Insufficient Treatment of Hypercholesterolemia among Patients Hospitalized with Chest Pain

ERIC E. HOWELL, M.D., SCOTT M. WRIGHT, M.D., DAVID E. BUSH, M.D., NISHA CHANDRA-STROBOS, M.D., CHARLES A. HENRIKSON, M.D.

Department of Medicine, Johns Hopkins Medical Institutions, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Summary

Background: Although morbidity and mortality from coronary artery disease can be improved with a variety of pharmacologic interventions, many patients remain undertreated.

Hypothesis: This study sought to assess whether hospitalization for possible coronary artery disease would prompt initiation of appropriate lipid-lowering therapy.

Methods: This prospective, observational study was conducted on consecutive patients with active chest pain admitted to the Emergency Department of the hospital for suspected myocardial ischemia. Elevated cholesterol, defined as low-density lipoprotein (LDL), was > 100 mg/dl with a prior history or a new diagnosis of coronary artery disease, or an LDL > 130 mg/dl without known coronary artery disease. Data were recorded at the time of admission, discharge, and at 4-month follow-up.

Results: Of the patients with hyperlipidemia, 65% men and 55% women were on medication at the time of admission ($p = 0.30$), while at discharge, 79% men and 60% women were on treatment ($p = 0.002$), with similar rates of treatment at 4-month follow-up ($p = 0.030$). At discharge, two variables were independently associated with patients receiving lipid-lowering therapy: age ≥ 65 years (odds ratio = 2.3; 95% confidence interval 1.2–4.5) and male gender (2.7; 1.5–5.0).

Conclusions: In patients hospitalized with chest pain, particularly in women, the initiation of treatment of hyperlipidemia frequently does not happen. This oversight repre-

sents a lost opportunity for making an impact on the health of this population.

Key words: hyperlipidemia, hospital medicine

Introduction

Not all populations with coronary artery disease (CAD) have similar outcomes: women, minorities, and the elderly have been shown to have substantially worse outcomes than men, Caucasians, and younger patients.^{1–3} However, even in these high-risk populations, it is now well established that lipid-lowering therapy affords major benefit with consequent primary and secondary prevention of CAD.^{4,5} Recent studies also demonstrate that despite these compelling data, many high-risk patients are undertreated or not treated at all.^{6–10}

For most patients, decisions about medical management occur in the outpatient setting. However, because hospitalizations represent significant events in any patient's medical history, strategies that intervene to promote health and reduce risk at the time of hospitalization can be invaluable. This principle is supported by several studies that substantiate that patients are more likely to meet treatment guidelines for hyperlipidemia if prescribed the medication at the time of discharge.^{10–12} This study was conducted to assess whether patients who had active chest pain in the Emergency Department and were admitted to the hospital for "rule out myocardial infarction (MI)" would prompt the initiation of lipid-lowering therapy for patients in whom this was indicated prior to discharge.

Methods

Population

This study was performed on the population in the Study of Nitroglycerin and Chest Pain (SNAP), which has been described previously.¹³ Patients admitted to the Emergency Department with chest pain at rest and subsequently admitted to the hospital with the preliminary diagnosis of "rule out MI" or "chest pain" during the study period were eligible for inclusion. This study was approved by the Johns Hopkins' institutional review board.

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Address for reprints:

Scott Wright, M.D.
Johns Hopkins Bayview Medical Center
Division of General Internal Medicine
4940 Eastern Avenue
Baltimore, MD 21224, USA
e-mail: smwright@jhmi.edu

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Treatment of Hypercholesterolemia

Based on the results of the West of Scotland Coronary Prevention Study,¹⁴ the Heart Protection Study,¹⁵ and the Adult Treatment Panel (ATP) III guidelines,¹⁶ elevated cholesterol for the present study was defined as low-density lipoprotein (LDL) > 100 mg/dl in patients with a prior history or a new diagnosis of CAD, or LDL > 130 mg/dl in patients without known CAD. In addition, elevated cholesterol could be self reported.^{14, 15} Patients in our study who met these definitions for hypercholesterolemia were considered to be appropriate candidates for lipid-lowering therapy, which was defined as any medication indicated for the treatment of hypercholesterolemia.

Follow-Up

Trained study investigators conducted telephone interviews with patients at approximately 4 months following the index hospitalization. Patient-reported hospitalization and testing within our hospital system were confirmed by review of electronic records. The Social Security death index was used to confirm all patient deaths and to determine the vital status of all patients who were lost to follow-up.¹³

Data Analysis

All data were collected on optically scannable forms that were read with TELEform Elite software (Cardiff Software, Vista, California). Data were compiled into a Microsoft Access (Redmond, Washington) database and analyzed using Systat (Richmond, California). Data are expressed as means ($\pm$ standard deviation) and percentages. Testing for significance was accomplished using *t*-tests and chi-square analyses.

Among the hospitalized patients with hyperlipidemia, bivariate analyses were used to characterize the association of individual attributes (such as age, gender, race, established CAD, and smoking status) with the likelihood of taking lipid-lowering medications. Logistic regression models were then used to identify independent associations between these individual variables and lipid-lowering medication use. The modeling included only variables that were statistically significant-

ly associated with the dependent variable (lipid-lowering medication) in the bivariate analysis at $p < 0.1$. Variables included in the models were checked for collinearity.

