Cholesterol-Lowering Benefits of a Whole Grain Oat Ready-to-Eat Cereal

Liz Johnston, MPH, RD, LD, Senior Scientist*‡
Helenbeth Reiss Reynolds, MPH, RD† • Mary Patz, RD, Clinical Dietitian*
Donald B. Hunninghake, MD, Professor of Medicine and Pharmacology,
Director, Heart Disease Prevention Clinic*
Kathleen Schultz, RD, LD, Clinical Dietitian*
Becky Westereng, RD, LD, Clinical Dietitian*

**University of Minnesota Heart Disease Prevention Clinic,*
401 East River Parkway, Box 192 UMHC, Minneapolis, MN 55455
†3460 Lawndale Lane, Plymouth, MN 55447

■ ABSTRACT

Medical nutrition therapy is the initial form of therapy for patients with elevated blood cholesterol levels and some dietary modification is currently recommended for all individuals with total serum cholesterol levels ≥ 200 mg/dl according to the National Cholesterol Education Program guidelines (1). In clinical practice it is estimated that the usual mean reduction in total cholesterol is in the range of 3–5%; when more restrictive diets are employed, it is estimated that an additional 3–5% reduction in total cholesterol may be achieved. Reductions in total cholesterol of 1% are predicted to produce a 2% reduction in coronary heart disease risk in studies of 5 years or less.

The cholesterol-lowering effects of a whole grain oat ready-to-eat cereal, Cheerios®, were evaluated in 135 men and women, ages 40-70 years, with mean LDL-C levels of 130-190 mg/dl and triglycerides ≤300 mg/dl. After following a Step One diet for 6 weeks, they were randomly assigned to either 3 oz of control cornflakes containing no soluble fiber or 3 oz of whole grain oat ready-to-eat cereal with 3.0 g soluble fiber both taken daily in two divided doses for a six-week treatment period. Compared to the control group, participants who consumed oat cereal achieved a 3.8% (9.1 mg/dl) reduction in total cholesterol ($p = 0.0008$), a 4.2% (6.7 mg/dl) reduction in LDL-cholesterol ($p = 0.0065$) and a 4.5% (5.7 mg/dl) decrease in apoB levels ($p = 0.02$) when compared to baseline values. The oat cereal did not significantly affect HDL-cholesterol, body weight, or total calories. Adherence to diet and cereals was excellent in both groups, with no significant side effects occurring. ■

KEY WORDS: hypercholesterolemia, whole grain oat cereal, soluble fiber, dietary fiber, serum total cholesterol, LDL-cholesterol, coronary heart disease

‡Address correspondence and reprint requests to L. Johnston.

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INTRODUCTION

Cardiovascular disease is the leading cause of death and disability in the United States. In 1996, nearly one million people died of heart disease and stroke, and an estimated $150 billion dollars was spent to treat these patients (2). Hypercholesterolemia has been identified as a major risk factor for coronary heart disease (3,4), and reductions in total serum and LDL-cholesterol have been shown to decrease the risk for future coronary events (5-11). There is a progressive increase in risk for developing coronary heart disease (CHD) as total and low-density lipoprotein cholesterol (LDL-C) levels increase; levels should therefore be kept as low as possible (12). The National Cholesterol Education Program

(NCEP) Adult Treatment Panel suggests desirable serum cholesterol levels for all Americans over 20 years of age to be 5.17 mmol/L (200 mg/dl) or less; levels >6.21 mmol/L (240 mg/dl) are considered to be high (13). Approximately 25% of the adult population over 20 years of age have serum cholesterol levels of 6.21 mmol/L or greater (14). Medical nutrition therapy consisting of a diet low in total fat and cholesterol has served as the cornerstone for treating elevated cholesterol for several decades. For many patients, however, the NCEP Step One diet (30% of calories from total fat, 10% from saturated fat, and <300 mg/day of cholesterol) or the Step two diet (7% of calories from saturated fat and <200 mg/day of cholesterol) are not sufficient to lower blood cholesterol into the desired range.

A practical approach to further reduce blood cholesterol is to consume oat-based cereal products on a daily basis. Numerous clinical trials and studies in free living populations have shown that the inclusion of foods rich in soluble fiber such as whole grain oats and oat bran reduced blood cholesterol beyond the effect of a low-fat, low-cholesterol diet (15-17).

Since medical nutrition therapy is the mainstay in the treatment of hypercholesterolemia, the objective of this study was to evaluate the effectiveness of a whole grain oat ready-to-eat cereal in reducing total and LDL-cholesterol levels when used as an adjunct to the Step-One Diet.

