Marine ω-3 Fatty Acid Intake

Associations with cardiometabolic risk and response to weight loss intervention in the Look AHEAD (Action for Health in Diabetes) study

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OBJECTIVE — To examine usual marine ω-3 fatty acid (mO-3FA) intake in individuals with diabetes; its association with adiposity, lipid, and glucose control; and its changes with behavioral lifestyle intervention for weight loss.

RESEARCH DESIGN AND METHODS — Cross-sectional and 1-year longitudinal analyses were performed on 2,397 Look AHEAD (Action for Health in Diabetes) participants. Look AHEAD is a cardiovascular outcome trial evaluating the effects of intensive lifestyle intervention for weight loss in overweight/obese subjects with type 2 diabetes.

RESULTS — Baseline mO-3FA intake was 162 ± 138 mg/day. It was inversely associated with triglycerides ($\beta = -0.41$, $P < 0.001$) and weakly with HDL ($\beta = 4.14$, $P = 0.050$), after multiple covariate adjustment. One-year mO-3FA and fried/sandwich fish intake decreased with intensive lifestyle intervention ($P < 0.001$).

CONCLUSIONS — mO-3FA intake in Look AHEAD participants was low but associated favorably with lipids. These results encourage investigation on the potential benefits of increasing mO-3FA intake in lifestyle interventions for weight loss in individuals with diabetes.

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Observational studies have suggested that marine ω-3 fatty acid (mO-3FA) intake may decrease coronary atherosclerosis progression in subjects with diabetes (1). However, only a fraction of participants in cardiovascular event studies have had diabetes. Concerns that high-dose mO-3FAs may worsen glucose control have reduced enthusiasm for their use in diabetes (2). Little is known regarding usual dietary mO-3FA intake and its association with metabolic disturbances in diabetes, and much less is known about the effects of weight loss interventions on mO-3FA consumption.

RESEARCH DESIGN AND METHODS

A total of 2,397 participants, corresponding to the first half of Look AHEAD (Action for Health in Diabetes) enrollees, completed the Look AHEAD food frequency questionnaire (LA-FFQ) (3). Look AHEAD is a multicenter randomized trial in overweight/obese individuals with type 2 diabetes, investigating the effects of intensive lifestyle intervention–induced weight loss on cardiovascular morbidity and mortality. Eligibility criteria included BMI ≥25 kg/m^2 (≥27 kg/m^2 if on insulin), age 45–76 years, A1C <11%, blood pressure ≤160/100 mmHg, and fasting triglycerides ≤600 mg/dl (4).

The LA-FFQ and its analysis were previously described (3). Eight line items inquire about seafood consumption. mO-3FA intake was estimated by adding eicosapentaenoic acid and docosahexaenoic acid intake from the LA-FFQ.

Statistical analysis

The baseline association between mO-3FA intake and weight, BMI, waist circumference, A1C, fasting glucose, and lipids was examined using multiple-variable linear regression. The final model included demographics, dietary variables, fitness (exercise capacity on graded exercise test), and class use of medications to control lipids and glucose. Comparisons between race/ethnicity groups were tested with ANCOVA. Differences in variable change at 1 year between intensive lifestyle intervention and the usual-care group (diabetes, support, and education) were analyzed with an unpaired t test and χ^2 test. Data were available for each variable analyzed in ≥99% of participants. An $\alpha < 0.05$ indicated significance.

RESULTS

Participant baseline characteristics do not differ from those of the overall Look AHEAD sample (5) with respect to sex, race/ethnicity, adiposity, or fitness. Age criteria change during the second year of study recruitment resulted in a slightly younger age in our subgroup (see Table S1, available in an online appendix at http://care.diabetesjournals.org/cgi/content/full/dc09-1235/DC1).

mO-3FA intake and metabolic variables at baseline

Mean mO-3FA intake was 162 ± 138 mg/day (median 120 mg/day). Intake was ≤200 mg/day in 75% of Look AHEAD

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Table 1—*Dietary intake of mO-3FAs and fried fish and HDL and triglyceride levels at baseline and 1 year*

	mO-3FA (mg/day)	HDL (mg/dl)	Triglycerides (mg/dl)	Subjects with fried fish/sandwich fish intake ≥1/week (%)
Baseline				
Overall (*n* = 2,397)	162 (138)	43 (11.3)	186 (125.6)	
African American (*n* = 331)	205 (186)*	48.2 (13.0)*	127.4 (99.8)*	
Caucasian (*n* = 1,552)	160 (130)	41.4 (10.7)	197.6 (127.01)	
Other (*n* = 76)	156 (117)	45.0 (12.1)	156.7 (90.7)	
Hispanic (*n* = 316)	152 (115)	42.4 (10.8)	191.7 (119.7)	
Native American (*n* = 122)	98 (117)	40.9 (9.0)	192.7 (156.1)	
Longitudinal				
ILI (*n* = 1,211)				
Baseline	160 (145)	43 (11.2)	189 (127.4)	5.62
Change at 1 year	−20 (137)†	3.5 (7.1)†	−34.9 (11.5)†	−3.56‡
DSE (*n* = 1,186)				
Baseline	160 (129)	42 (11.3)	182 (123.6)	6.16
Change at 1 year	0 (121)	1.4 (6.6)	−14.7 (98.7)	−0.93

