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ORIGINAL RESEARCH—PHARMACOTHERAPY

Comparison of the Effects of Testosterone Gels, Injections, and Pellets on Serum Hormones, Erythrocytosis, Lipids, and Prostate-Specific Antigen

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ABSTRACT

Introduction. Numerous testosterone (T) formulations are available, each with differing effects on serum parameters.
Aim. The aim of this study was to compare the long-term effects of topical, injectable, and implantable pellet T formulations in hypogonadal men.
Methods. Retrospective review of hypogonadal men treated with a single T formulation was performed: 47 men on T gels, 57 on injectable T, and 74 on T pellets were identified. Total T (TT), calculated free T (FT), estradiol (E), hemoglobin (Hgb), hematocrit (Hct), prostate-specific antigen (PSA), total cholesterol (Tchol), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol were evaluated at baseline and every 3–6 months for 3 years. Serum parameters were compared using a mixed model linear regression for repeated measures.
Main Outcome Measures. Effects of topical, injectable, and pellet T formulations on serum hormone levels, Hgb, Hct, lipid parameters and PSA.
Results. Men in the injectable T group were younger (42.5 ± 12.3 years) than in the gel (54.1 ± 9.8 years) or pellet groups (53.8 ± 13.0 years), and baseline FT, Hgb, and Hct were higher in the injectable T group than in gel or pellet groups. Increases in TT and FT were observed throughout follow-up in all groups. Increases in E were observed at in all T groups and throughout follow-up in injectable and gel groups. No PSA increases were observed. Erythrocytosis (Hct > 50%) was more common with injectable T (66.7%) than with T gels (12.8%) or pellets (35.1%, $P < 0.0001$). Transient changes in cholesterol, TG, and LDL were observed, and no significant changes were seen in HDL for any group.
Conclusions. All T formulations increase serum T and FT. More significant increases in E occur with injectable T and T gels. Changes in Hgb and Hct are most significant with injectable T, and effects on lipids are variable and inconsistent. Selection of T formulations must account for individual patient preferences and the effects of each formulation. **Pastuszak AW, Gomez LP, Scovell JM, Khera M, Lamb DJ, and Lipshultz LI. Comparison of the effects of testosterone gels, injections, and pellets on serum hormones, erythrocytosis, lipids, and prostate-specific antigen. Sex Med 2015;3:165–173.**

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Key Words. Testosterone Therapy; Testosterone Pellets; Testosterone Gel; Testosterone Injections; Erythrocytosis; Lipid Panel; Prostate Cancer

Introduction

Hypogonadism affects approximately 2–4 million men in the United States, and is characterized by low serum testosterone (T) levels in association with signs and symptoms of hypogonadism including fatigue, decreased libido, erectile dysfunction, depression, anemia, and decreased muscle mass and bone density [1,2]. In addition to ameliorating hypogonadal symptoms [1,3], T therapy (TTh) can lead to increased muscle mass and bone density [4–6], and reversal of the metabolic syndrome [2,7]. However, TTh is associated with potential adverse effects including elevated serum estrogen levels, gynecomastia, local reactions, alterations in serum lipids, erythrocytosis, testicular atrophy, male infertility, and cardiovascular effects [1,2,8–11].

Numerous T formulations are Food and Drug Administration approved in the United States for the treatment of hypogonadism. Several commonly used T formulations include injectables, transdermal gels, and implantable pellets [12]. While all T preparations are effective, the likelihood of associated side effects is determined by dosage, pharmacokinetics, and method of administration [12,13]. As such, the selection of T preparation should be a joint decision between the patient and physician, and includes consideration of treatment efficacy, cost, acceptability of the therapy by the patients, and likelihood of specific adverse effects [2,12]. However, a relative dearth of long-term data directly comparing the effects of T formulations in men on TTh limits physicians' ability to counsel their patients. To better understand how various T formulations impact not only serum T levels, but also the likelihood of related adverse effects, we retrospectively compared the long-term effects of injectable, transdermal, and subcutaneous T pellet formulations in hypogonadal men.

Aims

We sought to compare the long-term effects of topical, injectable, and implantable pellet T formulations in hypogonadal men on serum hormone, hemoglobin (Hgb), hematocrit (Hct), lipid, and prostate-specific antigen (PSA) levels. Our goal was to assess the unique and common effects of each T formulation in order to better inform selection of T formulations for individual patients. We hypothesized that different T formulations would have varying effects on both serum hormone parameters as well as the likelihood of adverse events.

Methods

Patient Identification and Data Acquisition

After approval by the Institutional Review Board of Baylor College of Medicine, retrospective review of hypogonadal men treated with a single T formulation between 2007 and 2012 was performed. Only men that were T naïve or those who had been off of T for 3 or more months prior to restarting TTh were included in the analysis. Men were diagnosed with hypogonadism using both clinical symptoms of hypogonadism, including erectile dysfunction, decreased libido, and/or decreased energy, as well as evidence of low serum T (≤350 ng/dL). All included men were diagnosed with secondary hypogonadism. We identified 47 men treated with T gels, 57 with injectable T, and 74 with subcutaneous T pellets that met our inclusion criteria. Men using T gels applied drug daily based on manufacturer's recommendations (Testim® 50–100 mg T [one to two packets applied to the shoulder area daily; Endo, Ballsbridge, Ireland], Androgel® 1.62% 20.25–80.1 mg T [two to four pumps applied to the skin daily; AbbVie, North Chicago, IL, USA]), and men on T pellets (75 mg crystalline T/pellet) were implanted with 10–14 pellets to achieve a peak serum T level of 500–800 ng/dL every 3–6 months [14]. Men on injectable T formulations injected 100–200 mg of T cypionate or enanthate intramuscularly weekly. If men developed serum estradiol (E) levels >5 pg/mL, the upper limit of our lab's reference range, they were treated with oral aromatase inhibitor (AI).

Patient demographics, total T, free T (FT), E, Hgb, Hct, PSA, total cholesterol (Tchol), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were evaluated at baseline and every 3–6 months for 3 years. All samples were analyzed in the Laboratory for Male Reproductive Research and Testing at Baylor College of Medicine on a single Beckman Coulter Access2 assay system (Beckman Coulter, Brea, CA, USA). Hormone levels were determined using