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Original article

Omega-3 fatty acids, inflammatory status and biochemical markers of patients with systemic lupus erythematosus: a pilot study☆

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ABSTRACT

Background: Studies have shown that omega-3 fatty acids reduce the concentrations of eicosanoids, cytokines, chemokines, C-reactive protein (CRP) and other inflammatory mediators.

Objective: To investigate the effects of omega-3 fatty acids on circulating levels of inflammatory mediators and biochemical markers in women with systemic lupus erythematosus (SLE).

Methods: Experimental clinical study (clinical trial: NCT02524795); 49 women with SLE (ACR1982/1997) were randomized: 22 to the omega-3 group (daily intake of 1080 mg EPA + 200 mg DHA, for 12 weeks) and 27 to the control group. The inflammatory mediators and biochemical markers at T0 and T1 in omega-3 group were compared using Wilcoxon test. U-Mann–Whitney test was used to compare variations of measured variables [ΔV = pre-treatment (T0) – post-treatment (T1) concentrations] between groups. $p < 0.05$ was considered significant.

Results: The median (interquartile range – IQR) of age was 37 (29–48) years old, of disease duration was 7 (4–13) years, and of SLEDAI-2K was 1 (0–2). The median (IQR) of variation in CRP levels between the two groups showed a decrease in omega-3 group while there was an increase in control group ($p = 0.008$). The serum concentrations of IL-6 and IL-10, leptin and adiponectin did not change after a 12 week treatment.

Conclusions: Supplementation with omega-3 had no impact on serum concentrations of IL-6, IL-10, leptin and adiponectin in women with SLE and low disease activity. There was a

☆ Study conducted at Unidade de Reumatologia, Hospital das Clínicas; Faculdade de Medicina, Departamentos de Sistema Locomotor, Cirurgia e Medicina Interna, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil.

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significant decrease of CRP levels as well as evidence that omega-3 may impact total and LDL-cholesterol.

Ácidos graxos ômega-3, estado inflamatório e marcadores bioquímicos de pacientes com lúpus eritematoso sistêmico: estudo piloto

Palavras-chave:
Ômega-3
Citocinas
Adipocinas
Proteína C-reativa
Lúpus eritematoso sistêmico

RESUMO

Introdução: Estudos têm mostrado que os ácidos graxos ômega-3 reduzem as concentrações séricas de eicosanoides, citocinas, quimiocinas, proteína C-reativa (PCR) e outros mediadores inflamatórios.

Objetivo: Investigar os efeitos dos ácidos graxos ômega-3 sobre os níveis circulantes de mediadores inflamatórios e marcadores bioquímicos em mulheres com lúpus eritematoso sistêmico (LES).

Métodos: Ensaio clínico randomizado (ensaio clínico: NCT02524795); foram randomizadas 49 mulheres com LES (ACR1982/1997): 22 para o grupo ômega-3 (dose diária de 1.080 mg de EPA + 200 mg de DHA durante 12 semanas) e 27 para o grupo controle. Os mediadores inflamatórios e marcadores bioquímicos em T0 e T1 no grupo ômega-3 foram comparados pelo teste de Wilcoxon. O teste U de Mann–Whitney foi usado para comparar variações das variáveis mensuradas [ΔV = concentrações pré-tratamento (T0) – concentrações pós-tratamento (T1)] entre os grupos. Um $p < 0,05$ foi considerado significativo.

Resultados: A mediana (intervalo interquartil – IIQ) da idade foi de 37 anos (29 - 48), a duração da doença foi de sete anos (4 - 13) anos e o *Systemic Lupus Disease Activity Index* (SLEDAI-2K) foi de 1 (0 - 2). A mediana (IIQ) da variação nos níveis de PCR entre os dois grupos mostrou um decréscimo no grupo ômega-3, enquanto houve um aumento no grupo controle ($p = 0,008$). As concentrações séricas de IL-6 e IL-10, leptina e adiponectina não se alteraram após um tratamento de 12 semanas.

