Angiology
The Journal of Vascular Diseases

VOLUME 46 DECEMBER 1995 NUMBER 12

Treating Hyperlipidemia in the Elderly

Richard M. Fleming, M.D., F.A.C.A., F.I.C.A.
Kristy Ketchum, R.D., L.D.
Diane M. Fleming, R.N., B.S.N.
and Ruth Gaede, R.N., M.S.N.

CEDAR FALLS, IOWA

ABSTRACT

Background: Determination of the effects of dietary modification and hyperlipidemic medications in the elderly (> sixty-five years of age) patient has not been significantly investigated to date despite knowledge that elevated cholesterol (TC) and triglyceride (TG) levels increase the risk of coronary artery disease (CAD).

Methods: Twenty-seven individuals were placed into one of three treatment groups and longitudinally followed up to examine the effects of diet and hyperlipidemic medications on TC and TG levels. Group 1 ($n = 14$) received neither dietary nor drug therapy. Group 2 ($n = 9$) received dietary counseling without concomitant hyperlipidemic medications. Subjects in group 3 ($n = 4$) underwent dietary instruction for six months and hyperlipidemic medication(s) for eighteen months.

Results: Subjects in group 1 demonstrated a statistical increase in TC ($P \leq 0.001$) during the study. Patients in groups 2 ($P \leq 0.001$) and 3 ($P \leq 0.05$) demonstrated statistical improvement in TC reduction during dietary counseling. The effect on TC was blunted in group 3 after dietary counseling was discontinued. Reductions in TG levels were significant ($P \leq 0.001$) only for patients in group 2.

Conclusion: Elderly individuals were able to significantly reduce both TC and TG levels by dietary modification alone. Minimal improvement was seen with the addition of hyperlipidemic medications.

From the Center for Clinical Cardiology and Research, in conjunction with Sartori Memorial Hospital, Cedar Falls, Iowa.

Introduction

Reversibility of coronary artery disease (CAD) by reduction of cholesterol levels has been documented in animal[1-10] models as early as 1971. Epidemiologic studies[11-14] have demonstrated a positive correlation between the intake of dietary cholesterol and serum cholesterol levels. Numerous studies[15-38] have examined the impact of risk factor (RF) modification in individuals ≤ sixty-five years of age as noted in Table I.

Table I

Studies Looking at Risk Factor Modification

Reference*	Number in Study	Age Range (years)	Sex
Clofibrate[15]	497	< 65	Both
Clofibrate[16]	717	40–69	Both
Clofibrate & Niacin[17]	8341	30–64	Males
North Karelia Project[18]	1683	25–59	Both
Belgian Heart[19]	19,390	40–59	Males
Western Electric[20]	1900	40–55	Males
MRFIT[21]	12,866	35–57	Males
LRC-CPPT[22]	3806	35–59	Males
Israeli Study[23]	10,059	> 40	Males
Probucol & Clofibrate[24]	1825	50–65	Males
Donolo-Tel Aviv[25]	2992	35–64	Both
Helsinki[26]	4081	40–55	Males
Clofibrate & Nicotinic Acid[27]	555	< 70	Both
PROCAM[28]	2754	40–65	Males
Niacin[29]	101	36–73	Both
Clofibrate[30]	40	< 65	Males
Diet & Colestipol[31]	30	38–65	Both
Colestipol[32]	42	< 65	Both
Cholestyramine[33]	116	< 65	Both
Clofibrate & Nicotinic Acid[34]	48	30–56	Both
Leiden Trial[35]	39	33–59	Both
Colestipol-Niacin[36]	162	40–59	Males
CLAS[37]	188	40–59	Males

*Denotes reference number as noted in the reference section.

Whereas reversibility of CAD has been demonstrated in younger[38] individuals, little work has been done[39-42] to determine whether individuals over sixty-five years of age can significantly lower their cholesterol levels, even though it is commonly accepted that elevated cholesterol[43,44] places the elderly at increased risk for atherosclerotic CAD.

This longitudinal study was designed to determine the effect of dietary counseling, hyperlipidemic medications, and the combined effect of diet and drug therapy on cholesterol (TC) and triglyceride (TG) levels in individuals ≥ sixty-five years of age.

