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The Effect of Fish Oil Supplements on Blood Pressure

ABSTRACT

We conducted a double-blind, placebo-controlled crossover study to determine the effects of fish oil supplementation on blood pressure in middle-aged men. Subjects were randomly assigned to consume either 20 g of fish oil or safflower oil for 12 weeks and then consume the other oil for an additional 12 weeks after a 4-week washout period. We found no significant changes from the pretreatment value in systolic or diastolic blood pressure with the use of fish oil supplements. In addition, there were no significant differences in the post-treatment blood pressures comparing the fish and safflower oil phases of the study. (*Am J Public Health.* 1993;83:267–269)

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Introduction

Recently, there has been considerable interest concerning the potential cardioprotective effect of consuming fish oil supplements containing high quantities of omega-3 polyunsaturated fatty acids.[1–3] It has been postulated that consumption of fish oil may reduce blood pressure by altering prostaglandin synthesis.[2,3] The initial studies on the effect of fish and fish oil consumption on blood pressure have produced mixed results.[4–8] A meta-analysis of the initial randomized trials failed to show a significant antihypertensive effect of consuming fish oil supplements.[9] As part of a double-blind randomized crossover trial of fish oil supplementation and cholesterol,[10] we had the opportunity to examine the effect of fish oil on blood pressure in a group of middle-aged hypertensive and normotensive men with hypercholesterolemia.

Methods

Participants were recruited at the Minneapolis Veterans Affairs Medical Center as part of a randomized double-blind, controlled, two-period crossover study investigating the effects of fish oil on serum cholesterol.[10] Participants were excluded if they were greater than 60 years old or had significant comorbid conditions. Individuals were designated as hypertensive if their mean diastolic blood pressure on three readings during the initial evaluation was greater than 90 mm Hg. Individuals were designated as normotensive if their initial mean diastolic blood pressure was 90 mm Hg or less and they were not receiving antihypertensive medications.

Blood pressure was measured at the right brachial artery in seated subjects using a mercury gauged sphygmomanometer. Blood pressure was measured at the initial visit (week −4) and at weeks 0, 12, 16, and 28. The mean of three readings

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TABLE 1—Comparison of the Change in Blood Pressure after Fish and Safflower Oil Supplementation

	Post Fish Oil (SD)	Post Safflower Oil (SD)	P
Hypertensive participants (n = 15)			
Systolic, mm Hg	2.3 (8.5)	3.9 (9.0)	0.31
Diastolic, mm Hg	4.7 (7.6)	2.8 (6.5)	0.45
Normotensive participants (n = 23)			
Systolic, mm Hg	1.5 (10.8)	−3.4 (10.4)	0.51
Diastolic, mm Hg	−2.1 (8.3)	−3.5 (9.4)	0.58
Total sample (n = 38)			
Systolic, mm Hg	1.8 (10.4)	−0.5 (10.4)	0.66
Diastolic, mm Hg	0.4 (9.0)	−0.9 (8.8)	0.74

was recorded at each visit. The blood pressure recorded at week 0 served as the baseline measurement. After a 4-week lead-in, eligible subjects were randomized to sequence 1 (with period 1 consisting of 12 weeks of safflower oil [control oil] followed by a 4-week washout and period 2 consisting of 12 weeks of fish oil [MaxEPA™, RP Scherer Corp, Troy, Mich] supplementation) or to sequence 2 (12 weeks of fish oil followed by a 4-week washout and then 12 weeks of safflower oil supplementation).[10] Oil was provided to participants in capsules containing 1 g (1 mL) of unflavored oil, and participants were instructed to consume 20 capsules per day in single or divided doses. Fish oil capsules contained 12% docosahexaenoic acid, 18% eicosapaentanoic acid, and 4.5 mg of cholesterol per capsule (thus, each subject consumed 6 g of omega-3 polyunsaturated fatty acids per day). Safflower oil placebo capsules contained 76% linoleic acid or 15.2 g of linoleic acid per day. Participants were instructed in the American Heart Association step one low cholesterol, low saturated fat diet by a registered dietitian and were advised to modify their diet to maintain weight constancy.

Baseline characteristics (age, percentage ideal body weight, and blood pressure) for study subjects according to sequence assignment were compared using Student's *t* tests. Changes in systolic and diastolic blood pressures from baseline for each period were compared using a modified *t* test for treatment effect as described for the analysis of crossover trials.[11,12] In addition, analyses included *t* tests for sequence effect (using $P = .10$ as the significance criterion) and period effect (using $P = .05$ as the significance criterion).[12,13] All tests for treatment effect included modification to adjust for possible period effects.[11] Sample size calculations were conducted for a two-period crossover trial.[11] With 19 subjects per sequence, the study had 95% power to detect a difference of 4 mm Hg in blood pressure change between fish oil and safflower oil ingestion.

