ON BEHALF OF THE EXUBERA PHASE III STUDY GROUP

From the [1]University of Birmingham and Heart of England, National Health Service Foundation Trust, Birmingham, U.K; the [2]Department of Diabetes and Metabolism, Bethanien Krankenhaus, Hamburg, Germany; the [3]Department of Respiratory Medicine, Hvidovre University Hospital, Hvidovre, Denmark; and [4]Pfizer, Sandwich, Kent, U.K.

Address correspondence to Anthony H. Barnett. Undergraduate Centre, Birmingham Heartlands Hospital, Bordesley Green East, Birmingham, B9 5SS, UK. E-mail: anthony.barnett@heartofengland.nhs.uk.

A.H.B. has received honoraria and research grants from Eli Lilly, Novo Nordisk, and Roche. M.D. has received honoraria from sanofi-aventis, Novo Nordisk, Eli Lilly, GlaxoSmithKline, and AstraZeneca. P.L. has served on an advisory panel and received consulting fees from sanofi-aventis and Pfizer.

DOI: 10.2337/dc-06-1466

© 2006 by the American Diabetes Association.

References

1. Mikhail N, Cope D: An open, randomized, parallel-group study to compare the efficacy and safety profile of inhaled human insulin (Exubera) with metformin as adjunctive therapy in patients with type 2 diabetes poorly controlled on a sulfonylurea (Letter). *Diabetes Care* 29:2332–2333, 2006
2. Barnett AH, Dreyer M, Lange P, Serdarevic-Pehar M, the Exubera Phase III Study Group: An open, randomized, parallel-group study to compare the efficacy and safety profile of inhaled human insulin (Exubera) with metformin as adjunctive therapy in patients with type 2 diabetes poorly controlled on a sulfonylurea. *Diabetes Care* 29:1282–1287, 2006
3. Monnier L, Lapinski H, Colette C: Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations with increasing levels of HbA_{1c}. *Diabetes Care* 26:881–885, 2003
4. Rosenstock J, Zinman B, Murphy LJ, Clement SC, Moore P, Bowering CK, Hendler R, Lan SP, Cefalu WT: Inhaled insulin improves glycemic control when substituted for or added to oral combination therapy in type 2 diabetes. *Ann Intern Med* 143:549–558, 2005
5. American Diabetes Association: Standards of medical care in diabetes (Position Statement). *Diabetes Care* 28 (Suppl. 1): S4–S36, 2005
6. American Diabetes Association: Standards of medical care in diabetes (Position Statement). *Diabetes Care* 27 (Suppl. 1): S15–S35, 2004

Antihypertensive Medications and the Risk of Incident Type 2 Diabetes

Response to Taylor et al.

Taylor et al. (1) reported that antihypertensive regimens containing either β-blockers or thiazide diuretics confer a greater risk of new diabetes when compared with ACE inhibitors or calcium channel blockers (CCBs). However, we feel that the interpretation of data provided by the authors warrants further discussion. It is unclear what medication classes were included in the "other" category for each cohort. The Nurse's Health Study (NHS) I (2) suggests a protective effect for ACE inhibitors, since the risk of diabetes is higher for patients on thiazides, β-blockers, "other" antihypertensives, and CCBs. In NHS II (2), for which more limited information was collected (only thiazides and "other"), the relative risk of new diabetes in the "other" group was significant and comparable to thiazides. In the all-male Health Professionals Follow-up Study (3), when information on CCBs and β-blockers was collected, the relative risk for "other" antihypertensives was no longer significant. Hence, we speculate that the "other" medications in NHS I and II may have been diabetogenic, and men on "other" medications in Health Professionals Follow-Up Study were protected from new diabetes by the addition of ACE inhibitors or CCBs or by other unknown mechanisms. Did male/female differences contribute to the incidence of new diabetes in these three studies instead of medications alone?

It is still debated whether thiazides and β-blockers promote diabetes and whether ACE inhibitors and CCBs are antidiabetogenic (4). The lack of prospective clinical trials evaluating the incidence of diabetes as a primary end point and the absence of placebo-controlled studies leaves physicians wondering whether a particular antihypertensive medication causes or prevents diabetes. However, Taylor et al. (1) have opened a new avenue in clinical research, providing preliminary evidence for the increased risk of new diabetes with the use of thiazides and β-blockers in men but not in women. This study also raises the possibility of male/female differences in relation to the effects of ACE inhibitors and CCBs in the prevention of new diabetes.

AIDAR R. GOSMANOV, MD, PHD, DMSC[1]
STEPHANIE CONNELLY, MD, MPH[1]
JAMES B. LEWIS, JR., MD[1]
NIYAZ R. GOSMANOV, MD[2,3]

From the [1]Department of Medicine, Division of General Internal Medicine, University of Tennessee Health Science Center, Memphis, Tennessee; the [2]Department of Medicine, VA Medical Center, Oklahoma City, Oklahoma; and the [3]Department of Medicine, Endocrine Section, University of Oklahoma Health Science Center, Oklahoma City, Oklahoma.

Address correspondence to Aidar R. Gosmanov, MD, PhD, DMSc, Department of Medicine, 842 Jefferson Ave., Room A601, University of Tennessee Health Science Center, Memphis, TN 38103. E-mail: agosmano@utmem.edu.

N.R.G. has received honoraria for speaking engagements from sanofi-aventis.

DOI: 10.2337/dc06-1067

© 2006 by the American Diabetes Association.

References

1. Taylor EN, Hu FB, Curhan GC: Antihypertensive medications and the risk of incident type 2 diabetes. *Diabetes Care* 29: 1065–1070, 2006
2. Feskanich D, Hunter DJ, Willett WC, Spiegelman D, Stampfer MJ, Speizer FE, Colditz GA: Oral contraceptive use and risk of melanoma in premenopausal women. *Br J Cancer* 81:918–923, 1999
3. Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ: Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 338:464–468, 1991
4. Padwal R, Laupacis A: Antihypertensive therapy and incidence of type 2 diabetes: a systematic review. *Diabetes Care* 27: 247–255, 2004

Antihypertensive Medications and the Risk of Incident Type 2 Diabetes

Response to Gosmanov et al.

We thank Gosmanov et al. (1) for their comments. As stated in our article (2) and the accompanying editorial (3), data on the specific use of ACE inhibitors were obtained only in the Nurses' Health Study (NHS) I and data for specific antihypertensive medication use in NHS II were limited to thiazide diuretic use. Thus, NHS II participants reporting the use of "other" antihypertensive medi-

Downloaded from http://diabetesjournals.org/care/article-pdf/29/10/2333/591574/zdc01006002333.pdf by guest on 30 May 2024