Original Article

Effect of omega-3 supplementation on inflammatory parameters in patients on chronic ambulatory peritoneal dialysis

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Abstract

Background: End stage renal disease (ESRD) is a state of micro inflammation that attenuates patient's life span and quality of life. Inflammatory markers like interlukin 6 (IL-6) and C- reactive protein (CRP) can predict inflammatory state in ESRD patients. Dietary limitations are risk factors for omega-3 deficiency in these patients. Omega-3 supplementation is an attractive material that proposed in inflammation modulation. The aim of this study is evaluation of effect of omega-3 supplementation on IL-6 and CRP level in chronic ambulatory peritoneal dialysis (CAPD) patients.

Materials and Methods: This randomized controlled double-blind clinical trial is performed in 40 CAPD patients in two academic hospitals in Isfahan, Iran. One group received 1000 mg omega-3 capsule (each capsule contains 180 mg Eicosapentanoic and 120 mg Dosahexanoic acid) three times a day orally for 8 weeks ($n = 20$) and the other matched group by placebo ($n = 20$). Serum level of IL-6 and quantitative CRP (Q-CRP) were measured in beginning and the end of the study. Finally all data were analyzed by SPSS version 18.

Results: Mean age of patients was 53 years old in omega-3 group patients and 54 years old in placebo group. There were not any differences in CRP and IL-6 level in the beginning and the end of study between two groups (*P*: 0.81 and 0.10 for CRP and 0.26 and 0.23 for IL-6, respectively).

Conclusion: Omega-3 supplementation did not effect on inflammatory markers (Q-CRP and IL-6) in CAPD patients after 8 weeks.

Key Words: C– reactive protein, chronic ambulatory peritoneal dialysis, interlukin 6, omega–3

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INTRODUCTION

Mortality in end stage renal disease patients (ESRD) is correlated with traditional and nontraditional or "novel" risk factors.[1] In Framingham Heart study, some characteristics like sex, hypertension, age, diabetes mellitus, smoking regarded as traditional risk factors. In addition, in some researches, some other risk factors including hypoalbuminemia, increased fibrinogen level and inflammation had related to cardiovascular mortality and morbidity referred as non-traditional risk factors.[2] Susceptibility to increasing inflammatory process look multiple reasons, perhaps of dialysis or non-dialysis factors.[3] In uremic patients, cytotoxines can generate excess

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oxidative stress that ultimately produce reactive oxygen species (ROS).[4,5] Therefore, advanced glycation endproducts (AGEs) are produced and convert short-lasting inflammatory responses to sustained pro-inflammatory reactions that induce atherosclerosis and calcifications.[6,7] Some inflammatory biomarkers are recognized in these processes that C-reactive protein (CRP) is the attractive molecules between them.[8] ESRD patients have elevated level of CRP due to dialysis membranes, fluid overload or chronic persistent infections caused by grafts and catheters.[9] According to one study, serum CRP level is associated with higher mortality independent of serum albumin level.[10] Another biomarker that was proposed as an useful molecule is interlukin-6 (IL-6) that acts as pro- and anti-inflammatory cytokine.[11] Serum level of IL6 in ESRD patients increases and its level do not change pre and post hemodialysis.[12] Some materials including fish oil could reduce atherosclerosis and inflammation *via* inhibition of lipid peroxidation.[13] However, some investigations describe the benefits of omega-3 supplementation in prevention of inflammation progression in hemodialysis patients.[14,15] But few studies are designed for effect of omega-3 in peritoneal dialysis patients, as a modality for renal replacement therapy.[16,17] In this study, we decided to evaluate the effect of omega-3 on IL6 and CRP, as inflammatory parameters, on CAPD patients.

MATERIALS AND METHODS

This randomized controlled double-blind clinical trial was carried out in two CAPD centers in two university hospitals in Isfahan, Iran. Patients with ESRD on continuous ambulatory peritoneal dialysis for at least 3 months and at least 18 years old enrolled in the study after agreement of consent form. If the patients had thrombocytopenia (PLT < 100,000/mm^3), steatorrhea, malignancy, abnormal coagulation profile or need for anticoagulation therapy, they exclude from the study.

All patients those were enrolled into the study were divided into two groups as shown in Figure 1. In case group (N = 40), they receive omega-3 capsule, three times a day for 2 months. Each 1 gram capsule (Omega-3, Zahravi co. Tabriz. Iran) contains Eicosapentanoic (180 mg) and Dosahexanoic (120 mg). In placebo group (N = 40) they receive placebo capsule, manufactured by the same as case group. All capsules have opaque enveloped and each patient receives the drugs for 2 months. After this, patient is admitted for evaluation of compliance, side effects and managing some possible problems. The next drugs enveloped were given them 1 month later. Serum levels of Interlukin-6 (IL-6) and C-reactive protein (CRP) were measured at beginning and the end of the study using auto analyzer, by standard kits.

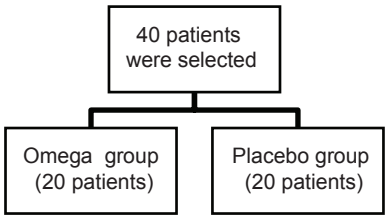

Figure 1: Flow diagram of the study process and patient selection

Patients were notified of the possibility of adverse effects such as abdominal pain, bloating, diarrhea, nausea and bleeding during the study. Incidence of these symptoms was evaluated by a specific questionnaire.

