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Effects of extra virgin olive oil and fish oil on lipid profile and oxidative stress in patients with metabolic syndrome

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ABSTRACT

Objective: The aim of this study was to verify if extra virgin olive oil and fish oil have a synergistic effect on lipid and oxidative stress parameters in patients with metabolic syndrome (MetS).
Methods: This intervention study included 102 patients (81 women and 21 men) with MetS (mean age 51.45 ± 8.27 y) from the ambulatory center of the University Hospital of Londrina, Paraná, Brazil. Patients were randomly assigned to one of four groups: Patients in the control group (CG) were instructed to maintain their usual diet; the second group (fish oil group [FO]) received 3 g/d of fish oil ω-3 fatty acids (10 capsules); the third group (extra virgin olive oil group [OO]) received 10 mL/d of extra virgin olive oil at lunch and dinner; and the fourth group (fish oil and extra virgin olive oil group [FOO]) received 3 g/d of fish oil ω-3 fatty acids and 10 mL/d of extra virgin olive oil. MetS related markers and oxidative stress were measured at baseline and after 90 d.
Results: Differences across treatment groups showed a statistically significant decrease ($P < 0.05$) in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) when FOO was compared with CG and OO, respectively. Hydroperoxides showed a significant decrease ($P < 0.05$) when FOO was compared with CG, whereas there was an increase in total peroxyl radical-trapping antioxidant potential/advanced oxidation protein products (TRAP/AOPP; $P < 0.05$) in FOO when compared with FO. In relation to baseline values, there was a significant decrease ($P < 0.05$) in LDL-C values, and TC/high-density lipoprotein cholesterol (HDL-C) and LDL-C/HDL-C indexes in FOO. There was also a decrease ($P < 0.05$) in hydroperoxides, in AOPP and in AOPP/TRAP index in FOO, and an increase ($P < 0.05$) in TRAP/AOPP index in FOO and in TRAP/uric acid ratio in OO.
Conclusion: The present study provides evidence that increased dietary ω-3 polyunsaturated fatty acids and extra virgin olive oil have beneficial synergistic effects on lipid metabolism and oxidative stress in patients with MetS.

Introduction

Metabolic syndrome (MetS) is a multicomponent disorder characterized by hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), hyperglycemia, abdominal obesity, and is closely linked to cardiovascular disease (CVD) and type 2 diabetes mellitus [1]. Patients with MetS have higher oxidative damage, caused by an imbalance between reactive oxygen/nitrogen species (ROS/RNS) production and antioxidant defenses [2]. Several studies have reported that a Mediterranean dietary pattern, in which olive oil is the main source of fat, is associated with a decrease in CVD and overall mortality [3,4,5]. Olive oil is rich in monounsaturated fatty acid (MUFA) and antioxidant compounds, mainly phenolic compounds, and is capable of reducing one or more risk factors of MetS [6]. Additionally, an Italian study showed that regular consumption of olive oil, compared with no or infrequent consumption, significantly

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reduced mortality risk by 24% in men and women with previous myocardial infarction [7].

The proposed mechanisms by which olive oil and mainly extra virgin olive oil can exert its beneficial effects on CVD risk include improvement of lipid profile, through a decrease in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and an increase in the ratio of HDL to TC [8,9,10,11], reduction in LDL-C susceptibility to oxidation, amelioration of oxidative vascular damage [10,12], and improved endothelial function and blood pressure [12,13].

Another intervention that may reduce CVD risk in patients with MetS is increasing the relative abundance of ω-3 polyunsaturated fatty acids (PUFAs), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in the diet [14]. Several studies have suggested that fish or dietary ω-3 PUFAs intake may have beneficial effects on the prevalence of MetS [15] and on its individual components [16].

The treatment of dyslipidemia is a cornerstone in the prevention of CVDs, and clinical trials have consistently demonstrated that a reduction in LDL-C levels is of primary importance in risk reduction [17]. Epidemiologic studies, which have been focused on the dietary consumption of fatty acids, have shown contradictory results for ω-3 and ω-6 PUFAs. Some studies have reported a reduction in TC and LDL-C concentrations [18,19]. Conversely, others have shown no change in TC or a slight increase in LDL-C [20]. The more consistent result using fish oil is the decrease in triacylglycerol (TG) levels [21].

Olive oil may act synergistically with fish oil by increasing the incorporation of ω-3 fatty acids in cell membranes [22,23]. A previous study verified that association of fish oil and extra virgin olive oil had more beneficial effects than isolated use of fish oil in patients with rheumatoid arthritis [24]. The main assumption was that extra virgin olive oil and fish oil would have a synergistic action on several parameters of MetS, which could be even superior to the expected benefit with the use of isolated oil.

As several features of MetS are associated with abnormal lipoprotein levels and oxidative stress markers, it is relevant to investigate whether these markers can be lowered by altering dietary fat intake, especially by MUFA and PUFAs. Although previous researchers have focused their studies on the effect of olive or fish oil on the incidence and prevention of MetS, the aim of present study was to investigate the effects of olive and fish oil on CVD risk factors and oxidative stress in patients with MetS.