Methods

Patient Population

Twenty-seven individuals sixty-five years or older were enrolled in an eighteen-month study designed to determine the impact of dietary counseling and hyperlipidemic medications on TC and TG levels. The study included 11 men and 16 women. Group 1 (n = 14) participants were advised by their cardiologist to reduce their intake of dietary cholesterol and fats and served as the "control" group. Subjects in this group did not receive dietary counseling or drug therapy. Dietary brochures were available regarding information about foods high in TC and TG, which patients were encouraged to read on their own.

Patients in group 2 (n = 9) received dietary counseling from either a cardiologist (RMF) trained in lipid disorders and/or a registered (KK) dietitian. Subjects in group 3 (n = 4) received dietary counseling for six months and hyperlipidemic medications for eighteen months.

Subject Enrollment

Patients were enrolled in the study if they had type IIa, IIb, or IV hyperlipidemia. Subject participation was voluntary, and those patients demonstrating ischemic changes on nuclear imaging[45] frequently requested specific dietary counseling, which placed them by definition into either group 2 or 3. Subjects were excluded from the study if they had hypercholesterolemia secondary to hypothyroidism, nephrotic syndrome, diabetes mellitus, obstructive liver disease, or drug effect caused by beta-antagonists, thiazide diuretics, progesterone, or anabolic steroids.

Dietary Counseling

Patients in group 2 (eighteen months) and 3 (six months) received instructions from either a registered dietitian and/or cardiologist as noted

Table II

Suggested Daily Dietary Guidelines (Percent of Calories) for Patients in Groups Two and Three

Constituent	Current* American Diet	Phase I* AHA Diet	Phase II* AHA Diet	Vegetarian Diet*
Total fat	42	< 30	< 20	< 10
Saturated	14–19	< 10	< 7	
Monosaturated		10–15	10–15	
Polysaturated		< 10	< 10	
Carbohydrate		50–60	50–60	75
Protein		15–20	15–20	15
Cholesterol	500 mg**	< 300 mg**	< 200 mg**	5 mg**

*Equals percent of daily calories, ** mg = milligrams.

above. Subjects were counseled individually for one hour during their first session. Follow-up sessions ranged from fifteen to thirty minutes depending upon the needs of the patient and significant other(s). Patients were advised to change their dietary habits to adopt a vegetarian life-style. If this could not be achieved, patients were encouraged to follow either phase II American Heart Association (AHA) standards or at least phase I AHA guidelines as noted in Table II. Since the study was designed to investigate what could be accomplished in the real world, patients and their families made the final decision regarding which of the dietary guidelines they would follow.

During each of the follow-up visits, patients in groups 2 and 3 were able to review their progress, assess individual dietary problems, and set future goals. Patients were encouraged about the progress they had made, with criticism limited to constructive comments.

Medications

Since the purpose of this study was not to compare specific hyperlipidemic agents, these medications were independently selected by the cardiologist(s) taking care of the patient. Selection consisted of HMG-CoA reductase inhibitors, bile acid sequestrants, fibric acid derivatives, and nicotinic acid. Combination drug therapy was also used at the discretion of the primary cardiologist and not influenced by the investigators. Medications were used according to guidelines outlined for each of the agents in the current *Physician's Desk Reference* (PDR) with appropriate monitoring of drug effect and side effects.

Lipoprotein Analysis

Subjects were asked to fast for a minimum of twelve hours prior to having blood drawn for serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels. TC and TG paramax reagent methods were used in the laboratory. HDL-C was measured by magnesium phosphotungstate precipitation and centrifugation method. Low-density lipoprotein cholesterol (LDL-C) was calculated as follows:

$$LDL\text{-}C = (TC) - (HDL\text{-}C) - (TG/5)$$

Statistical Analysis

Each lipoprotein was measured on scheduled visits as noted below. Results for each group were determined and described as mean ± standard deviation. Differences between groups and for differences within groups over time were analyzed by unmatched two-tailed t tests. Results of group differences were graphically depicted. Other statistical analyses of TC and TGs, including range, confidence intervals, and correlation among changes in weight, TC, and TG values, were done but yielded no additional useful information.

