Low Androgen Levels Linked to Diabetes in Men

BY DIANA MAHONEY
New England Bureau

Low androgen levels may be a risk factor for diabetes in men, a population-based study has shown.

In a sample of 1,413 adult men, concentrations of free and bioavailable testosterone in the low normal range were associated with diabetes independent of adiposity, reported Elizabeth Selvin, Ph.D., of Johns Hopkins Bloomberg School of Public Health, Baltimore, and colleagues. "To our knowledge, this is the first study to examine the association between sex steroid hormones and diabetes in a large, nationally representative male population," the authors wrote (Diabetes Care 2007;30:234-8).

The study sample included multiethnic U.S. men aged 20 years or older who participated in the morning session of phase I of the Third National Health and Nutrition Examination Survey (NHANES III), which was conducted between 1988 and 1991. "Morning session participants were chosen for this hormone study to reduce extraneous variation due to diurnal production of sex hormones," the authors wrote. As part of the survey, all of the study participants underwent an interview, an extensive physical examination, and collection of a blood sample.

Height, weight, and waist and hip circumferences were measured as part of the physical examination, and body mass index was calculated. Information on age, race/ethnicity, and diabetes status was collected by patient self-report. With respect to diabetes specifically, interviewers asked participants if they had ever been told by a health professional that they had diabetes or sugar diabetes, the authors noted.

The main hormone measurements of interest in the investigation included serum total testosterone as well as estimated bioavailable and free testosterone levels, which were calculated from serum total testosterone, sex hormone–binding globulin, and albumin concentrations. "Measurements of free and bioavailable testosterone levels more accurately represent concentrations readily available to tissues and metabolic processes," the authors stated.

In a multivariate model adjusted for age, race/ethnicity, and adiposity, there was no clear association of total testosterone concentration with diabetes; however, men in the lowest tertile (0.09 ng/mL or below) of free testosterone level were more than four times as likely to have prevalent diabetes, compared with men in the highest tertile (higher than 0.14 ng/mL).

Similarly, men in the lowest tertile of bioavailable testosterone (2.11 ng/mL or below) were nearly four times as likely to have prevalent diabetes as were men in the highest tertile (higher than 3.02 ng/mL), the authors reported, noting that "these associations persisted even after further adjustment for total cholesterol, triglycerides, and systolic blood pressure." In addition, the association with low free testosterone persisted even after the exclusion of men with clinically low levels of total testosterone (less than 3.25 ng/mL) and/or clinically low levels of free testosterone (less than 0.07 ng/mL), suggesting the observed associations were "not entirely driven by hypogonadal men," they said.

A sensitivity analysis that included 58 cases of undiagnosed diabetes showed no appreciable alterations in the adjusted models, the authors reported.

"The independent association of low free and bioavailable testosterone levels in our adjusted models suggest[s] that testosterone insufficiency may be a risk factor for diabetes," the authors wrote. Despite the fact that the directionality of the associations between low androgen levels and adiposity are unclear based on the analysis, "our data are consistent with the hypothesis that androgens may directly influence glucose metabolism and the development of insulin resistance independently of the effects of adiposity," they stated.

The study reported here is the third from the Hormone Demonstration Program, which is supported by the Maryland Cigarette Restitution Fund Research Grant Program at Johns Hopkins University. ■

Hypogonadism Raises Risk of CVD

BY NANCY WALSH
New York Bureau

MONTREAL — Hypogonadism should be considered a risk factor for cardiovascular disease in older men, Dr. Andre T. Guay said at a congress sponsored by the Canadian Society for the Study of the Aging Male.

He based that conclusion on an analysis of testosterone levels in 154 men with an average age of 53.5 who were seen at the erectile dysfunction (ED) clinic of the Lahey Clinic Medical Center, Peabody, Mass., where Dr. Guay is an endocrinologist.

Overall, 25% of the men had hypogonadism, defined as a free testosterone level below 10 pg/mL. Among men with low testosterone, 92.3% had insulin resistance, compared with 25.2% of those without low testosterone levels. High rates of metabolic syndrome also were seen among hypogonadal men, using both the NCEP criteria and the more stringent World Health Organization criteria for metabolic syndrome. (See box.)

In a previous study, 91% of the cohort of men seen in the ED clinic had cardiac risk factors. A total of 43% had hypertension, 73% had dyslipidemia, and 85% had a body mass index greater than 25 kg/m^2, Dr. Guay said.

Additionally, 43% of the men had metabolic syndrome, according to the National Cholesterol Education Program (NCEP) criteria, compared with 24% of the general population. Insulin resistance was found in 79%, compared with a 25% incidence in the general population.