Conclusões: A suplementação de ômega-3 não teve impacto sobre as concentrações séricas de IL-6, IL-10, leptina e adiponectina em mulheres com LES e baixa atividade da doença. Houve uma diminuição significativa nos níveis de PCR, bem como evidências de que o ômega-3 pode impactar sobre o colesterol total e LDL.

Introduction

Omega-3 fatty acids have been considered antiinflammatory lipids based on epidemiological studies of Greenland Eskimos, whose diet is rich in polyunsaturated fatty acids from fish. The prevalence of diseases with an inflammatory component such as acute myocardial infarction, diabetes mellitus, multiple sclerosis, asthma and thyrotoxicosis, was lower in the Eskimos compared to Western countries populations.[1]

Fatty acids of the omega-3 family [mainly the α-linolenic acid, eicosapentaenoic (EPA) and docosahexaenoic (DHA)], as well as those of the omega-6 family [represented mainly by linoleic acid and arachidonic acid (AA)] are essential for the synthesis of eicosanoids, prostaglandins, leukotrienes, thromboxanes and other oxidative factors, major mediators and regulators of inflammation.[2,3] Studies have shown that omega-3 fatty acids control inflammation by reducing C-reactive protein (CRP), eicosanoid proinflammatory cytokines, chemokines and other inflammatory mediators.[4–7] Furthermore, they present beneficial effects in the prevention and control of cardiovascular diseases, dyslipidemia and diabetes mellitus.[8–13]

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease characterized by loss of cellular immune regulation balance and increased levels of circulating inflammatory mediators.[14] Thus, omega-3 supplementation could represent additional therapy for individuals with SLE. However, little is known on the role of these fatty acids in patients with SLE, including the effects on inflammatory cytokine concentrations and on disease activity.

The aim of this study was to investigate the effects of omega-3 fatty acids on circulating levels of inflammatory mediators and biochemical markers in women with SLE.

Patients and methods

This is a clinical trial of the use of omega-3-polyunsaturated fatty acids in SLE patients followed at the Rheumatology Unit of Hospital das Clínicas, Universidade Federal de Minas Gerais, UFMG (clinical trial: NCT02524795). The Research Ethics

Committee of UFMG approved the study. All patients provided a written informed consent.

Study participants

Female patients who met the revised American College of Rheumatology (ACR) classification criteria for SLE (1982/1997),[15] aged over 18 years old and below 60 years old, taking stable doses of medications for SLE treatment in the last three months were included. Exclusion criteria were the following: pregnancy, disease duration of less than one year, allergy to fish, fish oil or any omega-3 product, omega-3 use within the previous six months and diagnosis of diabetes mellitus, liver disease, active nephritis, chronic renal failure, any type of infection at enrollment and/or throughout the study.

A total of 153 patients were screened for the trial and 66 patients were included, with 33 randomized to each arm. Twenty-two women in the study group and 27 in the control group completed the whole protocol and had both their first and 12-week visit assessments (Fig. 1).

Study design

A 12 week clinical trial of omega-3 fatty acids supplementation was conducted. Participants were seen at baseline (T0)

