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Comparative Effectiveness of Angiotensin-Converting Enzyme Inhibitor-Based Treatment on Cardiovascular Outcomes in Hypertensive Blacks Versus Whites

Gbenga Ogedegbe, MD, MPH,* Nirav R. Shah, MD, MPH,† Christopher Phillips, MD, MPH,‡ Keith Goldfeld, DrPH,* Jason Roy, PhD,§ Yu Guo, MA,‖ Joyce Gyamfi, MS,* Christopher Torgersen, MBA,* Louis Capponi, MD,¶# Sripal Bangalore, MD‖

ABSTRACT

BACKGROUND Clinical trial evidence suggests poorer outcomes in blacks compared with whites when treated with an angiotensin-converting enzyme (ACE) inhibitor–based regimen, but this has not been evaluated in clinical practice.

OBJECTIVES This study evaluated the comparative effectiveness of an ACE inhibitor–based regimen on a composite outcome of all-cause mortality, stroke, and acute myocardial infarction (AMI) in hypertensive blacks compared with whites.

METHODS We conducted a retrospective cohort study of 434,646 patients in a municipal health care system. Four exposure groups (Black-ACE, Black-NoACE, White-ACE, White-NoACE) were created based on race and treatment exposure (ACE or NoACE). Risk of the composite outcome and its components was compared across treatment groups and race using weighted Cox proportional hazard models.

RESULTS Our analysis included 59,316 new users of ACE inhibitors, 47% of whom were black. Baseline characteristics were comparable for all groups after inverse probability weighting adjustment. For the composite outcome, the race treatment interaction was significant ($p = 0.04$); ACE use in blacks was associated with poorer cardiovascular outcomes (ACE vs. NoACE: 8.69% vs. 7.74%; $p = 0.05$) but not in whites (6.40% vs. 6.74%; $p = 0.37$). Similarly, the Black-ACE group had higher rates of AMI (0.46% vs. 0.26%; $p = 0.04$), stroke (2.43% vs. 1.93%; $p = 0.05$), and congestive heart failure (3.75% vs. 2.25%; $p < 0.0001$) than the Black-NoACE group. However, the Black-ACE group was no more likely to develop adverse effects than the White-ACE group.

CONCLUSIONS ACE inhibitor–based therapy was associated with poorer cardiovascular outcomes in hypertensive blacks but not in whites. These findings confirm clinical trial evidence that hypertensive blacks have poorer outcomes than whites when treated with an ACE inhibitor–based regimen. (J Am Coll Cardiol 2015;66:1224–33)

From the *Department of Population Health, Center for Healthful Behavior Change, New York University School of Medicine, New York, New York; †Kaiser Permanente Southern California, Pasadena, California; ‡Morehouse School of Medicine, Atlanta, Georgia; ‖The Leon H. Charney Division of Cardiology, New York University School of Medicine, New York, New York; §Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, Pennsylvania; ¶New York City Health and Hospitals Corporation, New York, New York; and the #Division of General Internal Medicine, New York University School of Medicine, New York, New York. Dr. Bangalore has received honoraria from Abbott, Boehringher Ingelheim, Daiichi-Sankyo, Merck, Gilead, and Pfizer. Dr. Ogedegbe was supported by a grant from the National Heart, Lung, and Blood Institute, K24HL111315, in addition to the AHRQ grant R01HS018589. The AHRQ did not have any role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of this manuscript. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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In the United States, blacks have disproportionately higher hypertension-related morbidity and mortality than other racial/ethnic groups (1); plus, hypertension explains much of the variance in mortality between blacks and whites (2). Despite the higher rates of cardiovascular disease (CVD), blacks are underrepresented in randomized, controlled trials of therapeutic medications, with a participation rate of <30% in heart failure trials (3).