SUBJECTS AND METHODS

Subjects

The study was conducted with 135 volunteers (81 men, 54 women) diagnosed with mild to moderate primary hypercholesterolemia. The protocol and consent were approved by the University of Minnesota Research Subjects Review Board. The conditions and procedures of this study were explained, and written consent obtained from each participant. Subjects were included if they were 40-70 years old and had mean LDL-C levels between 3.37 mmol/L (130 mg/dl) and 4.9 mmol/L (190 mg/dl) at Weeks −4 and −2. The subjects agreed to maintain constant body weights (±5%) throughout the study. Subjects were excluded if their baseline triglycerides levels were greater than 3.39 mmol/L (300mg/dl); body weight was greater than 140% of ideal (based on 1983 Metropolitan height/weight standards), or if there was a history of major surgery in the previous three months. Subjects were also excluded for clinically significant metabolic, renal, hepatic, gastrointestinal, pulmonary, hematopoietic, thyroid, or cardiovascular diseases or a history of allergic reactions to corn, wheat, oats, or rice products. Subjects taking certain drugs i.e., corticosteroids, androgens, or lipid lowering drugs were excluded from the study and subjects taking other drugs potentially affecting lipids, i.e., estrogen, estrogen/progestin, thiazide diuretics, beta blockers and thyroid hormones were allowed, as long as they were on stable doses.

Study Design

This was a 12-week study consisting of a six-week pretreatment period of dietary reinforcement and qualification and a six-week treatment period. All subjects were instructed on the Step One diet at Week −6 by a registered dietitian. Qualifying lipid and lipoprotein determinations were done at Weeks −4 and −2 and subjects were randomly assigned to treatment or control at Week 0 (baseline). Subjects were stratified into four groups by gender and mean LDL-C values from Weeks −4 and −2. Subjects with LDL-C values <159 were assigned to one stratum and those with LDL-C values >159 to the other. Within each of the four strata, throughout the study subjects were randomly assigned to either the control cereal or the treatment cereal to maintain approximately equal numbers for each cereal during the course of the cereal assignment period. The total nutrient composition of the cereals used in the study are given in Table 1. The treatment group was given 3 oz of a whole grain ready-to-eat cereal

Table 1. Nutrition composition per 3 ounces (90g) of whole grain oat and control cereals

	Control Cereal	Whole Grain Oat Cereal
Calories	338.0	321.0
Protein (g)	5.4	9.9
Carbohydrate (g)	78.0	67.6
Fat (g)	1.4	5.2
Monounsaturated (g)	0.3	2.0
Polyunsaturated (g)	0.4	1.5
Saturated (g)	0.3	1.0
Cholesterol (mg)	0.0	0.0
Total fiber (g)	2.0	9.0
Water-soluble fiber (g)	0.1	2.9
Water-insoluble (g)	1.9	6.1

Cheerios®, composed of whole grain oat flour, starch, sugar, and salt with 3.0 g. of soluble fiber. The control group was given 3 oz of commercial cornflakes. This product contained degermed yellow corn meal, sugar, salt, and cereal malt syrup with no soluble fiber. Both cereals were produced with commercial cereal-processing equipment. Cereal was prepackaged into individual 45 g (1.5 oz) packets. Each subject was instructed to consume two packets of cereal daily: one as part of the morning meal and one in the evening. The diet was to remain otherwise stable. The treatment period consisted of four visits, weeks +2, +4, +5, and +6. Adherence to the regimen was monitored by subject interviews, daily logs of cereal intake, and by counting returned unopened packets of cereal at each visit.

Variables Measured

Lipid profiles were obtained at clinic visits which were made in the morning after a 12-h fast from food and liquid except water and a 24-h fast from alcohol. A clinical chemistry screen was obtained at Week −2. Apolipoproteins Al and B were measured at Weeks 0 and +6. Subjects were required to keep three-day food records at Weeks −6, 0 (baseline), and +6. A complete nutrient analysis was performed on the food records at Weeks 0 and +6 using the Nutrition Coordination Center (NCC), University of Minnesota Nutrition Data System, version 2.9. All food records were reviewed by NCC-certified registered dietitians. Dietary adherence was also evaluated by registered dietitians at weeks +2, +4, and +5.

