

Endocrine news



MEN'S HEALTH OBESITY

The Long Haul: Treating Men with Obesity with Testosterone

BY DEREK BAGLEY | JUN 2019

A study presented at ENDO 2019 shows that long-term testosterone therapy in men with obesity and hypogonadism can actually contribute to prolonged weight loss without an added risk for mortality or major cardiovascular incidents.

At a Glance

- Obesity – a complex physiological disorder – is more common in men with hypogonadism.
- A study presented at ENDO 2019 showed that men with hypogonadism and obesity lost weight and were able to keep the weight off long-term.
- Testosterone treatment not only reduced weight, but also the risk for mortality and major adverse cardiovascular events.

As obesity rates around the world continue to climb – the number has tripled since 1975 – physicians and health organizations continue to look at how to treat this disease. And it's widely agreed upon that obesity is a disease, since it's no longer solely a matter of "eat fewer calories," but a complex physiological disorder with various underlying causes as well as myriad comorbidities, both tangible and not. It's well documented that for people with obesity, lifestyle intervention alone can be ineffective,

especially in the long term, and for many patients, obesity can set off a vicious cycle from which it's difficult to escape.

But recent studies are producing glimmers of hope, and many of these studies were presented this past March at **ENDO 2019** in New Orleans. One such study showed that long-term testosterone therapy can help men with hypogonadism lose weight and maintain their weight loss. Obesity is common in men with hypogonadism, and the authors write in their ENDO presentation abstract that testosterone therapy has previously shown promising results in the long-term but not the short-term.

“Men with hypogonadism and obesity receiving long-term testosterone therapy achieved progressive and sustained weight loss, while untreated controls gained,” says lead study author Karim Haider, MD, a urologist and andrologist in private practice in Bremerhaven, Germany, who presented the 10-year results of the ongoing study at **ENDO 2019**. “The favorable decreases in weight and waist circumference may have contributed to the observed reductions in mortality and major cardiovascular events.”

Like Father, Like Son

In the early 1990s, Haider's father Ahmad, also a urologist and andrologist in private practice in Bremerhaven, Germany, started treating patients diagnosed with primary hypogonadism with testosterone therapy and within months these patients showed improvements in their motivation and energy levels, sexual function, compliance, and back pain. A few years later, Ahmad also began treating patients with hypogonadal symptoms but without a diagnosis of primary hypogonadism with testosterone and saw the similar results.

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In 2004, with the approval of testosterone undecanoate (TU) three-month injections, Ahmad recruited his son into the practice and the two, along with their colleagues, recorded urological parameters, blood parameters, and questionnaires in patients treated with injectable TU. They also collaborated with other specialists like orthopaedists, gastroenterologists, and the local diabetes center in order to include as many parameters as possible. “At every one of their visits in our office we encourage all of our overweight and obese patients to start exercising and to eat healthier,” Haider says. “When being treated with testosterone, these patients suddenly start to listen to our recommendations and come back asking

for more than just the usual template of exercises and food-tips we hand out. Hence, we do observe an increase in motivation and physical activity.”

For this current study, Haider and his colleagues followed 805 patients with hypogonadism who were, on average, in their late fifties to mid-sixties. The 462 (57.4%) patients with obesity were given the choice whether to be treated with long-term testosterone therapy with TU 1,000 mg every 12 weeks. Of these, 273 opted to receive testosterone, and the 189 who declined treatment served as controls. “We had many reactions, and most were positive,” Haider says. “[Seventeen] patients who at first refused treatment changed their mind after several years during which they encountered major adverse cardiovascular events and were strongly advised by their cardiologist to start the treatment.”

Over 10 years, the testosterone-treated men lost 20.3% of their baseline weight (50.5 lb; 22.9 kg); their waist circumference dropped by 12.5 cm (4.9 in). BMI decreased by 7.3 kg/m², and the waist-to-height ratio decreased by 0.07. By contrast, the untreated men gained 3.9% of their baseline weight (3.2 kg; 7.1 lb), and their waist size increased by 4.6 cm (1.8 in). In this group, BMI increased by 0.9 kg/m², and waist-to-height ratio increased by 0.03. During this time, 12 (4.4%) men in the testosterone group died, while in the untreated control group, 57 deaths (30.2%), 47 myocardial infarctions (24.9%) and 44 strokes (23.3%) occurred.

“The first big moment was when the reason for initiating this study was confirmed with significant changes in weight and waist circumference compared to the baseline,” Haider says. “This is something we realized the first time when the study was running for four years and four-year data were analyzed. We were then the first to publish weight loss as a result of testosterone therapy.”

No Prostate Cancer Risk

It’s well known that testosterone therapy changes body composition, during which patients lose fat mass and increase muscle mass. Testosterone therapy improves the structure and function of mitochondria, resulting in more energy expenditure. The authors write in their conclusion to the ENDO presentation abstract that long-term testosterone therapy in men with hypogonadism resulted in profound and sustained improvements in anthropometric parameters.

“Up to now we have not seen an increase in the risk of cardiovascular events during therapy although it was added by the FDA as a warning. On the contrary, we saw a much higher mortality and incidence of major adverse cardiovascular events in the untreated control group.” – Karim Haider, MD, urologist and andrologist, Bremerhaven, Germany

But it's not just decreases in BMI and waist circumference Haider and his team have observed in patients treated with testosterone therapy. Haider says they saw gastroenterological patients who reported remissions in their Crohn's disease once starting on testosterone therapy. Some of their patients with hypogonadism and type 2 diabetes receiving standard diabetes treatment went into remission and did not need their diabetes medication anymore.

"The fact that this study was the first to show that testosterone therapy does not increase the risk for prostate cancer was awarded with a presentation in the main plenary during the most important minutes of the 2014 annual meeting of the American Urological Association," Haider says. "Up to now we have not seen an increase in the risk of cardiovascular events during therapy although it was added by the FDA as a warning. On the contrary, we saw a much higher mortality and incidence of major adverse cardiovascular events in the untreated control group."

Hypogonadism: Lifelong Treatment

Haider credits the fact that medication adherence in the testosterone group was 100% as one of the most important explanations of their results, since all injections were performed in the clinic and all patients continuously have stable serum-testosterone levels. He also warns against stopping testosterone treatment in men who have lost weight or whose co-morbidities have improved. Haider points to another study in which patients stopped treatment after more than five years for approximately 18 months and then continued treatment again.

"The results were drastic worsening in every measurable parameter throughout the time without therapy, even worse than at baseline, and again an improvement when continuing the therapy," he says. "Similar results had been observed by various other researchers who tried stopping the treatment. Just like hypothyroidism, hypogonadism is a chronic disease which therefore requires lifelong treatment."

— *Bagley is the senior editor of Endocrine News. He wrote the extensive **ENDO 2019** wrap up in the May issue.*



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