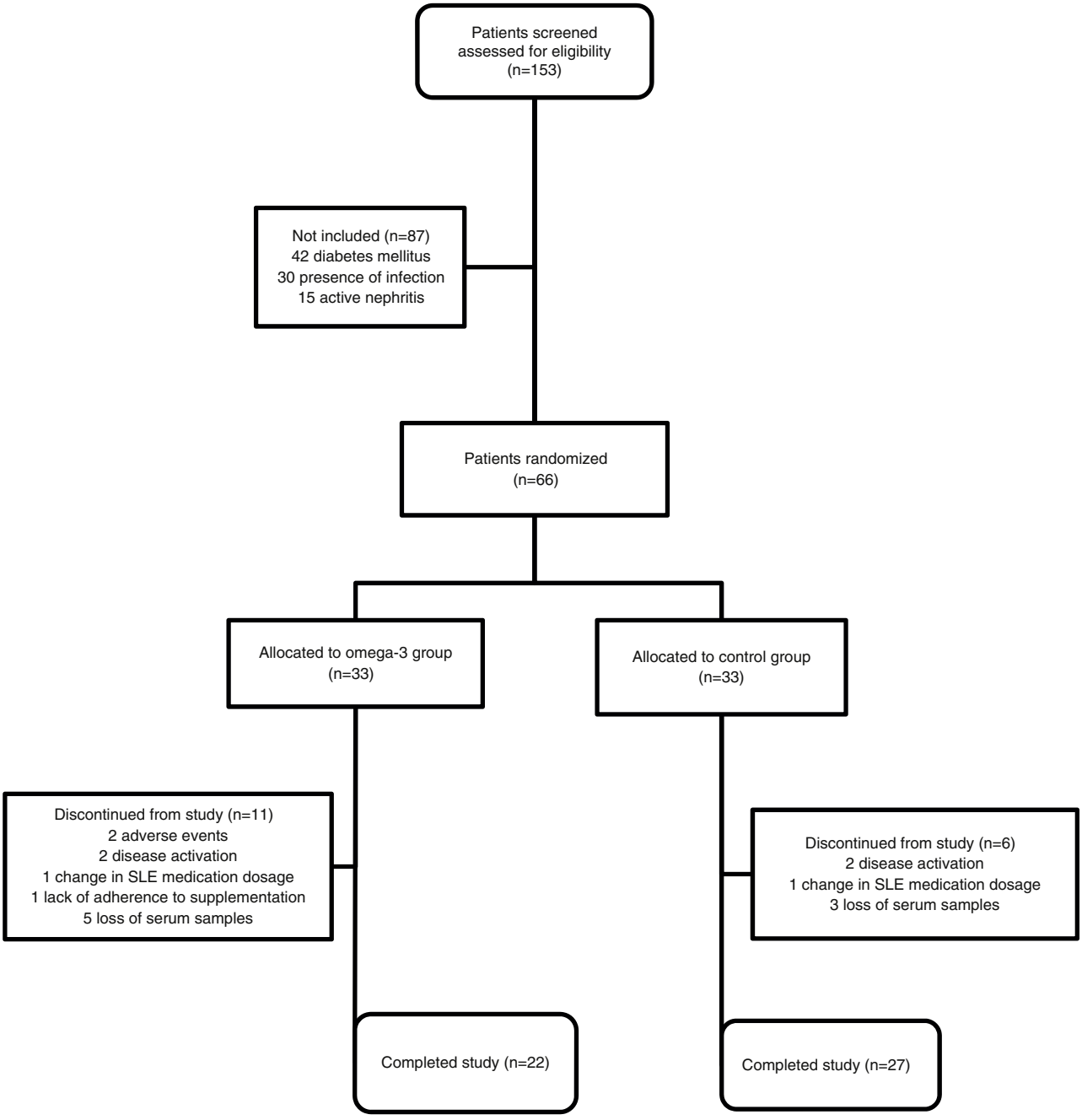

Fig. 1 – Study design.

Table 1 – Baseline (T0) characteristics of each group.

	Total n = 49	Omega-3 group n = 22	Control group n = 27	p[c]
Mucocutaneous disorders[a]	20 (40.8)	9 (40.9)	11 (40.7)	0.829
Arthritis[a]	3 (6.1)	1 (4.5)	2 (7.4)	0.724
Hematological disorders[a]	27 (55.1)	13 (59.1)	14 (51.9)	0.340
Lymphopenia[a]	26 (53.1)	13 (59.1)	13 (48.1)	0.233
Leukopenia[a]	10 (20.4)	3 (13.6)	7 (25.9)	0.390
Thrombocytopenia[a]	1 (2.0)	0	1 (3.7)	0.390
Nephritis[a]	11 (22.4)	5 (22.7)	6 (22.2)	0.861
Low C3[a]	9 (18.0)	2 (9.1)	7 (25.0)	0.146
Low C4[a]	10 (20.4)	3 (14.3)	3 (11.1)	0.102
Positive double strand antiDNA[a]	6 (12.5)	3 (14.3)	3 (11.1)	0.741
Current steroid dose (mg)[b]	5.0 (2.5–10.0)	5.0 (0.6–10.0)	5.0 (3.5–8.1)	0.745
Cumulative steroid dose (g)[b]	20.0 (12.2–37.8)	22.0 (12.7–56.7)	19.1 (12.1–30.5)	0.178
SLEDAI-2K[b]	1 (0–2)	0 (0–2)	2 (0–4)	0.072
BMI (kg/m^2)[b]	28.4 (25.7–30.9)	29.0 (25.7–30.7)	28.1 (25.2–31.4)	0.805
Body fat %[b]	36.9 (33.7–41.1)	37.7 (33.2–41.9)	36.0 (33.1–38.8)	0.512
Obesity[a]	17 (34.7)	8 (36.4)	9 (33.3)	0.689
Current immunosuppressor use[a]	33 (64.7)	13 (59.1)	20 (69.0)	0.465