Table III

Group Characteristics

	Age (Years)*	Weight (Pounds)*
Group 1	71 ±5	178 ±46
Group 2	71 ±3	166 ±15
Group 3	68 ±3	155 ±19

*Mean ± standard deviation.

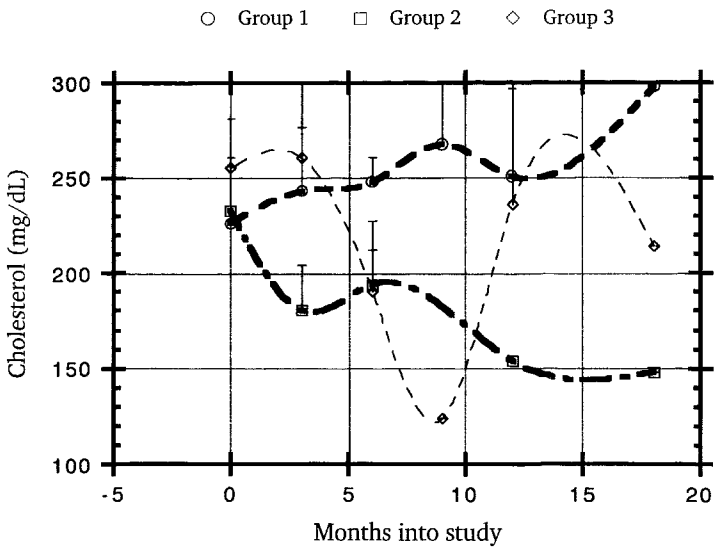

Figure 1. Results of changes in total cholesterol (TC) for each of the three treatment groups. Group 1 represents the control group and is noted by open circles and wide interrupted (— —) line. Subjects in this group showed an increase in TC during the study. Subjects in group 2 are represented by open squares and heavy interrupted line (— - —) line. There was an overall improvement seen in this group. Group 3 is represented by open diamonds and a thin (- - -) interrupted line. Subjects in group 3 demonstrated improvement while receiving dietary counseling. The standard deviation for each mean value is represented (T) by a vertical bar.

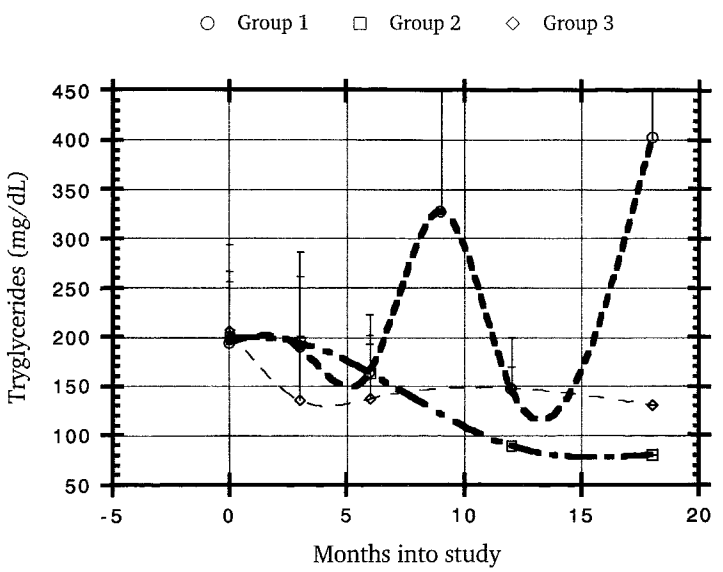

Figure 2. Results of Changes in Triglycerides (TG) for each of the three treatment groups. Group 1 represents the control group and is noted by open circles and wide interrupted (— —) line. Subjects in this group showed an increase in TG during the study. Subjects in group 2 are represented by open squares and heavy interrupted line (— - —) line. There was an overall reduction in TG seen for this group. Group 3 is represented by open diamonds and a thin (- - -) interrupted line. Subjects in group 3 demonstrated improvement while receiving dietary counseling, but no significant improvement once dietary instruction ceased. The standard deviation for each mean value is represented (T) by a vertical bar.

Results

Eleven men and 16 women enrolled in the study. Each individual's age and weight were recorded at entry and throughout the study. No significant differences in age or weight existed among the three groups of participants, as shown in Table III. Changes in weight did not correlate with changes in TC or TG values.

