Effects of Three Different Testosterone Formulations in Female-to-Male Transsexual Persons

Carla Pelusi, MD,* Antonietta Costantino, PhD,† Valentina Martelli, MD,† Martina Lambertini, MD,† Alberto Bazzocchi, MD, PhD,‡,§ Federico Ponti, MD,§ Giuseppe Battista, MD,§ Stefano Venturoli, MD,† and Maria C. Meriggiola, MD, PhD†

*Division of Endocrinology, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; †Department of Gynecology and Physiopathology of Reproduction, Center for Protection of Sexual Health, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; ‡Diagnostic and Interventional Radiology, The "Rizzoli" Institute, Bologna, Italy; §Department of Specialized, Diagnostic, and Experimental Medicine, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

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ABSTRACT

Introduction. Gender dysphoria is characterized by a strong discomfort with the gender assigned at birth and the urge to live as a member of the opposite gender. The acquisition of phenotypic features of the desired gender requires the use of cross-sex hormones. Female-to-male (FtM) transsexual persons are treated with testosterone to induce virilization.

Aim. The aim of the study was to assess the effects of three different testosterone formulations on body weight and composition and metabolic and bone parameters.

Methods. Forty-five FtM transsexuals were randomly assigned to receive testoviron depot (i.m.: 100 mg/10 days; n = 15), testosterone gel (50 mg/die; n = 15), and testosterone undecanoate (i.m.: 1,000 mg every 6 weeks for the first 6 weeks and then every 12 weeks, n = 15). FtM individuals were studied before, at week 30, and at week 54 of testosterone treatment.

Main Outcome Measures. Anthropometric, metabolic, bone, hematological, and biochemical parameters were evaluated at baseline and after 12 months of treatment.

Results. Lean body mass significantly increased and fat mass decreased in all groups. No modifications were reported in fasting insulin and insulin sensitivity index. High-density plasma lipoprotein levels declined significantly and low-density lipoprotein concentrations increased significantly in the three groups. The activated partial thromboplastin time and factor I did not change while prothrombin time significantly increased in all groups. At week 54, all subjects were amenorrheic and time to amenorrhea did not differ between the three groups. Current general life satisfaction was increased in all subjects after 1 year of treatment.

Conclusions. One-year testosterone administration in FtM transsexuals appears to be very safe with no differences among the testosterone formulations used. Our study is preliminary, and the detection of subtle or long-term differences in the effects of the three formulations may require further larger and longer term studies in this and other populations. **Pelusi C, Costantino A, Martelli V, Lambertini M, Bazzocchi A, Ponti F, Battista G, Venturoli S, and Meriggiola MC. Effects of three different testosterone formulations in female-to-male transsexual persons. J Sex Med 2014;11:3002–3011.**

Key Words. Testosterone; Transsexuals; Gender Dysphoria; Bone; Body Composition; Life Satisfaction

Introduction

Transsexuals require cross-sex hormones to acquire phenotypic features and secondary sexual characteristics of the sex opposite to their biological sex. To this end, biological female transsexual persons (female to male [FtM]) require treatment with testosterone (T) to induce virilization. Although there are no specific studies on the dose of T required to induce and maintain male sexual characteristics in these female persons, it is generally agreed that T levels should be maintained within the physiological range of normal men [1–4].

The most commonly used preparations have been injectable T esters (testoviron depot [TD]) administered in doses of 100–250 mg every 7–20 days. These formulations generate supraphysiological hormonal levels after injection with a rapid decline a few days before the next administration [5]. In recent years, new formulations that provide better pharmacokinetic profiles have become available such as daily administration of testosterone gel (T-gel) and long-acting testosterone undecanoate (TU) administered through intramuscular injections. These formulations are more conveniently administered and allow for maintenance of more stable levels of T and of its metabolites estradiol (E) and dihydrotestosterone [5–12]. The use and effects of these T formulations have been extensively studied as replacement therapy in hypogonadal men. In these subjects, they have been associated with a reduction of fat mass, an increase of lean mass, and possible positive effects on lipid profile and glycometabolic control [13–16]. Instead, the effect of androgen administration on healthy eugonadal females is less known. The few studies conducted in FtM transsexuals have shown that T administration may induce changes in body weight and composition with a shift toward a greater lean mass similar to T administration in hypogonadal patients; however, adverse effects on lipid profile and contrasting effects on insulin sensitivity have been reported [17–19]. Most studies have reported effects on short- or long-acting injectable T formulations while little data are available on the effects of transdermal T administration.

Aim

The aim of our study was to compare the effects of 1-year transdermal, short-acting, and long-acting intramuscular T injections in healthy FtM transsexual subjects on body composition, metabolic, safety parameters, and general life satisfaction.

Methods

A total of 45 healthy FtM transsexual persons were included in this study. All subjects were studied before, at week 30, and at week 54 of T treatment. A deviation of ±3 weeks was tolerated for injections.

Inclusion criteria were healthy by medical history and laboratory analysis and no use of medication for hypertension, hyperlipidemia, diabetes mellitus, and depression or any psychiatric drugs.

Three different hormone formulations were administered: TD (contains testosterone enanthate) i.m. at the dose of 100 mg, every 10 days (n = 15; TD group); T-gel at the dose of 50 mg/day, every evening between 8:00 and 10:00 PM (n = 15; T-gel group); or TU i.m. at the dose of 1,000 mg at week 0, week 6, and thereafter, every 12 weeks (n = 15; TU group).

Subjects were randomly assigned to receive TD, T-gel, or TU. All subjects were naïve of T and had not undertaken any genital surgery at admission nor throughout the duration of the study.

All subjects gave written consent to the use of T. The study was approved by the Ethical Committee of S. Orsola Hospital, Bologna.

Physical examination consisted of anthropometric assessment of weight, stature, and waist and hip circumferences, taken with participants dressed in a gown, according to standardized procedures. The waist circumference was measured midway between the iliac crest and lowest rib margin [20].

At the same time, body composition and bone mineral density (BMD) were measured by dual X-ray absorptiometry using the Hologic 49159 densitometer and standard QDR body composition software (Model QDR4500W, Software Level 11.2, Hologic Spine, Hologic, Bedford, MA,USA) with evaluation of body fat and lean mass, calculated using the female database provided by the manufacturer.

At baseline and week 54 of treatment, blood samples were drawn at 8:00 AM after a 12-hour overnight fast with determination of serum T, E, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), prolactin (PRL) and sex hormone-binding globulin (SHBG), hematocrit