BMI, body mass index.
[a] N (%).
[b] Median (interquartil range).
[c] Pearson's Chi-square, Fisher's exact or *U*-Mann–Whitney test.

and at week 12 (T1) for clinical, laboratory and nutritional assessment. Participants were also contacted by telephone at week 6 to check on compliance and any adverse events. The patients were randomized into one of two groups in a 1:1 ratio. Patients in the study group received, throughout 12 weeks, two tablets taken orally once daily of omega-3 fatty acids (540 mg of EPA and 100 mg of DHA; Hiomega-3 supplement of Naturalis® company - registered in the National Health Department number 4.1480.0006.001-4). Patients in the control group did not receive the nutrient nor any kind of placebo. All participants were instructed not to take omega-3 rich foods during the study period. The researcher (FMMS) who did clinical assessment and the inflammatory and biochemical data assessment was blind to randomization and intervention. Any adverse events observed during the study were recorded and managed according to local clinical practice.

Variables measured at each visit included: disease activity index, using the Systemic Lupus Disease Activity Index (SLEDAI-2k)[16]; damage index (Systemic Lupus International Collaboration Clinics/American College of Rheumatology damage index - SLICC/ACR)[17]; fasting lipid and glucose profile; standard laboratory tests to assess SLE (red and white blood count, platelet count, creatinine, urinalysis, urine protein/creatinine ratio, anti-dsDNA, anticardiolipin, C3 and C4 levels); cytokines (IL-6, IL-10), adipokines (leptin, adiponectin) C-reactive protein (CRP), nutritional assessment, and medications being used.

Nutritional status was assessed by body mass index (BMI) and patients were classified as malnourished (BMI ≤ 18.5 kg/m^2), normal weight (BMI = 18.6–24.9 kg/m^2), overweight (BMI = 25–29.9 kg/m^2) and obese (BMI ≥ 30 kg/m^2).[18] Body composition assessment was performed by using bioimpedance (RJL Quantum X®) and patients were classified in accordance to Gallagher et al. [19] as normal or above the recommended percentage body fat according to sex and age.

The IL-6 and IL-10 levels were assessed by ultrasensitive flow cytometry (Cytometric Bead Array), leptin and adiponectin levels by ELISA.

Outcome variables

The primary outcomes were median (interquartile range – IQR) variations [ΔV = pre-treatment (T0) – post-treatment (T1) concentrations], between groups, of serum cytokines, adipokines, C-reactive protein and biochemical markers (glucose and lipids) after a 12 week treatment.

Statistical analysis

The Statistical Package of Social Sciences Software (SPSS) version 19.0 (SPSS Inc., Chicago, IL, USA) was used. Comparison of groups at baseline (with *versus* without omega-3, with *versus* without excess weight and with adequate *versus* above recommended percentage body fat) were performed by nonparametric *U*-Mann–Whitney test for continuous variables, and Pearson's chi-square or Fisher's exact test for categorical variables. The median (IQR) of inflammatory and biochemical markers at T0 and T1 in omega-3 and in control group were compared using nonparametric Wilcoxon test.