Statistical analysis

This study has approved by Isfahan Kidney Diseases Research Center (project no. 391350) and ethical committee of Isfahan University of Medical Sciences. This study was registered in Iranian registry of clinical trials with ID number: IRCT201303052417N11.

All statistical analyses were performed with SPSS software (version 18.0 SPSS Inc, Chicago, IL, USA). Statistical analysis was done with χ_2 test, paired t-test and analysis of variance (ANOVA). A 2-sided probability value of <0.05 was considered statistically significant and a 95% confidence interval was used.

RESULTS

A total of 40 patients allowed to participating in this study. All candidates were randomized into either Omega-3 therapy (n = 20) or placebo therapy (n = 20). During this study, any patient describes significant side effects leading to drug discontinuation in both groups.

Demographic and baseline characteristics of all patients included in the study are shown in Table 1. Our data showed no significant difference between two groups regarding age, sex, body mass index (BMI), medication usage and cause of renal failure.

After 2 months, mean serum level of CRP were not shown significant differences analytic (P = 0.047 and 0.054 respectively). This finding was similar about IL-6 after 2 months supplementation between omega-3 and placebo groups (P = 0.064 and 0.066). Details of data are demonstrated in Tables 2 and 3.

DISCUSSION

Inflammation in ESRD patients is a destructive state that has an important role in atherosclerosis and cardiovascular diseases. This process is mediated by

Table 1: Demographic characteristics of CAPD Patients at the start of study

Variable	Omega-3 group	Placebo group	*P* value
Age (year)	57.7±16.3	59.36±13.4	0.6
Body mass index (BMI) (kg/m^2)	25.02±3.8	25.51±5.4	0.61
Sex (% male/% female)	53/47	60/40	0.671
Cause of kidney failure			
HTN	19 (42.22%)	9 (20%)	0.83
DM	17 (37.77%)	23 (51.11%)	
Other	9 (20%)	13 (28.88%)	

P value <0.05: Significant

Table 2: Comparison of Interlukin-6 (IL-6) and quantitative C-reactive protein (Q-CRP) in baseline and at 8 weeks in two groups

Variable	Groups	Time		Time	
		Beginning	*P* value	End	*P* value
CRP (mg/L)	Omega-3	2.65040±3.88	0.069	2.37155±3.38	0.047
	Placebo	12.36330±22.84	0.076	18.67655±35.36	0.054
IL-6 (pg/mL)	Omega-3	10.07±25.92	0.335	10.19±27.41	0.064
	placebo	16.46±26.01	0.336	21.48±30.75	0.066

Table 3: Comparison of Delta Interlukin-6 (IL-6) and Delta quantitative C-reactive protein (Q-CRP) in baseline and at 8 weeks in two groups

Variable	Groups	Mean	*P* value (two-tailed)
Delta CRP	Omega-3	−0.2789	0.308
	Placebo	6.3132	0.314
Delta IL-6	Omega-3	0.1211	0.218
	placebo	5.0263	0.223

some mediators like Interleukins, CRP and tumor necrotizing factor.[15,18,19] Some studies suggest that CRP is not only a marker of inflammation.

Inflammation but also be a direct mediator of vascular disease.[20] On the other hand, inflammation is a common process in renal failure that could predict outcome in chronic kidney diseases, in all stages.[21] Therefore, we can suppress this process with using substances that can suppress inflammation. Between these, omega-3,[18] magnesium,[22] Zinc[23] and dietary antioxidants[24] have been studied till now. Omega-3 fatty acids act via modulation of cell membrane and synthesis of lipid mediators. Omega-3 fatty acid is derived from α-linolenic acid (ALA) then converts to eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) in endoplasmic reticulum and peroxisomes, respectively.[25] Ultimately, anti inflammatory effects of omega-3 derived from down regulation of proinflammatory cytokines and cell surface molecules areinvolved in cell adhesion and activation.[26] For this reason, fish oil is used for some inflammatory states like in rhomatoid arthritis,[27] crohn,[28] Ig A nephropathy,[29] sepsis,[30] too.

Some studies are performed in end stage renal disease patients in order to evaluation and benefit assessment of omega-3 on inflammatory processes. Madsen *et al.*,[31] demonstrate that there was no significant differences in serum level of CRP in ESRD patients on hemodialysis after daily supplementation with 2.4 g omega-3 for 8 weeks compared to placebo group. Tayyebi *et al.*,[32] describe similar findings in their study but reveal significant decreases in serum level of TNF-α after 3 g omega-3 per day. Although Şahinarslan described that serum level of IL-6, TNF-α and CRP had no differences in two types of dialysis (hemodialysis or peritoneal dialysis), the most studies did in hemodialysis patients.[32] In our study, we did not find any significant changes in serum level of IL-6 and CRP after supplementation with omega-3. This finding is against the Tayyebi study, although that study was done in hemodialysis patients.[33]

CONCLUSION

Omega-3 supplementation did not have effect on inflammatory markers (Q-CRP and IL-6) in CAPD patients after 8 weeks.

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