*Differences across race/ethnicity groups were tested by ANOVA after adjusting for age, sex, and clinic site. African Americans had higher intake of mO-3FA, higher HDL, and lower triglycerides than Caucasians, Hispanics, and the other race/ethnicity group ($P < 0.05$ for all differences). †Differences between intensive lifestyle intervention (ILI) and diabetes, support, and education (DSE) in variable change from baseline were evaluated using the unpaired *t* test. ILI participants had lower mO-3FAs, higher HDL, and lower triglycerides than individuals in DSE ($P < 0.001$ for all differences). ‡Differences between ILI and DSE in the proportion of subjects eating fried fish/sandwich fish ≥1/week were tested with χ^2. There was a greater decrease of fried fish/sandwich fish intake in ILI than in DSE ($P < 0.001$). Percent subjects eating lean fish >1/week increased by 5.54% with ILI and by 1.27% with DSE ($P = 0.012$). Change in percent subjects eating fish rich in mO-3FAs did not differ between ILI and DSE at 1 year ($P = 0.421$).

participants and ≥1,000 mg/day in only 1%, with significant race/ethnicity differences (Table 1). mO-3FA intake was inversely associated with triglycerides (log-transformed) ($\beta = -0.41$, $P < 0.001$) and with a trend for increasing HDL ($\beta = 4.14$, $P = 0.050$), independently of multiple covariates (Table S2). No association was found between mO-3FA intake and each of cholesterol, non-HDL or LDL cholesterol, markers of adiposity, or glucose control ($P > 0.05$). African Americans, who consumed the most mO-3FAs, had the highest HDL cholesterol and the lowest triglycerides.

mO-3FA intake and HDL and triglyceride levels with intensive lifestyle intervention at 1 year

mO-3FA intake decreased with intensive lifestyle intervention but not with diabetes, support, and education at 1 year ($P < 0.001$) (Table 1). When investigating changes in type of fish consumed, we found an intensive lifestyle intervention–induced decrease in fried/sandwich fish consumption ($P < 0.001$) but not in lean or mO-3FA–rich fish. The small change in mO-3FA intake with intensive lifestyle intervention did not explain 1-year changes in HDL and triglycerides.

CONCLUSIONS— Look AHEAD offers a large sample of individuals with diabetes in whom a validated tool was used to estimate usual mO-3FA intake. mO-3FA consumption was found to be very low. An intake of ≥1,000 mg/day is recommended for people with diabetes (6–8). Despite the low levels, mO-3FA consumption was associated with lower triglycerides and with a trend for higher HDL. The relationship between mO-3FAs and each of HDL and triglycerides was independent of adiposity, fitness, lipid medications (including fibrates), glycemic control, and dietary variables that affect lipid levels, such as carbohydrate, fiber, and saturated fat. Likewise, the intake of linolenic acid, a precursor of eicosapentaenoic acid and docosahexaenoic acid, and consumption of its metabolic competitor linoleic acid, did not alter the relationship between mO-3FA intake and HDL and triglycerides.

Contrary to reports with high-dose mO-3FA (9,10), we did not find an unfavorable association between mO-3FA consumption and LDL cholesterol or glucose control. These findings encourage future outcome studies in individuals with diabetes evaluating lower intakes of mO-3FA than those previously investigated. A large trial with eicosapentaenoic acid supplementation in high-risk subjects found the greatest reduction in cardiovascular events in the subgroup with lower HDL and higher triglycerides (11), raising the possibility that mO-3FA may be of a particular benefit in individuals with diabetes, who characteristically display this lipid profile. The race/ethnicity differences in mO-3FA consumption and the question of whether specific groups might specifically benefit from interventions that increase mO-3FA intake are worthy of further study.

The decrease in mO-3FAs with intensive lifestyle intervention is not surprising given that the Look AHEAD intervention was not targeted at increasing mO-3FA intake. The decrease in mO-3FA intake paralleled a reduction in fried/sandwich fish intake, which is considered favorable (12).

Our results should be interpreted with caution. Look AHEAD did not evaluate supplement use and is subject to the limitations of information obtained by self-report (3). The favorable association between usual dietary mO-3FA intake and lipids at baseline encourages future research on the potential benefit of increasing consumption of mO-3FAs, in addition to modifying fish type, when planning lifestyle interventions for weight loss in individuals with diabetes.

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