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Angiotensin-converting enzyme (ACE) inhibitors are commonly prescribed for treatment of hypertension; however, despite their proven efficacy on blood pressure (BP) reduction (4), their relative effectiveness on cardiovascular (CV) outcomes in hypertensive blacks remains uncertain (5). Clinical trial evidence suggests that ACE inhibitors may not provide the same benefits in blacks compared with whites and, in fact, may cause harm (6–9). One retrospective study of 2,225 patients found a 19% rate of ACE inhibitor discontinuation due to adverse events (10). Among 15,100 blacks enrolled in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), those treated with ACE inhibitors had poorer CV outcomes and lesser decreases in BP than those randomized to a thiazide-type diuretic, chlorthalidone (5,9,11). The SOLVD (Study Of Left Ventricular Dysfunction) trial found a significant reduction in hospitalizations for congestive heart failure (CHF) among whites on an ACE inhibitor, but no such reduction was found in blacks (12). Despite the relatively lower clinical effectiveness of ACE inhibitor-based treatment in hypertensive blacks compared with whites enrolled in clinical trials, there are limited data on the comparative effectiveness of ACE inhibitor-based regimens on important health outcomes in hypertensive blacks compared with whites in clinical practice settings.

In this study, we evaluated racial differences in the comparative effectiveness and safety of ACE inhibitor-based regimens in hypertensive blacks compared with whites, using a longitudinal dataset derived from electronic health records (EHRs) of hypertensive patients who received care within New York City's Health and Hospital Corporation (HHC). We hypothesized that an ACE inhibitor-based regimen would be less effective and lead to higher rates of serious adverse effects (hyperkalemia) in blacks compared with whites.

METHODS

STUDY DESIGN, SETTING, AND POPULATION. This study was conducted in New York City's HHC, which oversees the city's public health care system in all 5 boroughs. The corporation consists of 11 acute care hospitals, 6 diagnostic and treatment centers, 4 long-term care facilities, a certified home health care agency, and more than 80 community health clinics. It is the largest municipal hospital and health care system in the country: a $5.4 billion public benefit corporation that serves 1.8 million New Yorkers. HHC provides care for approximately 20% of all general hospital discharges and more than 30% of all emergency department and hospital-based clinic visits in New York City. Approximately 35% of patients seen in the HHC system are black and 7% are white.

Using a retrospective cohort design, we extracted EHR data (BP measurements, weight, prescription refills, laboratory test results, clinical diagnoses, encounter diagnoses for outpatient visits, diagnostic imaging tests, and health care utilization) from HHC's clinical data warehouse. The study population was comprised of adult hypertensive patients (age ≥18 years), who received care between January 1, 2004, and December 31, 2009, and who met the following criteria: hypertension diagnosis (based on hypertension International Classification of Diseases-9th edition [ICD-9] code on ≥2 clinic visits) and prescribed an ACE inhibitor, β-blocker, thiazide-type diuretic, or calcium-channel blocker (CCB) for at least 6 months after their first date of entry into the HHC system. We excluded patients who were not self-identified as African American, black, or Caucasian, and those with a prior history of nonfatal acute myocardial infarction (AMI), nonfatal stroke, or CHF, because these medications are compelling indications for ACE inhibitor use. The study was approved by the institutional review boards of both the New York University School of Medicine and the HHC.

STUDY MEASURES AND OUTCOMES. The primary outcome was a composite of all-cause mortality, nonfatal AMI, and nonfatal stroke. Secondary outcomes included individual components of the composite outcome, CHF, kidney failure, and safety outcomes, which included severe side effects (hyperkalemia, defined as serum potassium >5.5 mEq/l, and hypokalemia, defined as a serum potassium of 2 to 3.5 mEq/l). All outcomes were extracted from the EHR using the corresponding ICD-9 codes from the patient's problem list and laboratory values. For these analyses, we followed patients for up to 2,000 days, with an average follow-up time of 4.5 years. For each

ABBREVIATIONS AND ACRONYMS

ACE = angiotensin-converting enzyme
AMI = acute myocardial infarction
BP = blood pressure
CCB = calcium-channel blocker
CI = confidence interval
CV = cardiovascular
CVD = cardiovascular disease
CHF = congestive heart failure
EHRs = electronic health records
HHC = Health and Hospital Corporation
HR = hazard ratio
ICD-9 = International Classification of Diseases-9th edition
IPTW = inverse probability of treatment weights
SBP = systolic blood pressure