All three groups began at comparable levels of TC and TG, as graphically illustrated in Figures 1 and 2. The results of these changes are shown in Tables IVA and IVB respectively. Subjects in group 1 received no dietary counseling or hyperlipidemic medications and demonstrated a statistical increase in TC ($P \leq 0.001$) and a nonstatistical increase in TGs during the eighteen-month study.

Table IVA

Average Cholesterol Levels for Scheduled Visits

Month	Group 1	Group 2	Group 3
Baseline	226	233	255
3	243	180	260
4	248	194	190
12	251	154	236
18	298	148	214

Table IVB

Average Triglyceride Levels for Scheduled Visits

Month	Group 1	Group 2	Group 3
Baseline	194	200	206
3	189	194	136
6	164	163	138
12	147	89	148
18	402	80	131

Subjects in group 2, who received dietary counseling only, demonstrated a 36% decrease in TC and a 60% decrease in TG levels. This reduction was statistically significant for both TC ($P \leq 0.001$) and TGs ($P \leq 0.001$) by the end of the study.

Subjects in group 3 showed a statistical reduction for TC ($P \leq 0.05$), but not TGs ($P = NS$) during the first six months of the study while receiving dietary instructions. The improvement in cholesterol was lost by the end of the study ($P = NS$) despite continuation of hyperlipidemic medications. Some improvement in TGs persisted when compared with baseline values, but no statistical difference ($P = NS$) was detectable. This improvement in TGs was much less pronounced than that seen for patients in group 2 who received dietary counseling for eighteen months without concomitant hyperlipidemic medications.

Subjects in groups 2 ($P \leq 0.05$) and 3 ($P \leq 0.05$) demonstrated significant improvements in TC as compared with subjects in group 1. Improvement was also seen in TG levels when subjects in groups 2 and 3 were compared with the control group.

Discussion

Twenty-seven people > sixty-five years of age were placed into one of three treatment groups designed to determine the effects of dietary counseling, hyperlipidemic medication(s), and combined therapy on TC and TG levels. No difference as a result of age, weight, or sex was determined

between groups. Patients who received no dietary counseling or medication(s) demonstrated an increase in both TC and TG values.

Subjects receiving dietary counseling demonstrated a significant reduction in TC levels. Once dietary counseling was discontinued for patients in group 3, TC levels increased toward baseline values despite the continued use of medications to reduce cholesterol.

Improvements in TG levels were seen for subjects in groups 2 and 3 while they were receiving dietary instruction aimed at reducing TC and TG levels. Patients in group 3 showed no improvement in TGs once dietary instruction ceased despite the continued use of medications aimed at reducing TG levels. Subjects in group 2 continued to show improvement throughout the study.

Conclusion

Elderly patients are continuing to make up an increasing percentage of the population. It has been shown that elevated levels of TC and TG continue to place these patients at an increased risk for CAD. Given the results of this study, it is clear that elderly individuals can effectively control and significantly reduce their risk of heart disease by dietary modification of cholesterol and fat intake. Some additional improvement is seen with hyperlipidemic medications as long as dietary counseling and modification occurs, but the effect of medication is blunted or lost when patients stop following dietary guidelines.

Richard M. Fleming, M.D., F.A.C.A., F.I.C.A.
Director, Center for Clinical Cardiology
and Research
305 Martin Drive, North
Bellevue, NE 68005

