

Are Statin Medications Associated with Lower Urinary Tract Symptoms in Men and Women? Results from the Boston Area Community Health (BACH) Survey

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PURPOSE: Statins may ameliorate lower urinary tract symptoms (LUTS) through anti-inflammatory or other pathways. We investigated the association between statin use and storage, voiding, and overall LUTS symptoms.

METHODS: The Boston Area Community Health Survey is an epidemiologic study of Boston, MA residents (2301 men; 3202 women) 30–79 years of age. LUTS, voiding, and storage symptoms were ascertained through an interviewer-administered questionnaire and defined as scores of greater than or equal to 8, greater than or equal to 5, and greater than or equal to 4, respectively, on relevant components of the American Urologic Association Symptom Index. Participants were included if they had a history of provider-diagnosed high cholesterol or recently used statin medications ($n = 1346$). Associations were estimated using odds ratios (ORs) and 95% confidence intervals (CI) from multivariate logistic regression.

RESULTS: In multivariate models, statin use had no association with LUTS (OR = 1.03, 95% CI: 0.70, 1.51) among women. No associations were observed for any LUTS among younger (<60) men, but among older (60+) men, we observed significant inverse associations for voiding (OR = 0.23, 95% CI: 0.08, 0.66), storage (OR = 0.24, 95% CI: 0.11, 0.56), and overall LUTS (OR = 0.15, 95% CI: 0.05, 0.44).

CONCLUSIONS: Our results suggest that use of statins is associated with a lower prevalence of urologic symptoms among older men but not among women or younger men.

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KEY WORDS: Urination Disorders, Statins, HMG-CoA, Epidemiology.

INTRODUCTION

Lipid regulators including statins were the most widely-sold prescription drugs in the United States in 2008, and are indicated for long-term use (1, 2). As such, their physiologic effects beyond their stated indication deserve research attention. Statins are hypothesized to improve kidney function and to slow the progression of chronic kidney disease as reflected in ongoing clinical trials, such as the Lipid-Lowering and Onset of Renal Disease Trial (3). The beneficial effects of statins may be through lipid-lowering or directly through anti-inflammatory effects on the kidney (3). An anti-inflammatory pathway is also of interest in the pathophysiology of lower urinary tract symptoms (LUTS) (4). Statins are hypothesized to affect smooth muscle (5), which could have beneficial effects on bladder fibrosis (6) and improve blood flow to the bladder (7). In the Boston Area Community Health (BACH) Survey, we observed a strong

inverse association (odds ratio [OR] = 0.24, 95% confidence interval [CI]: 0.08, 0.76) among women for painful bladder syndrome among users of statins versus nonusers (8). Atorvastatin and symptoms of LUTS have been examined among men in a clinical trial, but use was not found to improve existing lower urinary tract symptoms considering the International Prostate Symptom Score (IPSS), and did not improve other outcomes related to benign prostatic hyperplasia (9). To our knowledge, the relationship between statin medications and LUTS has not previously been considered in women. In this analysis, our objectives were to consider the symptomatic experience of LUTS among those on lipid-lowering treatments (compared to those with a history of high cholesterol, not currently drug-treated) in a population-based epidemiologic study of men and women, with separate considerations of voiding and storage symptoms.

MATERIALS AND METHODS

Study Design and Data Collection

The BACH Survey is supported by the U.S. National Institutes of Health (National Institute of Diabetes and Digestive and Kidney Diseases) and is a population-based,

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Selected Abbreviations and Acronyms

