Treatment of 161 Men with Symptomatic Late Onset Hypogonadism with Long-Acting Parenteral Testosterone Undecanoate: Effects on Body Composition, Lipids, and Psychosexual Complaints

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ABSTRACT

Introduction. Elderly men may suffer from late-onset hypogonadism (LOH). The long-term effects of long-acting testosterone undecanoate (TU) in a large number of LOH men have not yet been reported.
Aims. We analyzed the effects of normalization of plasma testosterone (T) in LOH men.
Methods. The records of 161 men with LOH (baseline T < 300 ng/dL) were reviewed and 100 men had used parenteral TU for >12 months. The mean duration of treatment was 90.6 weeks (54 to 150 weeks).
Main Outcome Measures. Body mass index (BMI), waist circumference, percentage body fat, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, prostate-specific antigen (PSA), and hematocrit were measured. Further the Aging Male Symptoms' scale (AMS) and the International Index of Erectile Function (IIEF-5 and 15) were scored.
Results. T therapy was associated with a significant decline in waist circumference ($P = 0.028$) and percentage body fat ($P < 0.001$), but no change of BMI. Total cholesterol and LDL cholesterol declined significantly ($P = 0.005$ and $P = 0.024$, respectively), with no significant changes of HDL cholesterol and triglycerides. The scores of sub-scales of AMS (psychological, somotovegetative and sexual factors) decreased ($P = 0.044$, $P = 0.200$ and $P = 0.071$, respectively). The mean IIEF-5 ($P = 0.011$) and IIEF-15 scores ($P = 0.021$) improved significantly. Erectile function domain, orgasmic function domain, sexual desire domain, intercourse satisfaction domain, and overall satisfaction domain improved. Median PSA rose from 0.95 (0.640; 1.558) ng/mL to 1.480 (1.015; 2.275) ng/mL ($P < 0.001$), with 11 patients >4 ng/mL (4.01–13.21). On biopsy there was no evidence for malignancy. The mean hematocrit level increased significantly from 42.3 ± 3.4% to 47.1 ± 3.8%.
Conclusions. Normalizing serum T in men with LOH resulted in improvement of the metabolic syndrome, mood and sexual functions and appeared acceptably safe. **Permpongkosol S, Tantirangsee N, and Ratana-olarn, K. Treatment of 161 men with symptomatic late onset hypogonadism with long-acting parenteral testosterone undecanoate: Effects on body composition, lipids, and psychosexual complaints. J Sex Med 2010;7:3765–3774.**

Key Words. Late-Onset Hypogonadism; Testosterone Deficiency Syndrome; Testosterone Undecanoate; International Index of Erectile Function; Prostate Safety; Sex Hormone Binding Globulin; Waist Circumference; Thai

Introduction

With aging, a significant percentage of men over the age of 60 years have serum testosterone levels below the lower limits of young adult (age 20–30 years) men [1]. Several recent studies have found that low testosterone level is a predictor of mortality in elderly men [2,3]. Numerous studies have found inverse associations between features of the metabolic syndrome and plasma testosterone [4]. Metabolic syndrome and diabetes are associated with low circulating testosterone—low testosterone

induces the metabolic syndrome, dramatically demonstrated in men with prostate cancer who undergo androgen ablation [5]. A recent study showed convincingly that acute androgen deprivation reduces insulin sensitivity [6].

The question arises then whether testosterone treatment has a role to play in the prevention and/or treatment of the metabolic syndrome and its sequels such as diabetes mellitus type 2 and cardiovascular disease. Testosterone treatment has a beneficial effect on visceral fat and other elements of the metabolic syndrome [7–9]. Evidently, the justification for testosterone treatment lies in a proper diagnosis of testosterone deficiency, and should be based on consistent symptoms and signs and unequivocally low serum testosterone. There is as yet no true consensus on what constitutes low testosterone values [10,11] and it may turn out to be impossible to define precise values of normal/abnormal plasma testosterone in an individual due to inherent properties of the biological action of testosterone on the person. Blood testosterone thresholds for androgen deficiency symptoms are highly consistent within a person but differ between men [12]. It appeared, additionally, that the various complaints of testosterone deficiency cannot be related to a specific threshold of testosterone concentrations. These vary with the various symptoms of testosterone deficiency [13]. These studies demonstrate that there is no clear cutoff point between normal and subnormal blood testosterone levels attempting to define whether a man is hypogonadal or not. Rather, symptoms accumulate gradually with decreasing testosterone levels, with the levels of testosterone differing between individuals and within a subject. Not all symptoms of testosterone deficiency will manifest themselves at the same blood testosterone levels.

Recently, the International Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood Institute representatives held discussions to attempt to resolve the remaining differences between definitions of metabolic syndrome [14]. Both sides agreed that abdominal obesity should not be a prerequisite for diagnosis but that it is 1 of 5 criteria, so that the presence of any three of five risk factors constitutes a diagnosis of metabolic syndrome: elevated triglycerides, low levels of high-density lipoprotein (HDL) cholesterol, elevated blood pressure, and raised fasting glucose and central obesity. A single set of cut points would be used for all components except waist circumference. In the interim, national or regional cut points for waist circumference can be used.

Although different cross-sectional and longitudinal studies have documented a strong association between hypogonadism and diabetes mellitus as well as with metabolic syndrome, only limited data have reported an improvement of insulin resistance treating hypogonadal diabetic subjects with testosterone [15]. Accordingly, the new International Society of Andrology (ISA), International Society for the Study of Aging Male (ISSAM), the European Association of Urology (EAU), European Academy of Andrology (EAA), and American Society of Andrology (ASA) recommendations [16] do not recommend widespread testosterone replacement therapy in subjects with metabolic syndrome or diabetes mellitus. The same guidelines, suggest that in men with hypogonadism and diabetes, testosterone treatment to relieve hypogonadal symptoms may have other unproven benefits for their metabolic status.

There are several studies that have investigated the effect of testosterone administration on features of the metabolic syndrome but they have predominantly been conducted in Caucasian populations and, in spite of the relevance of ethnicity for defining subjects suffering from the metabolic syndrome, studies in Asians are rare. This is a study of mostly elderly hypogonadal men with signs and symptoms of the metabolic syndrome.

Aims

The objective of this study was to investigate the effects of long-acting testosterone undecanoate (TU) on symptoms associated with 161 cases of LOH men.

Methods

Late-onset hypogonadism (LOH) is defined as "a clinical and biochemical syndrome associated with advancing age and characterized by typical symptoms and a deficiency in serum testosterone levels. It may significantly reduce quality of life and adversely affects the function of multiple organ systems" [16]. To meet the criteria for the diagnosis of LOH, the patients had to report symptoms of androgen deficiency, in addition to having had a serum testosterone level of <300 ng/dL or calculated free testosterone of <7.2 ng/dL. A diagnosis also made to exclude other diseases, such as karyotyping (Klinefelter syndrome), secondary hypogonadism, and a history of testicular or orchitis.