References

1. Tucker CF, Catsulis C, Strong JP, et al: Regression of early cholesterol induced aortic lesions in rhesus monkeys. Am J Pathol 65:493-514, 1971.
2. Eggen DA, Strong JP, Newman WP, et al: Regression of diet induced fatty streaks in rhesus monkeys. Lab Invest 31:294-301, 1974.
3. Kokatnur MG, Malcom GT, Eggen DA, et al: Depletion of aortic free and ester cholesterol by dietary means in rhesus monkeys with fatty streaks. Atherosclerosis 21:195-203, 1975.
4. Strong JP: Reversibility of fatty streaks in rhesus monkeys. Primates Med 9:300-320, 1976.
5. Armstong ML, Megan MB: Arterial fibrous proteins in cynomolgus monkeys after atherogenic and regression diets. Circ Res 36:256-261, 1975.
6. Malinow MR, McLaughlin P, Papworth L, et al: A model for therapeutic intervention on established coronary atherosclerosis in a non human primate. Adv Exp Med Biol 67:3-31, 1976.
7. Vesselinovitch D, Wissler RW, Hughes R, et al: Reversal of advanced atherosclerosis in rhesus monkeys. Part I. Light-microscopic studies. Atherosclerosis 23:155-176, 1976.
8. Weber G, Fabbrini P, Resi L, et al: Regression of arteriosclerotic lesions in rhesus monkey aortas after regression diet. Scanning and transmission electron microscope observations of the endothelium. Atherosclerosis 26:535-547, 1977.
9. Chakravarti RN, Kumar BS, Nair CR, et al: Reversibility of cholesterol adrenaline-induced atherosclerosis in rhesus monkeys. Evaluation of safflower oil and low-fat low-calorie diet. Atherosclerosis 28:405-416, 1977.
10. Hollander W: Studies on the progression and regression of coronary and peripheral atherosclerosis in the cynomolgus monkey. Part I. Effects of dipyridamole and aspirin. Exp Mol Path 30:55-73, 1979.
11. Connor WE, Cerqueira MT, Connor RW, et al: The plasma lipids, lipoproteins and diet of the Tarahumara Indians of Mexico. Am J Clin Nutr 31:1131-1142, 1978.
12. McGill HC: The relationship of dietary cholesterol to serum cholesterol concentration and to atherosclerosis in man. Am J Clin Nutr 32:2664-2702, 1979.
13. Glueck CJ: Dietary fat and atherosclerosis. Am J Clin Nutr 32:2703-2711, 1979.