To investigate the effect of omega-3 on inflammatory mediators and biochemical markers the variations of laboratory variables [ΔV = pre-treatment (T0) – post-treatment (T1) concentrations] between omega-3 and control groups were analyzed using *U*-Mann–Whitney test. All analyses were considered significant at a level of 2-sided 5% ($p < 0.05$).

Results

Seventeen randomized patients, out of 66, did not complete the trial (Fig. 1). Two patients interrupted supplementation due

Table 2 – Serum concentrations of cytokines, adipokines and biochemical markers of SLE patients at baseline (T0) by treatment groups.

	Omega-3 group $n=22$ Median (IQR)	Control group $n=27$ Median (IQR)	p[e]
IL-6 (pg/mL)	0.57 (0.40–2.90)[a]	1.09 (0.52–1.98)[b]	0.692
IL-10 (pg/mL)	19.05 (9.88–40.87)[c]	21.41 (6.72–51.64)[d]	0.699
Leptin (ng/mL)	80.03 (63.21–129.40)	58.12 (36.65–109.20)	0.067
Adiponectin (μg/mL)	42.30 (24.88–58.01)	40.08 (27.69–59.47)	0.817
Glucose (mg/dL)	77.5 (75.2–82.8)	78.0 (71.0–86.0)	0.958
Cholesterol (mg/dL)	168.0 (151.0–194.0)	182.0 (155.5–192.2)	0.899
LDL-c (mg/dL)	95.0 (80.0–116.0)	100.0 (84.5–111.8)	0.926
HDL-c (mg/dL)	52.0 (38.0–57.0)	53.0 (37.8–63.2)	0.498
Triglycerides (mg/dL)	88.0 (64.0–124.0)	79.5 (59.5–114.0)	0.311
CRP (mg/dL)	5.0 (4.9–8.1)	6.4 (4.9–11.6)	0.370

IL, interleukin; IQR, interquartile range; CRP, C-reactive protein.
[a] $n=21$.
[b] $n=26$.
[c] $n=14$.
[d] $n=21$.
[e] *U*-Mann–Whitney test.

to adverse events (one patient with diarrhea and the other reporting fish aftertaste). Both patients where discontinued from the trial. The final sample of this pilot study consisted of 49 patients. Cumulative revised ACR classification indicated mucocutaneous manifestations in 86.3% of the patients, hematological disorders in 80.0%, immunological disorders in 77.6%, arthritis in 66.7%, nephritis in 56.9%, serositis in 16.0% and neuropsychiatric disorders in 11.8%.

Baseline analysis

The median (IQR) of age was 37 (29–48) years old, of disease duration was 7 (4–13) years, of disease activity index was 1 (0–2) and of damage index was 0 (0–1).

Baseline (T0) clinical, laboratory and disease treatment characteristics, disease activity index and nutritional status of participants per treatment groups were not statistically different (Table 1).

Nutritional status of 49 patients, according to BMI, showed that 13 patients (26.5%) had normal weight, 19 (38.8%) were overweight and 17 (34.7%) were obese. This distribution was similar in both groups ($p=0.875$). Bioelectrical impedance analysis indicated that 29 (59.2%) patients had percentage body fat above recommended: 12 patients (54.5%) in the omega-3 group and 17 (63.0%) in the control group ($p=0.574$).

Serum concentrations of cytokines were similar in normal weight and excess weight participants (BMI $\geq 25\,kg/m^2$) [**IL-6:**1.38 (0.48–3.13) pg/mL *versus* 0.92 (0.40–1.95) pg/mL; $p=0.429$; **IL-10**: 19.30 (7.85–53.35) pg/mL *versus* 21.42 (9.40–51.16) pg/mL; $p=0.956$]. IL-10 levels were similar in both study groups considering patients with adequate and above recommended percentage body fat [16.26 (5.51–22.25) pg/mL *versus* 22.53 (9.78–55.79) pg/mL; $p=0.192$]. However, serum concentrations of IL-6 were higher in above recommended percentage body fat patients, showing a trend toward significance [0.48 (0.19–1.04) pg/mL *versus* 1.22 (0.47–2.38) pg/mL; $p=0.053$].