Results

Demographics

This study recruited 459 patients; 249 (54%) were women and 370 (81%) were Caucasians. As shown in Table 1, female participants were older and less likely to have a history of CAD or to be smokers (all $p < 0.05$). African-American participants were younger and less likely to have a prior history of CAD (both $p < 0.05$).

Of the 459 patients enrolled, 4-month follow-up information was obtained for 389 participants (84.7%); follow-up has been previously described.¹³

No significant differences were noted in the prescribing patterns of aspirin, blood pressure lowering, and diabetic medications at discharge when the data were compared by gender, race, or cardiac risk factors (all $p > 0.05$).

Treatment of Hyperlipidemia

Of the 459 patients enrolled, 52.1% met criteria for hyperlipidemia on admission. Men and women had similar rates of hypercholesterolemia (55.7 vs. 49.0%, respectively, $p = 0.15$). Of the patients with hyperlipidemia, 58% were on treatment for lipids on admission, compared with 69% at the time of discharge and 67% at follow-up. Of the patients who were on treatment at follow-up (122/137), 89% were receiving lipid-lowering medicine at the time of hospital discharge.

Rate of treatment by gender: At the time of admission, treatment of hypercholesterolemia with lipid-lowering medication was similar between men and women (61.5 vs. 54.9%, $p = 0.3$). At the time of discharge, treatment of hyperlipidemia in men increased significantly to 78.6% (+17.1%), while treatment for women increased only by 4.9 to 59.8% ($p = 0.002$). This treatment disparity continued at 4-month follow-up, with a higher proportion of men than women still taking lipid-lowering therapy (74.2 vs. 59.6%, $p = 0.03$).

TABLE 1 Characteristics of the 459 patients admitted to the hospital for chest pain or to rule out myocardial infarction

Characteristic	Men n = 210	Women n = 249	Caucasian n = 370	African American n = 83
Age, mean $\pm$ SD	55.3 $\pm$ 14.9	61.4 $\pm$ 15.6 ^a	60.0 $\pm$ 15.7	53.4 $\pm$ 14.7 ^b
Hyperlipidemia, n (%)	117 (55.7)	122 (49.0)	196 (53.0)	38 (45.8)
Coronary artery disease, n (%)	92 (43.8)	79 (31.7) ^a	148 (40.0)	21 (25.3) ^b
Hypertension, n (%)	123 (58.6)	152 (61.0)	217 (58.6)	56 (67.5)
Diabetes mellitus, n (%)	45 (21.4)	66 (26.5)	86 (23.2)	25 (30.1)
Smoking, n (%)	108 (51.4)	92 (36.9) ^a	167 (45.1)	32 (39.6)

^a $p < 0.05$ for comparison between men and women.

^b $p < 0.05$ for comparison between Caucasians and African Americans.

Abbreviation: SD = standard deviation.

Rate of treatment by race: When analyzed by race, Caucasian and African-American patients had similar rates of hyperlipidemia: 53.0 and 45.8%, respectively, $p = 0.12$ (Table I). These patients were also equally likely to be treated for hyperlipidemia at the time of admission, (59.7 vs. 50.0%, $p = 0.27$). At discharge, treatment for hyperlipidemia increased by about 10% in both groups, to 70.4% in Caucasians and to 60.5% in African Americans, $p = 0.23$. The rates of treatment between the two groups remained stable at 4 months (67.1 vs. 59.4%, $p = 0.40$) compared with those at the time of discharge.

Rate of treatment by cardiac risk factors: Of the patients with hyperlipidemia in our study ($n = 239$), 65.3% had two or more other cardiac risk factors, 30.1% had one other cardiac risk factor, and only 4.6% had no other cardiac risk factors. Patients with two or more additional risk factors were more likely to be on medication for hyperlipidemia on admission, at discharge, and at 4-month follow-up by 24.5, 20.9, and 12.3%, respectively, compared with patients with fewer risk factors (Table II). The likelihood of having hyperlipidemia and two or more additional cardiac risk factors (high risk) was comparable between men and women (65.8 vs. 64.7% $p = 0.864$). These high-risk men were more likely than their female counterparts to receive lipid-lowering treatment on admission (72.7% men vs. 60.8% women, $p = 0.113$), although the difference did not achieve statistical significance. The discrepancy in treatment between the genders widened and achieved statistical significance at discharge, at which time a greater percentage of men than their female counterparts were receiving lipid-lowering therapy (85.7 vs. 67.1%, $p = 0.006$). The difference was still present at 4-month follow-up (82.3 vs. 60.3%, $p = 0.01$).

Even when using a more conservative definition of hyperlipidemia—LDL > 160 for patients without multiple cardiac risk factors—our data show that women and men are treated similarly on hospital admission (63.7 men vs. 61.5% women, $p = 0.73$). However, upon discharge the treatment rate of men increases significantly compared with that of women (80.5 vs. 67.0%, $p = 0.022$). Although it was not statistically significant, at 4-month follow-up men were more likely to be treated with a lipid-lowering agent (men 75.5 vs. women 65.2%, $p = 0.124$).