Analytical Methods

Total cholesterol, triglyceride, and HDL-cholesterol were analyzed in a Centers for Disease Control (CDC) referenced laboratory, University of Minnesota, Minneapolis. Total plasma cholesterol was measured using a cholesterol esterase-cholesterol oxidase assay (Boehringer-Mannheim Diagnostics, Indianapolis, Indiana) on the Roche COBAS FARA centrifugal analyzer. Plasma triglycerides were determined by using a blanking reagent (Boehringer-Mannheim Diagnostics) and then using the same analyzer. HDL-cholesterol was measured by the same method as the total cholesterol after precipitation for the low-density lipoproteins and the very-low-density lipoproteins with a dextran sulphatemagnesium chloride reagent. Immunonepholemetry (ARAY, Beckman, Palo Alto, California) was used for measurement of Apolipoproteins. The LDL-cholesterol levels were calculated using the Friedewald formula: LDL-C = Total Cholesterol − (HDL-C + [Triglycerides/5]) (18).

Statistical Analysis

For lipid, blood pressure, and body weight measurements, baseline values for each subject were calculated as the mean of the measurements from Weeks −2 and 0. Final values were calculated as the mean of the measurements from Weeks +4, +5, and +6. Apolipoprotein baseline values were the measurement at Week 0 and apolipoprotein final values were the measurements at Week +6. Statistical analyses were performed on the changes in these measurements during the treatment phase which were calculated as the difference between the final and baseline values.

For the change in each lipid, Apolipoprotein B, blood pressure and body weight measurement, a three-way analysis of variance was done to evaluate whether there were differential cereal effects across the four strata. For all measurements the three-way ANOVA gave no evidence of differential cereal effects across the four strata. In fact, except for the LDL/HDL ratio there were no significant effects between strata (in the LDL/HDL ratio the high LDL baseline group had a significantly greater reduction in the ratio when compared to the low LDL baseline group $p = 0.016$). Consequently, 2 sample t-tests were used to assess the significance of differences in mean changes between the two cereal groups. All reported significance levels are two-sided and SAS statistical analysis software was used for all calculations.

Baseline nutritional values were the mean daily values from the three-day diet records returned at Week 0 and final nutritional values were the mean daily values from the three-day diet records returned at Week +6. Changes in nutritional intake during the treatment phase were calculated as the differences in the mean final and mean baseline values. As with the lipid values, differences in mean changes in nutritional intake between the two cereal groups were evaluated by two-sample t-tests.

RESULTS

Of the 135 randomized participants, 124 completed the study. Two subjects, of the 124, completed

weeks +4 and +5 but did not complete week +6. The mean of weeks +4 and +5 were used for these two subjects' final lipid values. One subject on the control cereal discontinued because of gastrointestinal complaints, two subjects could not be contacted and six subjects did not continue for reasons unrelated to study (primarily time or transportation difficulties). The control and oat cereal groups were well matched secondary to gender, age, weight, blood pressure, lipid and lipoprotein values, and dietary intake at baseline (Tables 2 and 3). Body weight did not change in the two groups during the course of the study. The mean blood pressure in the two groups were similar throughout the study. Life-style habits such as smoking, alcohol consumption, and exercise remained constant throughout the study for both groups. There were no significant changes in blood chemistries or complete blood counts (CBC) in the groups throughout the study (data not shown). The nutrient analysis confirmed adherence to the Step One diet throughout the study in both groups. Minor but statistically significant differences between control and treatment were posttreatment percent of calories from polyunsaturated fat 4.9 vs. 5.7 ($p = 0.013$), total dietary fiber posttreatment 20.2 vs. 24.8 ($p = 0.0005$), change in dietary fiber −3.1 vs. 3.2 ($p<0.00005$), soluble fiber posttreatment 6.0 vs. 9.3 ($p<0.00005$), change in soluble fiber −1.6 vs. 1.9 ($p<0.00005$), and change in insoluble fiber −1.5 vs. 1.4 ($p = 0.0002$). There were no statistically significant differences in mean changes between treatment groups during the cereal phase except for fiber components (the actual cereal compositions). There were no differences in the two groups in total and LDL-C baseline values (Table 4). There was no significant effect on HDL-C or triglycerides between cereal groups (Table 4). The

Table 2. Baseline characteristics

	Control Cereal Group	Whole Grain Oat Cereal Group
N	62	62
Gender (m/f)	38/24	40/22
Mean age (yr)	57.3	56.7
Body weight (kg)	79.5	83.9
BP (mm/hg)		
Systolic	124.2	123.2
Diastolic	78.6	76.8
Baseline lipids (mmol/l)		
Total cholesterol	6.14	6.19
LDL-Cholesterol	4.15	4.10
HDL-Cholesterol	1.25	1.28
Triglycerides	1.62	1.77

Table 3. Summary of dietary energy, carbohydrate, protein, fat, and fiber nutrient intake at baseline and after treatment[a]