Table 3 – Serum concentrations of cytokines, adipokines and biochemical markers at T0 and T1 in both groups.

Variable	Omega 3 group N=22			Control group N=27		
	T0 Median (IQR)	T1 Median (IQR)	p[a]	T0 Median (IQR)	T1 Median (IQR)	p[a]
IL-6 (pg/mL)[b]	0.57 (0.40–2.90)	1.10 (0.60–2.80)	0.821	1.09 (0.52–1.98)	0.88 (0.33–2.08)	0.946
IL-10 (pg/mL)[b]	19.05 (9.88–40.87)	29.90 (9.80–56.30)	0.363	21.41 (6.72–51.64)	26.08 (11.38–47.54)	0.332
Leptin (ng/mL)	80.03 (63.21–129.40)	93.20 (54.80–153.40)	0.506	58.12 (36.65–109.20)	77.20 (50.00–103.00)	0.416
Adiponectin (μg/mL)	42.30 (24.88–58.01)	44.9 (23.90–57.20)	0.465	40.08 (27.69–59.47)	44.50 (20.00–59.00)	0.462
Glucose (mg/dL)	77.5 (75.2–82.8)	83.0 (75.0–87.0)	**0.043**	78.0 (71.0–86.0)	77.5 (72.2–85.0)	0.354
Cholesterol (mg/dL)	168.0 (151.0–194.0)	188.0 (162.0–214.5)	**0.012**	182.0 (155.5–192.2)	176.0 (152.0–199.8)	0.067
LDL-c (mg/dL)	95.0 (80.0–116.0)	115.5 (90.0–129.2)	**0.003**	100.0 (84.5–111.8)	98.0 (76.0–125.0)	**0.019**
HDL-c (mg/dL)	52.0 (38.0–57.0)	53.0 (47.0–67.0)	0.537	53.0 (37.8–63.2)	53.5 (45.5–59.0)	0.857
Triglycerides (mg/dL)	88.0 (64.0–124.0)	70.0 (57.0–98.5)	0.520	79.5 (59.5–114.0)	87.0 (63.2–128.0)	0.657
CRP (mg/dL)	5.0 (4.9–8.1)	4.9 (4.9–7.2)	0.230	6.4 (4.9–11.6)	5.0 (4.9–11.6)	**0.009**

IL, interleukin; CRP, C-reactive protein.
[a] Nonparametric paired Wilcoxon.
[b] IL-6, Omega 3 Group $n=21$; control group $n=26$; IL-10, Omega 3 Group $n=14$; control group $n=21$.

Table 4 – Variation (ΔV) of serum cytokines and biochemical markers considering the end (T1) and the beginning (T0) of the study by treatment groups.

	Omega-3 group Median (IQR)	Control group Median (IQR)	p[e]
ΔV IL-6 (pg/mL)	0.12 (−1.19 to 1.45)[a]	−0.05 (−0.57 to 0.58)[b]	0.915
ΔV IL-10 (pg/mL)	1.32 (−8.94 to 18.80)[c]	1.04 (−7.17 to 12.19)[d]	0.920
ΔV Adiponectin (μg/mL)	0.6 (−3.2 to 11.8)	−3.4 (−6.6 to 5.8)	0.171
ΔV Leptin (ng/mL)	3.4 (−18.2 to 22.6)	0.0 (−16.3 to 28.0)	0.924
ΔV CRP (mg/dL)	0.0 (−1.5 to 0.0)	0.0 (0.0 to 1.5)	0.008
ΔGlucose (mg/dL)	−4.0 (−8.0 to 0.0)	−1.0 (−8.0 to 4.0)	0.496
ΔCholesterol (mg/mL)	14.0 (−2.5 to 27.2)	4.5 (−8.5 to 23.8)	0.477
ΔLDL-c (mg/dL)	17.0 (3.0 to 27.0)	10.5 (−2.5 to 20.8)	0.288
ΔHDL-c (mg/dL)	0.0 (−4.5 to 12.5)	−0.5 (−7.0 to 5.0)	0.536
ΔTriglycerides (mg/dL)	−1.0 (−39.2 to 22.8)	−4.5 (−17.8 to 16.8)	0.867

IL, interleukin; IQR, interquartil range; CRP, C-reactive protein.
[a] $n = 21$.
[b] $n = 26$.
[c] $n = 14$.
[d] $n = 21$.
[e] U-Mann–Whitney test.

