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Twice weekly intake of farmed Atlantic salmon (*Salmo salar*) positively influences lipoprotein concentration and particle size in overweight men and women

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ABSTRACT

The US Dietary Guidelines for Americans recommend twice weekly fish intake. Farmed Atlantic salmon is a good source of omega-3 (n-3) fatty acids which have positive lipid modifying effects; however, it is unknown whether these responses are dose-dependent. Our primary research objective was to determine the effect of dose-dependent intake of farmed Atlantic salmon on lipoprotein particle (P) size and concentration. We hypothesized that low-density lipoprotein (LDL)–P and high-density lipoprotein (HDL)–P size and concentration would increase with salmon intake in a dose-dependent manner. Overweight, adult participants (n = 19) were enrolled in a cross-over designed clinical trial evaluating intake of farmed Atlantic salmon. In random order, participants were assigned to 90, 180, or 270 g of salmon twice weekly for 4-week dietary treatments. Following a 4- to 8-week washout, participants crossed over to another dose of fish intake until all treatments were completed. Plasma lipid concentrations were determined and serum lipoprotein concentrations and particle size were determined by nuclear magnetic resonance. Intake of salmon reduced plasma and serum triglyceride (TG) concentrations and increased plasma HDL-C concentrations. The concentrations of large very low-density lipoprotein (VLDL)–P and chylomicron (CM)–P were reduced. Large LDL-P concentrations were increased in a dose-dependent manner. The mean size of VLDL-P was reduced and that of LDL was increased. Total TG was reduced as was the TG content of VLDL-P and CM-P. Twice weekly intake of farmed Atlantic salmon portions influences lipoprotein particle size and concentration in a manner associated with cardiovascular disease risk reduction.

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Abbreviations: C, cholesterol; CM, chylomicron; CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GFHNRC, Grand Forks Human Nutrition Research Center; HDL, high density lipoprotein; LCn-3, long chain omega-3; LDL, low density lipoprotein; NMR, nuclear magnetic resonance; P, particle; TG, triglyceride; VLDL, very low density lipoprotein.

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1. Introduction

Clinically, lipoprotein concentrations are evaluated to determine the risk of atherosclerosis [1]. Elevated concentrations of high-density lipoprotein cholesterol (HDL-C) and low concentrations of low-density lipoprotein cholesterol (LDL-C) are associated with reduced risk. Elevations in fasting and/or postprandial TG concentrations are seen to be atherogenic [2]. The lipoproteins responsible for transport of lipids include chylomicron (CM), very low-density lipoprotein (VLDL), LDL, and HDL with the classifications based upon the relative content of lipid and protein in each. The composition and physical structure of lipoprotein molecules is in constant flux and changes as the core contents are taken up by peripheral tissues The cholesterol and TG composition within the lipoprotein classes vary among individuals as a result of genetics [3,4], lifestyle [5,6], including diet [7,8], and drug therapy [9,10].

Elevated total and LDL-C and TG are associated with cardiovascular disease (CVD) risk; however, disease occurs among people with normal lipid levels [1]. Variation in the concentration and size of lipoprotein particles (P), particularly LDL-P and HDL-P, has an impact on their function and relationship to atherosclerosis development [11,12]. Individuals who have normal concentrations of cholesterol that are distributed in small, dense LDL-P may be at increased risk of coronary heart disease [13]. LDL-P size is an important CVD risk factor that correlates inversely with sub-clinical atherosclerosis as measured by intima-media thickening [14]. Although the total HDL-C concentration is associated with reduced CVD [15], it has been shown that, like LDL-P, small dense HDL-Ps are positively associated with increased risk of CVD [16] while an increased concentration of large HDL-Ps is considered protective [17,18]. VLDL-Ps are positively associated with CVD risk but a lower concentration of large VLDL-P is associated with reduced risk [16].

Consuming fatty fish and fish oil is associated with reduction of fatal coronary events [19]. The protective effect of fatty fish intake is ascribed to their content of the long-chain (LC) omega-3 (n-3) fatty acids [20] eicosapentaenoic acid (EPA) (20:5n-3) and docosahexaenoic acid (DHA) (22:6n-3). Supplementation with LCn-3 is an accepted therapy for the reduction of elevated blood TG levels [21,22] although it typically also results in increases in total cholesterol, HDL-C and LDL-C concentrations [23]. Controlled feeding studies show that fish intake increases large HDL-P concentrations [24,25]. Fish oil supplementation increases the content of large HDL-P and large LDL-P and reduces the size and concentration of VLDL-P [26,27], all changes that are associated with reduced risk of CVD [12].

The research objective of this study was to determine whether the intake of farmed Atlantic salmon (*Salmo salar*) would modify lipoprotein particle size and concentration in a manner associated with reduced CVD risk. Specifically, we hypothesized that LDL-P and HDL-P concentration and size would increase with salmon intake in dose-dependent manner. To test this hypothesis we performed an analysis of lipoprotein particle size and concentrations in a randomized, crossover-designed trial in which participants were fed 90 g, 180 g, and 270 g of farmed Atlantic salmon twice weekly in 4-week treatments.

2. Methods and materials

2.1. Study design and intervention

This investigation is an ancillary evaluation of a study which evaluated 19 participants in a cross-over designed clinical trial of farmed Atlantic salmon over three 4 week treatment periods. Complete details of the trial are provided elsewhere [28]. Here we report the plasma lipid concentrations and the serum lipoprotein particle concentration and size responses to the fish consumption. All study visits were at the US Department of Agriculture (USDA), Agricultural Research Service, Grand Forks Human Nutrition Research Center, Grand Forks, ND. The study was approved by the institutional review board at the University of North Dakota. Informed consent was obtained from all study participants prior to initiation of the study. The trial was registered at www.clinicaltrials.gov as NCT01183520.

2.2. Study population

Participants were recruited from the Greater Grand Forks Area, Grand Forks, ND. Sixty-one volunteers were screened for study participation. Twenty-two volunteers eligible for participation were initially randomized to treatment, although 3 withdrew prior to study initiation. Complete details of the study participant flow through the project are presented elsewhere [28]. The 19 participants who completed all aspects of the trial were men (n = 8) and women (n = 11) who were 51.6 ± 1.5 years (mean ± SE) and had an average body mass index of 29.2 ± 0.6 kg/m^2.

2.3. Dietary intervention

Dietary treatments consisted of farmed Atlantic salmon portions of 90 g, 180 g, or 270 g fed twice weekly. These treatments resulted in daily EPA and DHA intakes of 158 mg and 149 mg, 317 mg and 299 mg, and 475 mg and 448 mg, respectively. The fish fillets were served as prepared entrees on brown rice that were reheated by participants before consumption. Each participant completed all 3 of the 4-week dietary treatments in random order. Treatments were separated by 4- to 8-week washout periods. Throughout the trial participants consumed their habitual diets with the exclusion of fish and high n-3 foods, except for the fish provided.

2.4. Laboratory methods

Fasting blood samples were collected by venipuncture at Day 1 and 29 of each treatment. Serum was collected in tubes with no additive, allowed to clot at room temperature and then centrifuged at 3000 rpm at 4°C. Plasma was collected in tubes containing EDTA and prepared by centrifugation at 3000 rpm at 4°C. Plasma and serum samples were stored at –80°C until analysis.