

Lipoprotein levels in elderly patients with asthma

Paul L. Enright, MD,^a Elliott C. Lasser, MD,^b Beverly J. Ward, MS,^c and Russell P. Tracy, MD^d for the Cardiovascular Health Study Research Group Tucson, Ariz., San Diego, Calif., Seattle, Wash., and Colchester, Vt.

There is some evidence that persons with asthma have a lower risk of atherosclerotic heart disease. In one study, fewer calcified plaques were seen in the abdominal aorta and iliac arteries of 27 patients with asthma (mean age, 64 years) compared with a control group.¹ We hypothesized that elderly persons with asthma might therefore have lipoprotein profiles consistent with a reduced risk of atherosclerosis. The goal of this report is to explore the associations of lipoprotein levels with reported asthma in an elderly cohort.

METHODS

The Cardiovascular Health Study (CHS) is a prospective study of a general population sample designed to study the epidemiology and risk factors associated with cardiovascular disease in the elderly. The 1989-1990 CHS baseline examination provided comprehensive measures of cardiovascular disease and risk factors from a representative sample of 5201 elderly persons from four U.S. communities, as well as spirometry and standardized questions regarding asthma symptoms, a physician diagnosis of asthma, and therapy. Participants in the CHS were selected by using a Medicare eligibility list of persons aged 65 and older, provided by the U.S. Health Care Financing Administration. The CHS design and recruitment are described in detail elsewhere.² The subgroup of patients with asthma at the baseline examination was defined as those who reported a physician-confirmed history of asthma (ATS-DLD-78 question no. 20C). Examination components included spirometry, random-zero seated blood pressure, a physical examination, resting 12-lead electrocardiogram, coagulation factors, blood chemistry, and lipoprotein analyses after 12

Abbreviations used

CHS: Cardiovascular Health Study
HDL-C: High-density lipoprotein-cholesterol
LDL-C: Low-density lipoprotein-cholesterol

hours of fasting.³ Use of medications was assessed by inventory.

After excluding the 276 participants who were taking lipid-lowering drugs, we determined mean blood levels of total cholesterol, high-density lipoprotein-cholesterol (HDL-C), calculated low-density lipoprotein-cholesterol (LDL-C), fibrinogen, factor VII, and factor VIII in participants stratified by gender, smoking status, and asthma diagnosis. We performed *t* tests for each of these blood levels to test the hypothesis that they were the same for asthmatic and nonasthmatic subjects in each stratum.

To investigate the association of asthma with HDL-C, we then constructed gender-specific linear regression models with HDL-C as the dependent variable. We first offered for entry 16 variables previously found to be associated with HDL-C levels, including alcohol intake, estrogen use in women, body mass index, waist and hip size, age, clinic location, race, smoking status, diabetes, fasting glucose level, weekly exercise level, socioeconomic status, and the use of diuretics. In a second step, we then offered for entry into the models five indices of asthma: a diagnosis of asthma, an asthma severity score (0 to 6 with use of asthma medications or moderate to severe obstruction on spirometry giving a higher score), asthma duration (in years), current use of inhaled corticosteroids, and current use of oral prednisone. We did not attempt to correct for the possible effects of multiple comparisons, collinearity, and residual confounding in these analyses.

RESULTS

A total of 5201 participants (mean age, 73 years) were enrolled from May 1989 to June 1990 in the CHS; 43% were men, and 5% were nonwhite. Twelve percent were current cigarette smokers, and 42% were former smokers. Of the nonsmokers, 22% of the women and 29% of the men had a

From ^athe University of Arizona, Tucson; ^bUniversity of California, San Diego; ^cUniversity of Washington, Seattle; and ^dUniversity of Vermont, Colchester

Supported by National Heart, Lung and Blood Institute contract N01-87079.

Reprint requests: Richard Kronmal, PhD, Data Coordinating Center, 1501 Fourth Ave., Suite 2105, Seattle, WA 98101.

J Allergy Clin Immunol 1996;98:467-9.

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0091-6749/96 \$5.00 + 0 1/54/73131

TABLE I. Independent correlates of HDL-C (mg/dl)

Variable	Coefficient	p Value
Women only ($n = 2488$, adjusted $R^2 = 22\%$)		
Estrogen use	+10.0	<0.00001
Alcohol intake	+0.593	<0.00001
BMI (kg/m^2)	-0.715	<0.00001
Waist size (cm)	-0.180	<0.00001
Hip size (cm)	+0.228	0.0001
Non-white race	+6.68	<0.00001
Diabetes diagnosis	-2.92	0.0008
Glucose intolerance	-2.49	0.0002
Fasting glucose	-0.039	0.0001
Current smoking	-3.12	0.0002
Higher income level	+0.436	0.003
Asthma diagnosis	+3.00	0.010
Asthma severity		NS
Oral prednisone		NS
Asthma duration		NS
Inhaled steroids		NS
Men only ($n = 1981$, adjusted $R^2 = 18\%$)		
Alcohol intake	+0.428	<0.00001
Non-white race	+8.00	<0.00001
Waist size (cm)	-0.141	0.0049
BMI (kg/m^2)	-0.326	0.018
Age (yr)	+0.157	0.0010
Diabetes diagnosis	-1.90	0.0026
Exercise/wk	+0.444	0.0003
Diuretic use	-1.82	0.0041
Higher income level	+0.495	0.0009
Clinic	0.658	0.0050
Asthma diagnosis	+2.56	0.027
Asthma severity	+0.483	0.0008
Oral prednisone	+4.76	0.0002
Asthma duration		NS
Inhaled steroids		NS

Participants taking lipid-lowering drugs were excluded. Exercise per week was estimated from self-reported activities with units $\text{Kcal}/\text{wk} \times 1000$.