Parameter	Control Cereal Group n = 60		Whole Grain Oat Cereal Group n = 60	
	Baseline	Posttreatment	Baseline	Posttreatment
Total energy (kcal)	2007.7	2024.9	1923.6	1935.2
Total CHO (g)	302.9	310.7	268.6*	274.3*
(% of total energy)	60.7	62.6	56.4**	57.6***
Total protein (g)	74.1	76.9	75.5	82.6
(% of total energy)	15.4	15.5	16.2	17.5***
Total fat (g)	59.2	53.8	60.7	57.6
(% of total energy)	25.6	22.5	27.7	25.5*
Saturated fat (g)	19.3	17.3	19.6	18.0
(% of total fat)	8.4	7.2	8.9	8.0
Monosaturated fat (g)	22.5	20.6	23.8	21.7
(% of total fat)	9.7	8.6	10.8	9.6
Polyunsaturated fat (g)	12.5	11.4	12.3	12.8
(% of total fat)	5.4	4.9	5.7	5.7*
Cholesterol (mg)	177.3	170.1	195.1	168.5
Total dietary fiber (g)	23.3	20.2	21.6	24.8***
Water soluble (g)	7.6	6.0	7.4	9.3***
Water insoluble (g)	15.5	14	14	15.4

[a] Analyzed from three-day food records using University of Minnesota NDS, vesion 2.9; dietary contributions from cereals are included. See Table 1 for contributions from cereals. Calories from the nutrients (as % of calories) are calculated on a per person basis and hence will not completely agree with percents based on the overall average gram consumption.

[b] p value footnotes are for comparing cereals at baseline and posttreatment.

* $p \leq 0.05$ and $> .01$.

** $p \leq .01$ and $> .001$.

*** $p \leq .001$.

Table 4. Effects of whole grain oat or placebo cereals on serum lipids, apolipoproteins, and triglycerides[a]

Parameter	Control Cereal Group n = 62 Baseline	Posttreatment	Change From Baseline	Percent Change From Baseline	Whole Grain Oat Cereal Group n = 62 Baseline	Posttreatment	Change From Baseline	Percent Change From Baseline
Total cholesterol (mmol/L)	6.14 ± 0.54	6.23 ± 0.54	0.09 ± 0.39	1.7 ± 6.2	6.19 ± 0.55	6.04 ± 0.61	−0.14 ± 0.37	−2.3 ± 6.1
LDL-Cholesterol (mmol/L)	4.15 ± 0.42	4.15 ± 0.42	0.0 ± 0.34	0.3 ± 8.3	4.10 ± 0.45	3.93 ± 0.49	−0.18 ± 0.36	−4.0 ± 8.6
HDL-Cholesterol (mmol/L)	1.25 ± 0.27	1.25 ± 0.28	0.00 ± 0.10	0.0 ± 8.2	1.28 ± 0.31	1.29 ± 0.33	0.02 ± 0.08	1.1 ± 6.5
LDL:HDL	3.48 ± 0.83	3.47 ± 0.83	−0.01 ± 0.33	0.20 ± 10.4	3.39 ± 0.85	3.21 ± 0.78	−0.18 ± 0.35	−4.9 ± 9.1
Triglycerides (mmol/L)	1.62 ± 0.70	1.85 ± 0.84	0.23 ± 0.45	16.2 ± 26.4	1.77 ± 0.69	1.81 ± 0.71	0.03 ± 0.39	3.9 ± 21.5
APO A-1 (mg/dl)	129.7 ± 19.2	131.1 ± 17.5	1.39 ± 10.1	1.6 ± 8.2	134.8 ± 22.0	134.2 ± 22.4	−0.6 ± 11.3	−0.1 ± 9.2
APO B (mg/dl)	125.6 ± 17.9	129.1 ± 18.7	3.6 ± 13.8	3.5 ± 11.6	124.2 ± 15.1	122.1 ± 14.7	−2.1 ± 12.1	−1.2 ± 10.3
Weight (lb)	174.8 ± 26.3	175.9 ± 26.6			184.7 ± 30.6	185.4 ± 30.6		

[a] All values are mean ± standard deviation. Mean percent change calculated from baseline on a per person basis.
* For LDL and LDL/HDL ratio, 61 subjects in the control group and 62 subjects in the treatment group.
Apo A-1 and Apo B, 59 subjects in both the control and treatment groups.

difference in mean cholesterol change between treatment and control groups is −0.24 mmol/L (9.1 mg/dl) with a standard error of 0.07 and a p value of 0.0008 (Table 5). The difference in mean LDL cholesterol change between treatment and control groups is −0.17 mmol/L (6.7 mg/dl) with a standard error of 0.06 and a p value of 0.0065. The difference in mean Apolipoprotein B change between treatment and control groups was 5.7 mg/dl (Table 5).

