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Brief report

Effect of soy product kinako and fish oil on serum lipids and glucose metabolism in women with metabolic syndrome

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ABSTRACT

Objectives: At the doses typically used to treat hypertriacylglycerolemia, fish oil may increase low-density lipoprotein (LDL) cholesterol and blood glucose levels. The aim of the present study was to verify whether soy could attenuate the effects of fish oil on blood lipids and carbohydrate metabolism in patients with metabolic syndrome.

Methods: Sixty-five women (47.9 ± 9.98 y) were studied with the use of a parallel, randomized design. The control group maintained the usual diet; the second group received 29.14 g/d of soy (kinako); the third group received 3 g/d of fish oil *n*-3 fatty acids; and the fourth group received fish oil (3 g/d) and kinako (29.14 g/d). Assessments were performed at baseline and after 45 and 90 d.

Results: In relation to baseline values, fish oil increased ($P < 0.05$) total and LDL cholesterol, glucose, insulin, and homeostasis model assessment of insulin resistance levels after 90 d. Comparisons among groups demonstrated a decrease ($P < 0.05$) in total cholesterol in the fish oil and kinako group after 90 d as compared with the fish oil group. LDL cholesterol decreased ($P < 0.01$) in the kinako group as compared with the fish oil group. Blood glucose and homeostasis model assessment of insulin resistance levels decreased after 90 d ($P < 0.01$ and $P < 0.05$, respectively) and insulin levels decreased ($P < 0.05$) after 45 d when the kinako group was compared with the fish oil group.

Conclusions: The present study showed that kinako moderates the adverse effects of high doses of fish oil on LDL cholesterol, total cholesterol, and glucose metabolism levels.

Introduction

Metabolic syndrome comprises pathologic conditions that include insulin resistance, arterial hypertension, visceral adiposity, and dyslipidemia, which favor the development of cardiovascular diseases and type 2 diabetes [1].

Fish or fish oil consumption has been recommended for the primary prevention of death from coronary heart disease and after a coronary event to reduce the risk of death related to coronary heart disease, largely because the properties of these substances are understood to prevent fatal coronary heart disease and sudden cardiac death [2].

The reported effects of fish oil *n*-3 fatty acids (eicosapentaenoic C20:5*n*-3 and docosahexaenoic C22:6*n*-3 acids) could be expected to prevent hypertriacylglycerolemia [3]. However, there are reports of increased total cholesterol and low-density lipoprotein (LDL) cholesterol levels [4] as well as hyperglycemia or the worsening of type 2 diabetes mellitus [5] with *n*-3 fatty acids in doses of more than 3 g/d.

Alternatively, soy-based products and soy components are involved in the improvement of blood lipid profiles and particularly in the decreasing of total and LDL cholesterol [6]. Soy products can also reduce blood glucose levels among postmenopausal women with type 2 diabetes mellitus [7] and metabolic syndrome [8]. As a result, the use of soy products

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could conceivably counterbalance the effects of a high dosage of fish oil *n*-3 fatty acids (ie, 3 g/d) in patients with metabolic syndrome.

In a recent report [9], we demonstrated that both fish oil and soy decreased blood pressure among patients with metabolic syndrome. In the present study, the same cohort of patients was studied to verify whether 29.14 g/d of soy could attenuate the effects of 3 g/d of fish oil on blood lipids and carbohydrate metabolism.

Materials and methods

Sixty-nine patients (N = 69) were randomized and began participation in the study. The mean age of the patients was 47.9 ± 9.98 y. The exclusion criteria were the presence of thyroid, renal, hepatic, gastrointestinal, or oncological disease and the use of lipid-lowering drugs, estrogen replacement therapy, drugs for the treatment of hyperglycemia, fish oil, or soy supplements.

All procedures were approved by the Ethical Committee of the University of Londrina, Paraná, Brazil. Written informed consent was obtained from all study subjects.

Patients were randomly assigned to one of four groups after stratification by age and body mass index. The first group (control group, n = 15) was only directed to maintain the usual diet; the second group (kinako group, n = 15) received 29 g/d of kinako (toasted ground soybeans with 50 mg of isoflavones and 12.95 g/d of soy protein) at lunch and dinner; the third group (fish oil group, n = 19) received 3 g/d of fish oil *n*-3 fatty acids (10 capsules); and the fourth group (fish oil and kinako group, n = 16) received 3 g/d of fish oil *n*-3 fatty acids and 29 g/d of kinako. Each fish oil capsule contained 180 mg of eicosapentaenoic acid and 120 mg of docosahexaenoic acid that originated from sardines. The capsules were given at breakfast, lunch, and dinner. All of the groups were evaluated at the beginning of the study and after 45 and 90 d. Fish oil capsules were provided by Opção Fenix (São Paulo, Brazil), and kinako was provided by Good Soy (Uberaba, Minas Gerais, Brazil).

Anthropometric measurements and biochemical parameters were assessed at the beginning of the study and after 45 and 90 d.