BMI, Body mass index; NS, not significant.

history of coronary heart disease (myocardial infarction, angina, or bypass surgery), and 24% of the women and 36% of the men had major electrocardiographic abnormalities.⁴

Six percent (309) of the participants reported a history of asthma, and 59% of these were women. One third of those with asthma reported a concurrent diagnosis of chronic bronchitis or emphysema. Of those with asthma, 30% were currently taking either a theophylline preparation or an inhaled sympathomimetic medication; 13.6% were using an inhaled corticosteroid, and 10.4% were taking oral prednisone.

In the bivariate analyses, mean HDL-C and

fibrinogen levels were significantly higher in participants with asthma when compared with the others: HDL-C, 57.1 mg/dl versus 53.8 ($p = 0.002$); fibrinogen, 332.1 units versus 319.6 ($p = 0.007$). Mean factor VII, factor VIII, LDL-C, and total cholesterol levels were not significantly different in those with asthma compared with the others.

Mean factor VIII, fibrinogen, and HDL-C levels were significantly higher (and LDL-C levels were lower) in the 185 participants taking oral steroids (prednisone, for any reason, as assessed by medication inventory): HDL-C, 57.8 versus 53.8 ($p = 0.005$); LDL-C, 127.3 versus 132.7 ($p = 0.042$); fibrinogen, 335.9 versus 319.9 ($p = 0.001$); factor VIII, 132.9 versus 121.3 ($p < 0.0001$). Mean HDL-C was also significantly higher in the 116 participants currently using inhaled corticosteroids (presumably only for treatment of asthma): 59.7 versus 53.8 ($p < 0.0001$); and factor VIII was lower: 114.6 versus 121.9 ($p = 0.014$).

Variables that were independently associated with HDL-C levels in the gender-specific linear regression models are shown in Table I. Estrogen use and current smoking in women, alcohol intake, race or ethnicity, measures of habitus, a history of diabetes, fasting glucose level (in women), socioeconomic indicators, and exercise level in men were all significant predictors of HDL-C level. After correcting for these covariates, a diagnosis of asthma also entered the models for men and women ($p = 0.027$ and 0.010 , respectively). Participants with asthma had a mean HDL-C value of 3 mg/dl higher than the others. The asthma severity score and the use of oral corticosteroids also entered the model for men only ($p < 0.001$). Neither the duration of asthma nor the use of inhaled corticosteroids for treatment of asthma was an independent predictor of HDL-C in models including asthma diagnosis.

DISCUSSION

The association of asthma with high HDL-C levels is surprising because chronic inflammatory disease in other organ systems is associated with lower HDL-C levels. A likely explanation is that corticosteroid therapy is associated with high HDL-C levels. Prednisone use was indeed a significant independent predictor of HDL-C levels in elderly men: mean HDL-C levels were 4.7 mg/dl higher in asthmatic men taking prednisone, after correcting for other factors. However, this was not true in women, and the use of *inhaled* steroids for treatment of asthma was not independently associated with HDL-C levels in men or women.

Long-term administration of corticosteroids may have different effects on lipid profiles than short-term therapy. In one study, patients taking a short-term tapering oral prednisone burst for treatment of rheumatic disease demonstrated significant increases in total cholesterol and HDL-C, 1 month later, but no changes in triglycerides or LDL-C.⁵ The association of higher HDL-C levels in elderly CHS participants with asthma, independent of corticosteroid therapy, suggests that other mechanisms exist. We also found evidence for a dose-response relationship in elderly men: those with more severe asthma (more frequent attacks or more severe airway obstruction) had significantly higher HDL-C levels than those who were currently free of symptoms. A possible explanation is that some CHS participants with asthma had recently taken a short course of prednisone (raising HDL-C) but were not *currently* taking it at the time of their clinic visit when medication use was ascer-

tained. Another theory is that the increased work of breathing, which occurs because of bronchospasm in asthma, is a type of regular exercise that raises HDL-C.

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Anaphylaxis caused by linseed (flaxseed) intake

Lidia Alonso, MD, María Luisa Marcos, MD, Juan Guillermo Blanco, MD,
Jose Antonio Navarro, MD, Sonsoles Juste, MD,
María del Mar Garcés, MD, Reyes Pérez, MD, and
Pedro Jaime Carretero, MD *Burgos, Spain*

Flax is a plant that belongs to the Linaceae family. It comes from Central Asia, and it has been cultivated for 5000 years. Egyptians, Hebrews, Greeks, and Romans used the seeds as food and the fibers to weave clothes, sails, and other items. Nowadays, linseed oil is extracted from this plant, and this oil is mainly used in the preparation of varnish, paint, linoleum, and soap. Linseed oil has recently been used as a laxative.¹ We report the case of a 40-year-old woman who had an anaphylactic reaction after the intake of linseed oil.

From Sección Alergología, Hospital General Yagüe, Burgos, Spain.

Reprint requests: Lidia Alonso, MD, Sección Alergología, Hospital General Yagüe, E-09005 Burgos, Spain.

J Allergy Clin Immunol 1996;98:469-70

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0091-6749/96 \$5.00 + 0 1/54/73138

Abbreviation used

SDS-PAGE: Sodium dodecylsulfate-polyacrylamide gel electrophoresis

CASE REPORT

A 40-year-old woman with no personal or familial history of atopy took linseed oil as a laxative. Ten minutes after the intake of the first spoonful, she experienced ocular pruritus and weeping, followed by strong palmar pruritus and generalized urticaria, nausea, and vomiting. She was treated in the emergency department, and the symptoms were promptly reversed.

Skin prick tests were done with a battery of commercially available allergens (Laboratory Ifidesa-Aristegui, Bilbao, Spain), which included: *Dermatophagoides ptero-*