Compliance was based on the number of returned, unopened packages, participant interviews, and daily cereal intake logs. Participants consumed 93.8% of the whole grain oat cereal and 93.5% of the placebo cereal. No serious adverse reactions were reported in either group. Five participants reported mild gastrointestinal side effects. Three of the five reporting gastrointestinal complaints were in the placebo group: one reported flatus, two reported increased constipation (one discontinued the study for this reason). The remaining two participants reporting gastrointestinal complaints were in the whole grain oat cereal group. One individual reported increased flatus, one reported increased stool frequency.

DISCUSSION

This study evaluated the effectiveness of a ready-to-eat breakfast cereal made of whole grain oats in a double-blind, randomized trial. The two groups were well matched for age and baseline weight. The dietary analysis included the dietary contributions from the treatment and control cereals.

Results of this clinical study demonstrate that two daily servings of 1.5 oz (45 g) of a whole grain oat ready-to-eat cereal reduced total cholesterol levels by 3.8% (−0.24 mmol/L) and LDL-C levels by 4.2% (−0.17 mmol/L) respectively when compared to control. Apolipoprotein B levels were reduced, while HDL cholesterol levels were not changed.

The lipid-lowering effect of this ready-to-eat cereal is similar to studies using hot oatmeal and oat bran (15, 16) as well as a previous study evaluating the effect of a whole grain oat ready-to-eat cereal (17). When hypercholesterolemic subjects added oatmeal to a prudent low-fat, low-cholesterol diet, serum cholesterol was lowered an additional 3.1% (19). An earlier clinical study (n = 43) (20) using Cheerios® resulted in a significant reduction in both total cholesterol (4.4%) and LDL cholesterol (4.9%) when compared to baseline. There was no significant effect on HDL-C or triglycerides. These data indicate that a whole grain oat ready-to-eat cereal as part of a low-fat, low-cholesterol diet can be as effective as hot oat cereals such as oatmeal or oat bran in the treatment of elevated blood cholesterol.

These findings translate to a simple and practical

approach to help reduce blood cholesterol levels since whole grain oats are well tolerated and may be appropriate for long-term use when factors such as: safety, subject tolerance, and ease of availability are considered. The addition of the whole grain oat cereal was easily incorporated into the daily lifestyles of these subjects.

The precise mechanism responsible for the cholesterol-lowering effect of soluble fiber is not clear. Several possible mechanisms have been proposed: binding of bile acids in the small intestine (21) leads to increased fecal bile acid excretion (22) and primarily bile acid synthesis (23, 24); reduced fat and cholesterol absorption (25, 26); a reduced rate of carbohydrate absorption leading to lower serum insulin concentrations and hence less stimulus for cholesterol and lipoprotein synthesis (27); and inhibition of cholesterol synthesis by short-chain fatty acids generated during colonic fermentation of soluble fiber (28).

β-glucan, a viscous fiber contained in oats, appears to be a primary component that elicits the cholesterol-lowering effect of oat cereals (29, 30). Animal studies have shown that higher levels of intestinal contents viscosity are associated with a reduction in both plasma and liver cholesterol (31, 32). The results of the current study are further supported by Gallaher et al. (33), who used an animal model to demonstrate that the intestinal contents viscosity of a whole grain oat ready-to-eat cereal is not significantly different than oatmeal or oat bran. β-glucan is not the only component in oats that may favorably effect blood lipids. Oats also contain plant sterols, a lipid fraction high in tocotrienols and monounsaturated fatty acids (34). The ratio of arginine to lysine contained in oats is also associated with cholesterol lowering in animals (35).

The available clinical and animal data along with this clinical trial indicate that a whole grain oat ready-to-eat cereal contains the efficacious compounds needed to achieve an additional cholesterol-lowering effect in humans with mild to moderate hypercholesterolemia when used as an adjunct to a low-fat, low-cholesterol diet. This study demonstrates that individuals can adhere to a cholesterol-lowering diet that includes a whole grain oat cereal that is readily available, convenient to consume, and easy to incorporate into a daily eating plan.

Table 5. Differences between changes in treatment and control groups for lipids and apolipoprotein B

Mean cholesterol	-9.1 mg/dl
Mean LDL cholesterol	-6.7 mg/dl
Mean Apo B	-5.7 mg/dl

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