Serum leptin concentrations were higher in excess weight patients comparing to normal weight ones [84.0 (52.9–12.3) ng/mL *versus* 47.6 (33.5–73.5) ng/mL; $p = 0.033$], and in individuals with above recommended percentage body fat compared to those with normal percentage body fat [93.8 (56.5–143.6) ng/mL *versus* 45.8 (33.5–63.6) ng/mL; $p = 0.002$]. In contrast, adiponectin levels did not differ between groups [normal weight: 46.4 (34.6–61.0) μg/mL *versus* excess weight: 42.5 (24.7–58.0) μg/mL; $p = 0.571$; and normal percentage body fat: 46.4 (35.1–59.4) μg/mL *versus* above recommended percentage body fat: 42.9 (24.3–59.6) μg/mL; $p = 0.365$].

Serum levels of IL-6, IL-10 and adipokines, serum fasting glucose, lipid profile and C-reactive protein at baseline were similar in omega-3 and control groups (Table 2).

The serum levels of IL-6 and IL-10, leptin and adiponectin did not change after a 12 week treatment. The concentrations of fasting blood glucose, total cholesterol and LDL-cholesterol increased in the omega-3 group, and of LDL-cholesterol increased in control group, although they remained within normal limits (Table 3).

Comparison of variations (ΔV) between the two groups

The median (IQR) variations (ΔV = T1-T0) of cytokines, adipokines, fasting glucose and lipids concentrations were similar for the two groups (Table 4). The median (IQR) in CRP levels variation between the two groups is represented in Fig. 2, showing a decrease in the omega-3 group while there was an increase in the control group ($p = 0.008$).

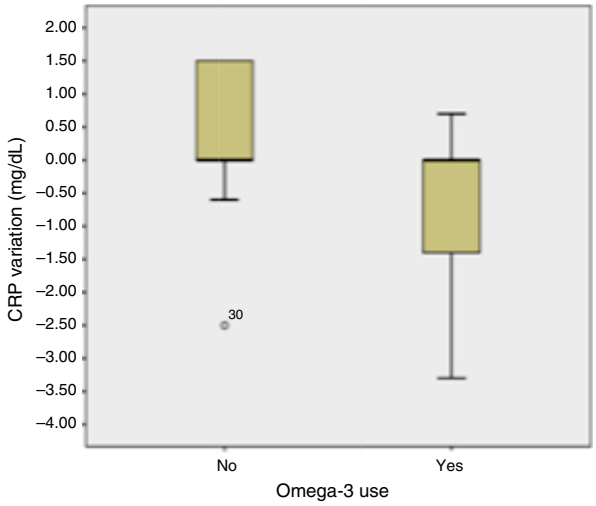

Fig. 2 – Box-plot of median (range) of C-reactive protein levels variations (ΔV) between T0 and T1 in treatment and control groups.

Discussion

Supplementation with omega-3 (2 g: 1080 mg of EPA and 200 mg of DHA) for 12 weeks had no impact on serum concentrations of IL-6 and IL-10 cytokines as well as on adipokines (leptin and adiponectin) in 49 women with SLE and low disease activity. Bello et al.[20] reported similar results studying 85 SLE patients who presented no reduction in inflammatory mediators levels (sICAM-1, sVCAM-1 and IL-6) after the use of higher doses of this fatty acid (3 g of omega-3: 1800 mg of EPA and 1200 mg of DHA) for 12 weeks. In contrast, in healthy subjects, cell culture studies demonstrated that EPA and DHA can inhibit the production of IL-6, TNF-α, IL-1 and IL-1β.[7,8,21,22] In a review study, we found conflicting results of the effects of omega-3 on disease activity, on cytokines and on biochemical markers levels, due to the many different methods used.[23]