Methods and materials

Participants

This intervention study included 102 patients (81 women and 21 men) with MetS (mean age 51.45 ± 8.27 y) from the ambulatory center of the University Hospital of Londrina, Paraná, Brazil. Patient motivation was related to the intake of a nonpharmacologic therapy that was practically without side effects. The exclusion criteria were CVDs (except hypertension); thyroid, renal, hepatic, gastrointestinal, oncologic diseases; or acute infection and utilization of lipid-lowering drugs, estrogens replacement therapy, drugs for hyperglycemia; and intake of fish oil or antioxidant supplements. Patients who were taking antihypertensive drugs were not excluded and were allowed to continue taking their prescribed dosage. None of the participants followed a specific diet before the start of the study. The patients were instructed not to change their usual diets, alcohol intake, level of physical activity, or other lifestyle factors throughout the intervention period. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human patients were approved by the Ethical Committee of the University of Londrina, Paraná, Brazil (study protocol CEP 258/08). Written informed consent was obtained from all patients. Anthropometric measurements, oxidative stress, and biochemical parameters were assessed at the beginning of the study and after 90 d. MetS was defined following the Adult Treatment Panel III criteria [25]. When three of the following five of the characteristics were verified, a diagnosis of MetS was performed

1. Abdominal obesity: waist circumference ≥102 cm in men and ≥88 cm in women;
2. Hypertriglyceridemia ≥150 mg/dL (1.695 mmol/L);
3. Low levels of HDL-C: ≤40 mg/dL (1.036 mmol/L) in men and ≤50 mg/dL (1.295 mmol/L) in women;
4. High blood pressure: ≥130/85 mm Hg; and
5. High fasting glucose: ≥100 mg/dL (5.5 mmol/L).

Experimental protocol

Patients were randomly assigned to one of four groups. Patients in the first group (control group [CG], n = 42) were instructed to maintain their usual diet. The second group (fish oil group [FO], n = 21) received 3 g/d of fish oil ω-3 fatty acids (10 capsules). The third group (extra virgin olive oil group [OO], n = 13) received 10 mL/d of extra virgin olive oil at lunch and dinner. The fourth group (fish oil + extra virgin olive oil group [FOO], n = 26) received 3 g/d of fish oil ω-3 fatty acids and 10 mL/d of extra virgin olive oil. Each fish oil capsule contained 180 mg EPA and 120 mg DHA originated from sardines. The capsules were given at breakfast, lunch, and dinner. Fish oil capsules were provided by Opção Fenix (São Paulo, Brazil). The extra virgin olive oil was added to salads at lunch and dinner. Each 10 mL olive oil contained 6.4 g oleic acid. The participants were instructed to refrain from resting after meals to avoid any unpleasant effects. All the groups were evaluated at the beginning of the study and after 90 d.

Steps taken to optimize compliance

Before each trial began, it was ensured that the patients understood that they could be allocated to any group. Boxes of fish oil capsules were handed out at the initial interview and at the two later visits. The participants were asked to return the boxes at each visit so the number of capsules taken could be estimated by questioning the patients and by counting the remaining capsules. Extra virgin olive oil compliance was measured by questioning the patients, counting the extra virgin olive oil bottles consumed, and the quantity that remained in the bottle when patients returned for their clinical and nutritional evaluations.

Anthropometric and blood pressure measurements

Height and weight were measured in the morning with participants wearing light clothing, but no shoes. After 5 min of rest, each participant had his or her blood pressure measured on the left arm while in a sitting position. We considered the current use of antihypertensive medication as an indication of high blood pressure. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured at the umbilical level with the participants standing after normal expiration and the hip girth was measured at the widest part of the hip and, the waist-to-hip ratio was calculated.

Biochemical and inflammatory biomarkers measurements

After fasting for 12 h, the participants underwent the following laboratory blood analysis: glucose, TC, HDL-C, LDL-C, TG, and uric acid, which were evaluated by a biochemical auto-analyzer (Dimension Dade AR, Dade Behring, Deerfield, IL, USA), using Dade Behring® kits. Plasma insulin levels were determined by microparticle enzyme immunoassay (Axsym, Abbott Laboratory). Serum high-sensitivity C-reactive protein (hs-CRP) was measured using a nephelometric assay (Behring Nephelometer II, Dade Behring, Marburg, Germany). All samples were centrifuged at 3000*g* for 15 min, and plasma or serum aliquots were stored at −70 °C until assayed. Inter- and intraassays coefficient of variances were <10%, as determined in human serum.

The homeostasis model of assessment in insulin resistance (HOMA-IR) was used as a surrogate measure of insulin sensitivity [26].

HOMA-IR = fasting insulin (μU/mL) × fasting glucose (nmol/L)/22.5.

Oxidative stress measurements

The samples for evaluating oxidative stress and total antioxidant capacity (TAC) were performed with EDTA as anticoagulant and antioxidant. All samples were centrifuged at 3000*g* for 15 min and plasma aliquots stored at −70 °C until assayed.

The analysis of plasma hydroperoxide concentrations by tert-butyl hydroperoxide-initiated chemiluminescence assay was evaluated as described previously [27] and reported previously [28]. The results were expressed in counts per minute.