Using only laboratory-proven hyperlipidemia using serum testing, and excluding patients with a self-reported diagnosis

of hyperlipidemia, men and women were treated similarly for hyperlipidemia on hospital admission (men 26.0 vs. women 24.5%, $p = 0.86$), but men were more likely to be discharged on lipid-lowering therapy (men 66.0 vs. women 38.8%, $p = 0.007$). At 4-month follow-up, men remained on lipid-lowering therapy more often than women (66.6 vs. 44.7%, $p = 0.053$).

Multivariate analyses: At discharge, the two variables that were independently associated with patients on lipid-lowering therapy were age ≥ 65 years (odds ratio = 2.3; 95% confidence interval 1.2–4.5) and male gender (2.7; 1.5–5.0).

At 4-month follow-up, the only variable independently associated with lipid-lowering therapy was a personal history of CAD (3.1; 1.6–5.9). At this time, neither gender (1.8; 0.9–3.3) nor older age (1.0; 0.5–2.0) remained statistically significant.

Discussion

Modification of reversible risk factors including tobacco use, hypertension, and hypercholesterolemia has been associated with improved outcomes, both as primary and secondary therapeutic strategies.¹⁷ Treatment of hyperlipidemia has been a recent area of major interest, with increasing evidence suggesting that lowering LDL is effective in both primary and secondary prevention of CAD^{4, 5, 10, 12} and is cost effective.¹⁸ This study's data show that usage of lipid-lowering therapy is suboptimal, even among high-risk patients who are admitted to the hospital with chest pain. These findings are consistent with the EUROpean Action on Secondary Prevention by Intervention to Reduce Events (EUROASPIRE) and EUROASPIRE II studies, which focused on European patients with known CAD, in which more than one-half of patients requiring lipid therapy were either undertreated or not treated at all.^{6, 7} In our study, women with hyperlipidemia were discharged on lipid-lowering medication less frequently than their male counterparts. This finding remained consistent even when the data were analyzed with potential confounders accounted for, such as more conservative LDL goals for low-risk patients and an analysis excluding those patients who self reported the diagnosis of hyperlipidemia.

TABLE II Treatment of hypercholesterolemia at the time of admission, on discharge, and at 4-month follow-up based on cardiac risk factors other than elevated low-density lipoprotein cholesterol

	n	Treatment rate on admission n (%)	Treatment rate on discharge n (%)	Treatment rate at 4-month follow-up n (%)
Hypercholesterolemia and < 2 other cardiac risk factors	83	35 (42.2)	46 (55.4)	43/73 (58.9)
Hypercholesterolemia and ≥ 2 other cardiac risk factors	156	104 (66.7) ^a	119 (76.3) ^a	94/132 (71.2)
Men with hypercholesterolemia and ≥ 2 other cardiac risk factors	77	56 (72.7)	66 (85.7)	53/64 (82.3)
Women with hypercholesterolemia and ≥ 2 other cardiac risk factors	79	48 (60.8)	53 (67.1) ^b	40/63 (60.3) ^b

^a $p < 0.05$ for comparison between patients with < 2 and ≥ 2 coronary risk factors.

^b $p < 0.05$ for comparison between men and women with ≥ 2 coronary risk factors.

Decisions about whether to initiate lipid-lowering therapies are sometimes left to the primary care providers (following discharge) because of the established doctor-patient relationships and because it will be the responsibility of these physicians to monitor the patients for side effects and titrate dosing. However, our 4-month follow-up data suggest that patients who leave the hospital without lipid-lowering treatment do not get started on such therapy. Patients in whom these medications are initiated continue to take them. Such findings are consistent with previous studies^{10, 11} and highlight the importance of seizing the therapeutic opportunity among inpatients being evaluated for suspected myocardial ischemia.

Study Limitations

Several limitations of this study should be considered. First, as with all observational studies, the associations noted cannot prove causality. Second, again due to the observational nature of the study, it was not possible to determine the number of patients who were able to achieve LDL goals on treatment. Third, the study was conducted at a single institution; nonetheless, the care of these patients occurred in a wide variety of clinical settings staffed by a diverse spectrum of physicians and practitioners. Fourth, the predominance of Caucasian patients limited the study's power to detect differences between patients of different races. Fifth, the decision about whether to treat hyperlipidemia is complex and may involve issues such as insurance status. Our analyses did not include such factors. Sixth, we relied on self reporting of cardiac risk factors in addition to chart audits. Finally, continuous variables (such as blood pressure and cholesterol level) were treated as though they were dichotomous (present or absent) both for ease of analysis and because this is how they are considered in practice guidelines.¹⁶

Conclusion

This study confirms that hypercholesterolemia is a common problem in a general population admitted with chest pain to the hospital. Despite the established benefits of lipid-lowering treatment in primary and secondary prevention, such therapy is initiated less frequently than it should be, particularly in women. The decision not to initiate therapy, whether calculated or an oversight, represents a lost therapeutic opportunity.

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