
Medscape Medical News

Testosterone Replacement Improves Exercise Capacity in Men With CHF

Yael Waknine

June 8, 2005 (San Diego) — Testosterone replacement therapy significantly improves exercise capacity and quality of life in men with moderate to severe chronic heart failure (CHF), according to the results of a 12-month, double-blind, placebo-controlled trial presented here at ENDO 2005, the 87th Annual Meeting of the Endocrine Society.

"Heart failure is associated with a high mortality rate and gradual deterioration that affects patients' outlook and quality of life," Hugh T. Jones, MD, colead investigator, told Medscape. "We previously did a pilot study that was published in *Heart* in 2004, in which men treated with testosterone showed very significant improvements in functional capacity [FC] — they were actually walking a mean 65 m further at three months compared with those who had received placebo."

Dr. Jones is a consultant endocrinologist at the University of Sheffield's Academic Unit of Endocrinology and Barnsley District General Hospital in the U.K.

In a follow-up study, investigators randomized 76 men (mean age, 64 years) with moderate to severe CHF (New York Heart Association [NYHA] class 2 - 4; mean ejection fraction [EF], 32.5% ± 1.3%) to receive 12 months of testosterone replacement therapy (Androderm 5-mg patch, made by Watson Laboratories, Inc.) or placebo. Improvements in FC were assessed using the incremental shuttle walk test (ISWT).

Although testosterone therapy is generally contraindicated in patients with CHF, Dr. Jones explained that the recommendation is based on studies in which testosterone was administered to supraphysiological levels that caused fluid retention. "What we did was increase testosterone levels

to within the physiological range — the average increase in testosterone was only 5.3 nmol (160 ng/dL), a small increase that did not cause edema."

Results showed that testosterone replacement therapy improved FC throughout the 12-month period, relative to placebo (*P* = .006), although the effect was most significant at six months (mean increase in ISWT, 18% ± 7%; 95% confidence interval [CI], 4% - 31%; mean increase in distance, +38 ± 13 m; 95% CI, 11.6 - 64 m).

In addition, 35% of patients treated with testosterone improved by at least one NYHA class for the study period, compared with 8% of those administered placebo (*P* = .01).

"Exercise capacity improved significantly in patients who were taking testosterone, but deteriorated in those who were receiving placebo. NYHA class also improved in one third of patients, and there are not many drugs for heart failure that do that," noted Dr. Jones.

Secondary findings showed that patients treated with testosterone also maintained left ventricular cavity length, which decreased in the placebo group (difference, -8.4 ± 0.28 mm; *P* < .0001); no other changes were observed in dimensions, fractional shortening, or EF. "In patients treated with placebo, the heart length deteriorated and became globular, which is a sign of worsening heart failure," Dr. Jones pointed out.

Testosterone therapy also resulted in maintenance of systolic blood pressure (difference, -6 ± 6 mm Hg; *P* = .01) and increased general muscle function as determined by dominant handgrip strength (*P* = .04).

"In general, patients treated with testosterone maintained their cardiac and general muscle state, whereas those who were treated with placebo experienced deterioration," said Dr. Jones, adding that testosterone therapy can also improve mood and cognitive function. "Patients who were treated with testosterone felt better about themselves and were able to do more than they had been capable of prior to therapy."

According to Dr. Jones, testosterone may also benefit patients with CHF-related cachexia who are losing weight and muscle mass. "Testosterone treatment has also been shown to help men with AIDS-related cachexia and ours is the only study of note to show a parallel benefit in men with CHF."

Skin reactions were the most frequently reported adverse events associated with testosterone patch therapy and may be avoided with use of more recently approved testosterone formulations.

There was no evidence of edema or fluid retention, and no significant changes were observed in serum brain naturetic peptide, tumor necrosis factor, prostate-specific antigen, or hematocrit levels.

"Men with CHF, especially those with low testosterone levels, may benefit from testosterone replacement therapy in improved exercise function and quality of life, maintenance of blood pressure for a period, and the potential for improved NYHA class," Dr. Jones concluded. "More studies are

needed before the full safety of testosterone in heart failure can be established."

The study was supported by a grant from the National Heart Research Fund (U.K.), and the study medication was provided by Watson Laboratories, Inc., the maker of testosterone extended-release transdermal film (Androderm).

ENDO 2005: Abstract PI1-294. Presented June 4, 2005.

Reviewed by Gary D. Vogin, MD