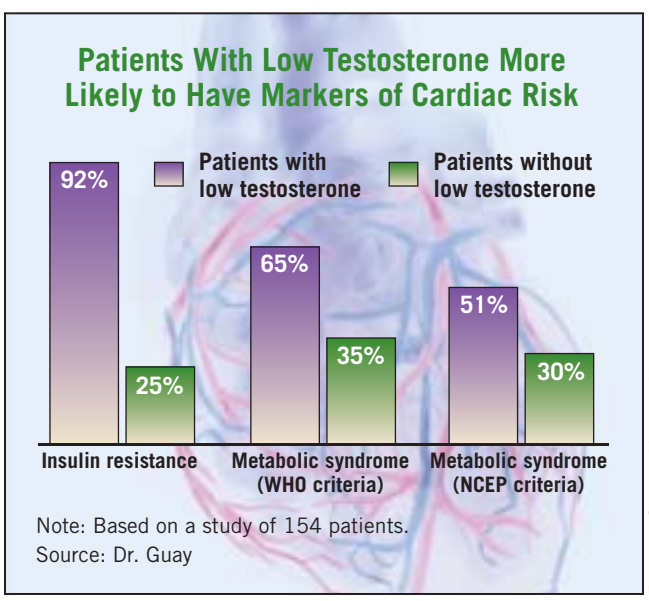
These findings suggest that ED may be an early warning sign of cardiac disease, he said.

The new findings on hypogonadism go beyond the link between ED and cardiac risk, suggesting that low testosterone also may be associated with cardiovascular disease, according to Dr. Guay.

Several large reviews have indicated that men with low testosterone have increased cardiovascular risks, with a high incidence of metabolic syndrome and insulin resistance.

"There are associations, but that doesn't necessarily prove cause and effect," Dr. Guay said in an interview. "However, we know that testosterone can positively affect endothelial function, increasing blood flow, and we know that even acute stimulation of testosterone can decrease insulin resistance, which is the basis of the metabolic syndrome and many chronic diseases. Testosterone must therefore have a protective effect on the vascular lining where atherosclerosis begins."

The study findings suggest that "when patients present with ED, you should immediately look for major cardiac risks and either treat or refer for treatment. It also may be that we should be checking the testosterone level in every man with ED," he said at the meeting, which was cosponsored by the International Society for the Study of the Aging Male. ■



ELSEVIER GLOBAL MEDICAL NEWS

Sildenafil Relieves ED, Lower Urinary Tract Symptoms

TUCSON, ARIZ. — Monotherapy with sildenafil provides relief for men with both erectile dysfunction and lower urinary tract symptoms, Dr. Jay Young and his associates reported in a poster at the annual meeting of the North American Primary Care Research Group.

The study randomized 369 men, aged 45 years and older, with lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) to sildenafil (Viagra) 50 mg or placebo nightly or 30-60 minutes before sexual activity. After 2 weeks, the sildenafil dose was titrated to 100 mg with the option of returning to 50 mg if 100 mg was not tolerated.

Overall, 189 patients were treated with sildenafil and 180 patients took placebo. The cause of ED was organic in the majority of patients, with an average duration of about 5 years in both groups.

The intent-to-treat analysis included 366 men. Those receiving sildenafil had significantly greater mean improvement in erectile function domain scores on the International Index of Erectile Function, compared with placebo-treated patients (9.2 vs. 1.9), and in their International Prostate Symptom Scores (IPSS) (–6.3 vs. –1.9), Dr. Young reported.

He has been an investigator for, owns stock in, and is on the speaker's bureau of Pfizer Inc., which sponsored the study.

Secondary end points were also significantly improved in sildenafil- vs. placebo-treated men, including irritative and obstructive symptoms, the IPSS quality-of-life question, and Benign Prostatic Hyperplasia Impact Index (BPHII) scores.

Maximum urinary flow rate (Qmax) increased slightly for both groups but was not significantly different between groups.

"The improvement in IPSS and BPHII score with no concomitant improvement in Qmax suggests that a new pathophysiology paradigm may be needed to explain the etiology of LUTS," said Dr. Young, director of clinical research at South Orange County Medical Research Center in Laguna Woods, Calif.

A previous study, presented at the 2006 annual meeting of the European Association of Urology, reported that the combination of sildenafil 25 mg/day and the α_1-blocker alfuzosin (Uroxatral) 10 mg/day was more effective than either agent was alone in men with previously untreated LUTS and ED.

It is possible that further improvement in LUTS would have been observed if alfuzosin had been added to the sildenafil in the current trial; however, that was not done, said Carl Clay, Ph.D., senior medical writer with Complete Healthcare Communications, which fielded questions on the study for Dr. Young.

Nine sildenafil patients dropped out of the current study because of adverse events, compared with two in the placebo group. The most common events were headache, dyspepsia, and respiratory tract infection.

—Patrice Wendling

Pages 18a—18b