Results

Thirty-eight participants were enrolled and completed the protocol. There were no significant differences in the baseline values between sequence groups. Participants ingested over 90% of the oil capsules as determined by a count of unused capsules. Compliance was also confirmed by plasma phospholipid analysis. Side effects of belching, loose stools, and other gastrointestinal symptoms were reported in 42% of the subjects taking fish oil and 40% of subjects taking safflower oil. These symptoms were minor and did not require specific intervention or therapy.[10]

Table 1 lists systolic and diastolic blood pressure changes for study subjects while they were ingesting fish and safflower oil. There was no evidence for sequence effect in any analyses of the primary outcome or in any subgroup analyses (all Ps $> .25$). For one subgroup, there was a suggestion of a period effect (for normotensive subjects' change in diastolic blood pressure; $P = .03$). For all other analyses, there was no evidence of a period effect (all Ps $> .10$). As can be seen, there were no significant differences in blood pressure change between the fish oil and safflower oil phases of the study. Subgroup analyses of hypertensive and normotensive subjects also failed to show any significant differences in blood pressure changes between the two study phases (Table 1).

Discussion

In the current study, we failed to detect any significant changes from pretreatment values in systolic or diastolic blood pressure with the use of fish oil supplements. Also, a subgroup analysis of patients with hypertension failed to demonstrate any significant change from pretreatment values when comparing the fish and safflower oil phases of the study. The study had sufficient power to conclude with 95% confidence that fish oil supplementation does not lower diastolic blood pressure by more than 4 mm Hg when compared with safflower oil.

The reason for the varied results from the different trials is not immediately apparent. The trials differed in size, types of participants, design, type and amount of fish oil supplementation, and measurements.[2–9] Although several recent trials have demonstrated that consumption of omega-3 polyunsaturated fatty acids results in a modest decrease in blood pressure, the precise effect and amount of fish oil needed to produce an antihypertensive effect have been inconsistent. A study by Knapp and FitzGerald[14] reported that very large doses of fish oil (15 g of omega-3 polyunsaturated fatty acids or 50 mL of fish oil) reduced blood pressure in men with mild essential hypertension, whereas a lower dose of fish oil (3 g of omega-3 polyunsaturated fatty acids or 10 mL of fish oil) produced no significant changes. Surprisingly, alteration in the synthesis of prostaglandins did not appear to be the direct mechanism for this effect. On the other hand, Bonaa and coworkers[15] did not note any dose effect and found that a modest dose of fish oil (6 g of fish oil or 5 g of omega-3 polyunsaturated fatty acids per day) significantly reduced the blood pressure in a portion of their study population. Kestin et al.[16] noted a significant reduction in subjects' systolic but not diastolic blood pressure after consumption of 3.4 g of omega-3 polyunsaturated fatty acids over a 6-week period. In a randomized crossover trial, Radack et al.[17] found that consuming 2.0 g of omega-3 polyunsaturated fatty acids decreased systolic blood pressure by 4.1 mm Hg and diastolic blood pressure by 2.4 mm Hg. However, Margolin and coworkers,[18] in another randomized crossover trial, noted a significant reduction in systolic and diastolic blood pressures in both the fish oil group (consuming 4.7 g of omega-3 polyunsaturated fatty acids per day) and control groups. There were no significant differences between the groups.

The effect of fish oil supplementation on blood pressure remains inconclusive and controversial. It is premature to recommend fish oil as an effective means to control hypertension. The studies that have shown a beneficial effect usually required large doses of fish oil, and thus should be viewed as pharmacologic intervention trials and not as nonpharmacologic or dietary trials. Consumption of such large amounts of fish oil is relatively expensive and inconvenient. The known side effects may be bothersome and will potentially reduce compliance if applied to a general population of hypertensive patients. Although these studies were careful to avoid significant weight gain, consumption of large quantities of fish oil has a high caloric value. Annoying problems with abdominal bloating and diarrhea may also limit its use. Finally, there is concern about possible serious, long-term toxicity (e.g., the risk of significant bleeding, deterioration in glycemic control, and elevation in low-density lipoprotein cholesterol).[2,3,10,16] Fish oil has no clear advantage over conventional antihypertensive medications that are currently available. □

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