AUA-SI = American Urologic Association Symptom Index
BACH = Boston Area Community Health Survey
BMI = body mass index
BPH = benign prostatic hyperplasia
CI = 95% confidence interval
IPSS = International Prostate Symptom Score
LDL = low density lipoprotein
LLM = lipid-lowering medication
LUTS = lower urinary tract symptoms
ORs = odds ratios
SE = standard error
SES = socioeconomic status

epidemiologic cohort study conducted among 5503 men and women aged 30–79 residing in Boston, Massachusetts. A multistage, stratified cluster sampling design was used to recruit approximately equal numbers of persons in prespecified groups defined according to age (30–39, 40–49, 50–59, 60–79), race and ethnic groups (black, Hispanic, white), and gender. This analysis was cross-sectional using baseline data collected between April 2002 and June 2005 during a 2-hour, in-person interview conducted by a trained, bilingual interviewer after acquisition of written informed consent. Interviews for 63.3% of eligible persons were completed, with a resulting study population of 2301 men and 3202 women comprised of 1767 black participants, 1877 Hispanic participants and 1859 white participants. A nonfasting venous blood sample (20 ml) was collected as close to awakening as possible. All protocols and procedures were approved by the Institutional Review Board of New England Research Institutes. Further details of the study design and procedures are available (10).

Urologic Symptoms and Cholesterol Measures

LUTS were defined using the American Urologic Association Symptom Index (AUA-SI, equivalent to the IPSS scale) that measures seven urologic symptoms (11). Higher scores indicate more symptoms (score range, 0–35). We defined the presence of LUTS as a score of 8 or more, corresponding to the presence of moderate to severe symptoms, with further stratification by voiding (obstructive) symptoms and storage (irritative) symptoms. Consistent with a prior study (12), our operational definition for the presence of storage symptoms was a score of 4 or higher (possible range, 0–15) for the three relevant questions (frequency, urgency, nocturia). This cutpoint corresponds with the convention of using 8+ on the full AUA-SI scale to indicate “moderate and higher.” A subscale of voiding symptoms was created from the four symptom-specific questions (possible range, 0–20) for questions related to incomplete emptying, intermittency, weak stream, and hesitancy, with a cutpoint of 5 or higher to create a dichotomous

variable to indicate the presence of “moderate and higher” voiding symptoms.

To date, cholesterol measurements in the BACH Survey have been conducted on 1899 (82.5%) of 2301 men who donated a blood sample, but measurements are not yet conducted on 1872 women donors. As such, we used a self-report of health care provider diagnosis of high cholesterol in our analyses.

Medication Use

BACH participants were asked to gather all medications used in the past 4 weeks for label recording by the interviewer. In addition, participants were asked whether they were taking drugs for specific indications, such as “any medications for cholesterol or fats in your blood?” Medication labels and/or responses were coded using the Slone Drug Dictionary (13), which links medications to their components and classifies them using a modification of the American Hospital Formulary Service Drug Pharmacologic Therapeutic Classification System (14). We first considered the prevalence of use of any prescription antilipemic (including statins, fibric acid derivatives, bile acid sequestrants, niacin, and ezetimibe) as use of lipid-lowering medications (LLM). As the vast majority of these (>90%) were statins, the analyses presented in this study are confined to persons who used statins only versus persons who did not use any LLM.

Covariates

Race/ethnic groups were self-identified and were considered to measure health disparities. A socioeconomic status (SES) variable was constructed as a function of standardized income and education variables for the Northeastern United States and reclassified into low, middle, and high (15). Depressive symptoms were considered present among participants with at least five of eight symptoms on the abridged Center for Epidemiologic Studies Depression Scale (16). Other comorbidities were based on the query, “Have you ever been told by a health care provider that you have or had...?” A composite yes/no variable for cardiac disease was made from any report of myocardial infarction, angina, congestive heart failure, and coronary artery bypass or graft surgery. Similarly for vascular disease, a composite yes/no variable was made from a history of pulmonary embolism, deep vein thrombosis, carotid artery surgery, Raynaud’s disease, peripheral vascular disease, intermittent claudication, aortic aneurysm, or surgery or angioplasty for arterial disease of the leg. Body mass index (BMI) was calculated from interviewer-measured weight and height. The mean of two interviewer-measured blood pressure values were used to define a case of measured hypertension using the cutpoints in the Seventh Report of the Joint National

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