Metabolic syndrome was defined with the use of the Adult Treatment Panel III criteria as recommended by the National Cholesterol Education Program of the National Heart, Lung, and Blood Institute [10]. Waist circumference, body weight, and height were measured, and body mass index was calculated (kg/m^2). After fasting for 12 hours, the patients underwent laboratory blood analysis for the following: glucose, total cholesterol, high-density lipoprotein cholesterol, LDL cholesterol, and triacylglycerol (TG). Blood samples were evaluated with the use of a biochemical autoanalyzer (Dimension Dade AR, Dade Behring, Deerfield, IL, USA) with Dade Behring kits. Plasma insulin levels were determined with the use of microparticle enzyme immunoassay (MEIA, AXSYM, Abbott Laboratories, Wiesbaden, Germany). The homeostasis model assessment of insulin resistance (HOMA-IR) was used as a surrogate measure for insulin sensitivity [11] in accordance with the following formula: HOMA-IR = insulin fasting (μU/mL) × glucose fasting (nmol/L)/22.5.

All data are presented as means ± standard deviations. Significance was set at a P value of < 0.05. Distribution of age and number of medications was analyzed with Fisher's exact test. The analysis of variance was performed with the percentage of change from baseline and post hoc comparisons (Tukey's honestly significant difference test). Both tests (Fisher's and Tukey's) were used to compare differences among the means of treatment.

Results

Four patients withdrew from the study. Despite the known influence of antihypertensive medications (ie, diuretics and β-blockers) on lipid and glucose metabolism, we could not ask the patients to stop using these medications during the study because of their medical necessity. However, there was no statistically significant difference between groups that were taking these drugs and those that were not when they were compared.

The parameters related to body composition (body mass index and waist circumference) showed no statistically significant results after 45 and 90 d in relation to the baseline values of all groups (Table 1).

With regard to baseline values, the fish oil group presented statistically significant decreases in TG values ($P < 0.05$) and significant increases ($P < 0.05$) in total cholesterol and LDL cholesterol values after 45 and 90 d. In the group in which fish oil was associated with kinako, TG also decreased significantly after 90 d ($P < 0.05$). After an initial increase after 45 d ($P < 0.05$), total cholesterol and LDL cholesterol values returned to normal values after 90 d.

Differences across treatment groups showed a statistically significant increase ($P < 0.05$) in total cholesterol values in the fish oil group after 90 d as compared with the fish oil and kinako group, whereas LDL cholesterol significantly increased in the fish oil group as compared with the control group ($P < 0.01$) and the kinako group ($P < 0.05$).

With respect to carbohydrate metabolism, a worsening of metabolic conditions was also seen in the fish oil group, whereas there was an improvement in the kinako group. In relation to the baseline values, in the fish oil group there was a significant increase ($P < 0.05$) in blood glucose, insulin, and HOMA-IR values after 90 d. At the same time, the kinako group had decreased values of glucose ($P < 0.05$), insulin ($P < 0.05$), and HOMA-IR ($P < 0.01$) after 45 and 90 d.

Differences between treatment groups verified a statistically significant increase in blood glucose after 45 and 90 d ($P < 0.05$ and $P < 0.01$, respectively), in insulin levels after 45 d ($P < 0.05$), and in HOMA-IR after 45 and 90 d ($P < 0.05$) when the fish oil group was compared with the kinako group.

Discussion

To our knowledge, this is the first study to report that kinako (29.14 g/d) attenuates some adverse effects of high fish oil intake (3 g/d). Several other reports have also verified an increase in LDL and total cholesterol levels when fish oil is used at doses of more than 3 g/d [4]. The assumption is that an increase in the concentration of LDL cholesterol as a result of the intake of fish oil results directly from the enhanced conversion of very-low-density lipoproteins to LDL. Although *n*-3 fatty acid–enriched LDL particles may be larger and therefore less atherogenic than control LDL particles [4], they are still atherogenic [12]. Two meta-analyses showed that both isolated soy protein supplementation [13] and soy isoflavones [6] decreased LDL and total cholesterol levels. The recommendation for the intake of soy protein or isoflavones to benefit cardiovascular and overall health has changed to intact soy products, which were used in the present study [8,14].

At the same time, TG levels decreased after fish oil consumption throughout the study and after 90 d in the group that received both fish oil and kinako. A decrease in serum TG generally occurs in the range of 3 to 4 g/d [4]; this is an expected and beneficial effect of fish oil on the blood lipid profile [15]. Balk et al [16] pooled the results of 21 trials that involved about 8000 patients who were taking *n*-3 fatty acids and found similar results to those obtained during the present study, including significant decreases in TG levels and significant increases in LDL cholesterol levels.

Adverse effects on glucose metabolism have been verified in small-scale clinical trials when *n*-3 fatty acids were used in doses of more than 4 g/d [5,17,18]. Interestingly, our data showed both increasing fasting glucose and insulin concentrations after 90 d but not after 45 d; this seems to demonstrate, as previous studies have done, that increases in glucose metabolism were both time- and dose-dependent.

Alternatively, several reports have demonstrated beneficial effects of soybeans on the glucose metabolism of healthy women [19] and of patients with type 2 diabetes [7] and metabolic syndrome [14]. In the current study, as well as in the study by Jayagopal et al [7], the effects of soy on the reduction of insulin resistance occurred without a change in the body weight.