14. Simons LA: Interrelations of lipids and lipoproteins with coronary artery disease mortality in 19 countries. Am J Cardiol 57:5G-10G, 1986.
15. Dewar HA, Arthur JB, Ashby WR, et al: Trial of clofibrate in the treatment of ischaemic heart disease. Five-year study by a group of physicians of the Newcastle upon Tyne region. Br Med J 4:767-775, 1971.
16. Alstead S, Aitchison JD, Barr JB, et al: Ischaemic heart disease: A secondary prevention trial using clofibrate. Report by a research committee of the Scottish Society of Physicians. Br Med J 4:775-784, 1971.
17. The Coronary Drug Project Research Group: Clofibrate and niacin in coronary heart disease. JAMA 231:360-381, 1975.
18. Puska P, Virtamo J, Tuomilehto J, et al: Cardiovascular risk factor changes in a three-year follow-up of a cohort in connection with a community programme (the North Karelia Project). Acta Med Scand 204:381-388, 1978.
19. Kornitzer M, Backer GD, Dramaix M, et al: The Belgian Heart Disease Prevention Project. Modification of the coronary risk profile in an industrial population. Circulation 61:18-25, 1980.
20. Shekelle RB, Shryock AM, Paul O, et al: Diet, serum cholesterol, and death from coronary heart disease. The Western Electric Study. N Engl J Med 304:65-70, 1981.
21. Kjelsberg MO: Multiple Risk Factor Intervention Trial. Risk factor changes and mortality results. JAMA 248:1465-1477, 1982.
22. Lipids Research Clinics Program: The Lipid Research Clinics Coronary Primary Prevention Trial Results. I. Reduction in incidence of coronary heart disease. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA 251:351-374, 1984.
23. Goldbourt U, Holtzman E, Neufeld HN: Total and high density lipoprotein cholesterol in the serum and risk of mortality: Evidence of a threshold effect. Br Med J 290:1239-1243, 1985.
24. Miettinen TA, Huttunen JK, Naukkarinen V, et al: Multifactorial primary prevention of cardiovascular diseases in middle-aged men. Risk factor changes, incidence, and mortality. JAMA 254:2097-2102, 1985.
25. Brunner D, Weisbort J, Meshulam N, et al: Relation of serum total cholesterol and high-density lipoprotein cholesterol percentage to the incidence of definite coronary events: Twenty-year follow-up of the Donolo-Tel Aviv Prospective Coronary Artery Disease Study. Am J Cardiol 59:1271-1276, 1987.
26. Frick JH, Elo O, Haapa K: Helsinki Heart Study: Primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. N Engl J Med 317:1237-1245, 1987.
27. Carlson LA, Rosenhamer G: Reduction of mortality in the Stockholm Ischaemic Heart Disease Secondary Prevention Study by combined treatment with clofibrate and nicotinic acid. Acta Med Scand 223:405-418, 1988.
28. Assmann G, Schulte H, Munster DR: The Prospective Cardiovascular Munster (PROCAM) Study: Prevalence of hyperlipidemia in persons with hypertension and/or diabetes mellitus and the relationship to coronary heart disease. Am Heart J 116:1713-1724, 1988.
29. Alderman JD, Pasternak RC, Sacks FM, et al: Effect of a modified, well-tolerated niacin regimen on serum total cholesterol, high density lipoprotein cholesterol and the cholesterol to high density lipoprotein ratio. Am J Cardiol 64:725-729, 1989.
30. Cohn K, Sakai FJ, Langston MF: Effect of clofibrate on progression of coronary disease: A prospective angiographic study in man. 89:591-598, 1975.
31. Kuo PT, Hayase K, Kostis JB, et al: Use of combined diet and colestipol in long-term (7 to 7 and ½ years) treatment of patients with type II hyperlipoproteinemia. Circulation. 59:199-214, 1979.
32. Nash DT, Gensini G, Esente P: Effect of lipid-lowering therapy on the progression of coronary atherosclerosis assessed by scheduled repetitive coronary arteriography. Int J Cardiol 2:43-55, 1982.
33. Levy RI, Brensike JF, Epstein SE, et al: The influence of changes in lipid values induced by cholestyramine and diet on progression of coronary artery disease: Results of the NHLBI Type II Coronary Intervention Study. Circulation 69:325-337, 1984.
34. Nikkila EA, Viikinkoski P, Valle M, et al: Prevention of progression of coronary atherosclerosis by treatment of hyperlipidaemia: A seven year prospective angiographic study. Br Med J 289:220-223, 1984.
35. Arntzenius AC, Kromhout D, Barth JD, et al: Lipoproteins and the progression of coronary atherosclerosis. The Leiden Intervention Trial. N Engl J Med 312:805-811, 1985.
36. Blankenhorn DH, Nessim SA, Johnson RL, et al: Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. JAMA 257:3233-3240, 1987.
37. Blankenhorn DH, Johnson RL, Nessim SA, et al: The Cholesterol Lowering Atherosclerosis Study (CLAS): Design, methods, and baseline results. Controlled Clinical Trails 8:354-387, 1987.
38. Ornish D, Brown SE, Scherwitz LW, et al: Can lifestyle changes reverse coronary heart disease? Lancet 336:129-133, 1990.
39. Fleming RM, Rater D, Ketchum K: Reducing cholesterol and triglycerides in the elderly patient by diet alone. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Sessions of the AHA. Published Sept. 1993, p 127.
40. Fleming RM, Rater D: Dietary changes without medication can equally reduce cholesterol in both the

young and older patient. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Sessions of the AHA. Published Sept. 1993, p 128.

41. Fleming RM, Rater D, Ketchum K: Studying the effect of medications on cholesterol and triglycerides in subjects not receiving dietary counseling. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Sessions of the AHA. Published Sept. 1993 p 128.
42. Fleming RM, Ketchum K: Dietary reinforcement is an integral component of cholesterol reduction. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Sessions of the AHA. Published Sept. 1993, p 128.
43. Benfante R, Reed D: Is elevated serum cholesterol level a risk factor for coronary heart disease in the elderly? JAMA 263:393, 1990.
44. Shipley MJ, Pocock SJ, Marmot MG: Does plasma cholesterol concentration predict mortality from coronary heart disease in elderly people? 18 year follow up in Whitehall Study. Br Med J 303:89, 1991.
45. Fleming RM, Rose CH, Feldmann KM. Comparing a high dose dipyridamole SPECT imaging protocol with dobutamine and exercise stress testing protocols. Angiology 46:547-556, 1995.