pars Azemoon Co, Tehran, Iran). The ethic committee of Tabriz University of Medical Sciences reviewed and approved the study which is in compliance with the Declaration of Helsinki. Statistical significance was assessed by T-Test and Difference between groups were considered significant when $P \leq 0.05$. To compare probable effects of supplement versus placebo, the researchers used an independent sample T-Test and Mann-Whitney test.

RESULTS

At the end of study, 83 patients completed 3 months follow-up; forty patients treated with fish oil and 43 patients treated with placebo (7 patients did not complete the study protocol). The patient's demographic data and baseline characteristics of the two groups are shown before in the other our double-blind randomized controlled trial project for investigation effect of fish oil supplements on serum paraoxonase activity in female patients with rheumatoid arthritis [13].

No significant difference was present between fish oil or placebo treated groups in regard of ages, disease duration, and post menopauses, type of conventional therapy, BMI, swollen and tender joints number and DAS28 at the beginning of the study. The serum levels of SOD, GPX, MDA, TA and hs-CRP at the baseline and following of 3 months of treatment with fish oil or placebo have been shown in Table **1**.

There was no statistically difference between two groups. There weren't any correlation among DAS and antioxidant serum levels.

The results of analyzes in two groups showed no statistically significant correlation after three months intervention between superoxide desmotaz action, glutation peroxidaz enzyme levels change, total serum antioxidant levels with each other's and disease severity ($p>0.05$ in all cases). Also, there has not been seen any statistically significant correlation between change of antioxidant enzymes (superoxide desmotaz, glutationperoxidaz) action levels with lipid peroxidation index (MDA) and disease activation score (DAS) in two groups ($p>0.05$in all cases).

DISCUSSION

Increase of oxidative stress and decrease of included enzymes in this process had been shown in several diseases; especially rheumatoid arthritis [14-16]. The present study was designed to determine the effect of fish oil supplement versus placebo in Iranian patients with RA. The result of study didn't show any effect on oxidative serum level in RA. This study didn't demonstrated significant differences among placebo and fish oil in RA on superoxide desmotaz, glutation peroxidaz action and serum total antioxidant level after receiving 3 month fish oil.

The finding emerging from the present study does not lend support to those of Kermes *et al.* [17] that showed 6 gram daily fish oil decreased symptom of patient with RA.

The finding call into the question finding of Berbert [18] that showed pain and morning stiffness statistically significant decreased and hand fingers grasping force increased with fish oil after 12week and After 24 weeks, disease progression improved with supplement. Change of food regimen in patients with RA showed that serving of 15% of food regimen of omega-3 statistically significant differ disease activation, due to high action of antioxidant enzymes such as superoxidd esmotaz and pathologic survey of tissue samples showed that omega-3 induced decrease of inflammation synovial tissue [19]. One American study in 1997 showed that superoxide desmotaz action increased and serum MDA decreased in patients that 7% their food regimen included fish oil for 2-6 weeks [20].

We haven't found any clinical trial study about the effect of fish oil in RA. A number of limitation restrict generalization of the finding from this study, First, we used low dose of fish oil due to its price, Second, we couldn't evaluate effect of other drugs in patient with RA and other explanations are deferent in dosage of fish oil supplement and duration of treatment.

CONCLUSION

The findings emerging from the present inquiry suggested that FO with 1 gram daily dose didn't have effect on serum antioxidant level and activity of disease in RA.

CONFLICT OF INTERESTS

The authors declare no conflict of interests that exist.

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