Adverse Cardiovascular Events Reported in Testosterone Trial in Older Men

June 30 2010

(PhysOrg.com) -- A clinical trial of testosterone treatment in older men, reported June 30 online in the *New England Journal of Medicine*, has found a higher rate of adverse cardiovascular events, such as heart attacks and elevated blood pressure, in a group of older men receiving testosterone gel compared to those receiving placebo. Due to these events, the treatment phase of the trial was stopped.

Decreased muscle strength may contribute to difficulties in mobility, such as in walking or climbing stairs, which can limit older persons' independence. Testosterone treatment has been shown to improve muscle strength in some older men, but it is not yet known whether it would reduce mobility limitations in older men with low testosterone levels. The TOM (Testosterone in Older Men) Trial was designed to address this question. It was a randomized, double-blind, placebo-controlled clinical trial of the effects of six months of testosterone gel treatment on strength and ability to walk and climb stairs in 209 older men with low testosterone levels and mobility limitations. The testosterone gel used in this study was administered to the skin daily. The 209 men in the trial had an average age of 74 and high rates of chronic diseases such as diabetes and cardiovascular disease.

The treatment phase of the trial was stopped on Dec. 31, 2009, following a review by the study's Data and Safety Monitoring Board (DSMB). The DSMB is an independent panel of medical and statistical experts set up from the start of the trial to check regularly for the occurrence of adverse health events in participants and to detect any possible risks

from treatment. In December 2009, the board found that 23 of the 106 men who had received testosterone experienced adverse cardiovascular-related events during the study, compared to five of the 103 men who received placebo. The cardiovascular-related events included heart attack, heart rhythm disturbances and elevated blood pressure, and one death from a suspected heart attack. The DSMB weighed the severity of the adverse events in relation to the potential benefits and recommended that participants stop taking study medications and that enrollment be stopped.

As soon as the DSMB made its recommendation, the treatment phase of the trial was halted. All participants were promptly notified and asked to meet with study physicians to discuss any questions they might have. The men who experienced cardiovascular events were treated by their personal physicians for their specific conditions. No new participants will be enrolled in the study. The study team will continue to monitor the health of all participants for at least another year after stopping testosterone use to further evaluate effects of the treatment.

The report in the New England Journal of Medicine provides detailed information about the outcomes and adverse events in participants. The authors note that physicians and patients, especially older men, should consider this study's findings on adverse effects along with other information on the risks and benefits of testosterone therapy. They also note that further research is needed to clarify the safety issues raised by this trial.

The authors caution that the ability to draw broader conclusions about the safety of testosterone therapy based on these findings is constrained by several factors, including this study's small size and the fact that the study's population was older and had higher rates of chronic diseases and mobility limitation than individuals in most other studies.

In addition, the trial's eligibility criteria excluded men with severely low testosterone levels, limiting the ability to make inferences about safety in this population. The authors also note that the testosterone doses and serum levels in this trial may be higher than those usually used in clinical practice and in some previous clinical trials.

Provided by National Institutes of Health