This paper indicates an effect of omega-3 on CRP levels as there was a significant variation of serum levels between groups: there was a decrease in the omega-3 group while there was an increase in the control group. Studies in healthy subjects and in patients with chronic inflammatory diseases including diabetes, coronary heart disease, ulcerative colitis, dyslipidemia and rheumatoid arthritis,[24–30] have shown that consumption of omega-3 fatty acids is inversely associated

with serum CRP. No information could be found in the literature about the effects of omega-3 on CRP levels in SLE patients.

The higher serum concentrations of leptin described in this study in overweight individuals and in those with above recommended percentage body fat were also observed by other researchers.[31–34] Studies evaluating leptin levels in SLE patients are consistent and indicate higher levels of leptin compared to control subjects, even after statistical adjustment for body mass index (BMI), hypertension, hyperlipidemia and diabetes.[35–38] This finding suggests that adipose tissue could have a significant role in SLE inflammatory response. In contrast to obesity and metabolic diseases, elevated systemic and local levels of adiponectin are present in patients with inflammatory and immune-mediated conditions, like SLE.[31] Since adiponectin has been found to present both pro and anti-inflammatory activities, controversial findings have been observed on the role of total adiponectin in systemic autoimmune and inflammatory diseases.[32]

To our knowledge, the analysis of serum leptin and adiponectin levels after omega-3 fatty acid supplementation in SLE patients is original data of our study. In healthy subjects the results are conflicting. Ramel et al.[39] found that daily consumption of 1.3 g EPA + DHA caused a significant reduction in serum levels of leptin, noting that there was concomitant weight loss of about 1 kg in these individuals, which could bias these results. Itoh et al.[40] reported that after treatment with daily doses of 1.8 g of EPA there was a significant increase in adiponectin production in obese rodents and humans. Studies evaluating omega-3 and omega-6 concentrations in red cell membranes demonstrated positive association between omega-3 with increased adiponectin and decreased leptin serum levels, indicating a potential effect of this fatty acid in controlling inflammation.[41,42] However, other authors showed no relationship between the consumption of this nutrient and serum concentrations of those adipokines.[43,44]

An increase of total serum cholesterol ($p = 0.012$) and LDL-c ($p = 0.003$) in patients receiving omega-3 fatty acid was seen in our study, as well as an increase in serum LDL-c ($p = 0.019$) in control group individuals. Nonetheless, the median serum concentrations between T1 and T0 remained within the laboratory normal levels. In accordance with our findings, Bello et al.[20] and Wright et al.[44] also described an increase in total cholesterol and in LDL-c in SLE patients who received omega-3. Studies in non SLE subjects with hypertriglyceridemia demonstrated increased serum levels of LDL-c after supplementation with this fatty acid.[45,46] This is a clinically important finding, since SLE patients are at increased risk of atherosclerotic cardiovascular disease, which is one of the leading causes of mortality in these individuals.[47–50] Interestingly, in two meta-analysis of population with high risk of cardiovascular and cerebrovascular diseases there was no reduction in the frequency of cardiovascular events, coronary and cerebrovascular as well as overall mortality with this supplementation.[51,52]

In the present study, the low levels of inflammation of the SLE patients may have contributed to the absence of changes in serum cytokine levels after omega-3 supplementation. Therefore, it is not possible to rule out a potential reduction in serum concentrations in patients with moderate to high inflammatory activity indexes. Longer periods of supplementation would yield different results? Larger doses could be beneficial with no risks to the patients? These questions can only be answered by long term randomized studies in which compliance must be controlled by omega-3 cell uptake, which we did not perform.

In conclusion, in this 12 weeks study in low disease activity lupus patients, the supplementation with omega-3 fatty acids was not associated with changes in serum levels of IL-6, IL-10, leptin and adiponectin, although a significant decrease of CRP concentrations was observed.

Conflicts of interest

The authors declare no conflicts of interest.

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