

Androgens and Diabetes in Men

Results from the Third National Health and Nutrition Examination Survey (NHANES III)

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OBJECTIVE— Low levels of androgens in men may play a role in the development of diabetes; however, few studies have examined the association between androgen concentration and diabetes in men in the general population. The objective of this study is to test the hypothesis that low normal levels of total, free, and bioavailable testosterone are associated with prevalent diabetes in men.

RESEARCH DESIGN AND METHODS— The study sample included 1,413 adult men aged ≥ 20 years who participated in the morning session of the first phase of the Third National Health and Nutrition Examination Survey, a cross-sectional survey of the civilian, noninstitutionalized population of the U.S. Bioavailable and free testosterone levels were calculated from serum total testosterone, sex hormone-binding globulin, and albumin concentrations.

RESULTS— In multivariable models adjusted for age, race/ethnicity, and adiposity, men in the first tertile (lowest) of free testosterone level were four times more likely to have prevalent diabetes compared with men in the third tertile (odds ratio 4.12 [95% CI 1.25–13.55]). Similarly, men in the first tertile of bioavailable testosterone also were approximately four times as likely to have prevalent diabetes compared with men in the third tertile (3.93 [1.39–11.13]). These associations persisted even after excluding men with clinically abnormal testosterone concentrations defined as total testosterone < 3.25 ng/ml or free testosterone < 0.07 ng/ml. No clear association was observed for total testosterone after multivariable adjustment (P for trend across tertiles = 0.27).

CONCLUSIONS— Low free and bioavailable testosterone concentrations in the normal range were associated with diabetes, independent of adiposity. These data suggest that low androgen levels may be a risk factor for diabetes in men.

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Abbreviations: AAG, androstenediol glucuronide; NHANES III, Third National Health and Nutrition Examination Survey; SHBG, sex hormone-binding globulin.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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It has been suggested that sex steroid hormones may play a causal role in the development of insulin resistance and type 2 diabetes (1,2). There is a growing amount of literature examining the role sex steroid hormones may play in the development of diabetes and cardiovascular disease in women, but there has been relatively less attention paid to this association in men. Men with endocrine disorders that are associated with low testosterone levels (hypogonadism), such as Klinefelter's and Wolfram's syndromes, have an elevated risk of developing insulin resistance and diabetes (3,4). However, the association between sex steroid concentrations within the normal range and diabetes risk in men in the general population has not been well characterized.

Obesity, one of the most important underlying causes of insulin resistance, is associated with low testosterone levels in men (5–7) and may partially or wholly mediate the process by which endogenous sex hormones influence diabetes risk. Many previous studies have been conducted in small, highly selected populations or convenience samples and/or did not rigorously measure or control for the possible effects of adiposity. The present study was undertaken to investigate the association between sex steroid hormones and diabetes in the general adult male population in the U.S. Specifically, we hypothesized that low levels of total, free, and bioavailable testosterone would be associated with prevalent diabetes. We also hypothesized that this association would persist after controlling for the potentially confounding effects of adiposity. Estimates from this study are nationally representative of the U.S. adult male population in 1988–1991.

RESEARCH DESIGN AND METHODS

Between 1988 and 1994, the National Center for Health Statistics conducted the Third National Health and Nutrition Examination Survey (NHANES III). NHANES III was designed as a cross-sectional study using a multi-stage-stratified, clustered probability sample of the U.S. civilian noninstitutionalized population. To ensure adequate