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Case Report

Two Transgender Men Receiving Subdermal Testosterone Pellets for Gender Affirmation

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ABSTRACT

Background/Objective: Testosterone treatment is employed in transgender men to help them affirm their gender. Our objective is to report the cases of 2 transgender men who received subdermal testosterone pellets as the mode of testosterone administration.
Case Report: Both patients presented for discussion of testosterone therapy. Patient 1 was a 47-year-old transgender male. He had bilateral mastectomy and total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO). Physical exam was significant for obesity. He was on injectable testosterone for 9 years and experienced voice deepening, facial hair growth, temporal hair thinning, and increased skin oiliness, but was interested in a long-acting testosterone formulation. Pellets were well tolerated, but the patient ultimately chose to return to injections. Patient 2 was a 20-year-old transgender male with no history of gender-affirming surgeries. Physical exam was pertinent for a thin, masculinized individual. He started on testosterone gel, but switched to weekly injections, on which he experienced voice deepening, increased skin oiliness and cessation of menses. Due to pain with injections and desire for a long-acting formulation, he elected to try pellets.
Discussion: The dose of testosterone pellets used in transgender men are similar to those employed for testosterone replacement in hypogonadal cisgender men.
Conclusion: Subdermal testosterone pellets may be suitable as a means of delivering testosterone in transgender men, but the 2 cases reported here do not permit firm conclusions. Given the widespread use of testosterone for gender affirmation in transgender men, a prospective controlled study of subdermal testosterone pellets seems indicated.

Introduction

A major aspect of the treatment of transgender men to help them affirm their gender is to administer testosterone to achieve testosterone levels seen in cisgender men. The usual methods for testosterone replacement are injectable and transdermal testosterone formulations.[1] Testosterone pellets have been used in cisgender men for physiological testosterone replacement, but there is currently a scant amount of literature related to this method. Here, we report the cases of 2 transgender men who elected to try subdermal testosterone pellets as a means of receiving testosterone in amounts like those that cisgender men are exposed to.

Case Report

Patient 1 was a 47-year-old transgender man who presented for discussion of his testosterone treatment options. His past medical history was significant for asthma treated with albuterol and budesonide, fibromyalgia, osteoarthritis involving the neck and bilateral shoulders, and generalized anxiety disorder (GAD) managed with escitalopram. The patient had no history of obstructive sleep apnea (OSA) and was a smokeless tobacco user.

Prior to presentation, Patient 1 had been on injectable testosterone for 9 years as a component of gender affirmation. On injections, he had experienced anticipated effects from testosterone, including voice deepening, facial hair growth,

Abbreviations: BMI, body mass index; FDA, food and drug administration; GAD, generalized anxiety disorder; IM, intramuscular; OSA, obstructive sleep apnea; TAH-BSO, total abdominal hysterectomy with bilateral salpingo-oophorectomy.

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temporal hair thinning, and increased skin oiliness. One year after beginning testosterone therapy, he underwent bilateral mastectomy. He obtained a TAH-BSO 7 years thereafter. Patient 1 was satisfied with weekly testosterone injections but intrigued by long-acting pellets.

On physical exam, vital signs included a blood pressure of 126/85,pulse of 74, and oxygen saturation of 95%. Body mass index (BMI) was 36.5 kg/m^2.

Before beginning pellets, Patient 1 was on weekly testosterone cypionate 0.55 mL (110 mg) intramuscular (IM) injections. Total testosterone 2 weeks prior to pellet insertion was 894 ng/dL (300-890 ng/dL by immunoassay), measured 2 days after IM injection. Insertion of testosterone pellets was performed in a clinic setting. Each pellet is 75 mg of testosterone. The procedure involved making a small incision in the upper outer quadrant of the hip. A trocar with a sharp ended stylet was inserted into the subcutaneous tissue in line with the femur. The stylet was exchanged for testosterone pellets, which were advanced into the tissue. The trocar was then removed, and the incision was closed with a butterfly bandage.

Patient 1 received subdermal testosterone pellets for a period of 45 weeks. Initially, 450 mg of testosterone was inserted, and the patient achieved a total testosterone of 366 ng/dL after 4 weeks (Fig. 1). After 11 weeks, total testosterone fell to its lowest at 246 ng/dL, after which 675 mg of testosterone was inserted. Total testosterone 4 weeks later was 572 ng/dL; levels fell to 305 ng/dL after 17 weeks. At 18.5 weeks, 750 mg of testosterone was inserted; total testosterone rose to its highest measured level at 1234 ng/dL within 1 week and decreased to 396 ng/dL by 15.5 weeks. Mean serum total testosterone in Patient 1 with 450, 675, and 750 mg was 307, 450, and 718 ng/dL, respectively. At the highest testosterone level, 17-β-estradiol reached its maximum of 104 pg/mL (11.3-43.2 pg/mL by immunoassay); at the lowest testosterone level, it was 15.5 pg/mL. The lowest hematocrit across pellet use was 46.4%, measured 4 weeks after insertion of 450 mg of testosterone (Fig. 1). The highest hematocrit, 53.9%, occurred 15 weeks after insertion of 750 mg of testosterone.

Patient 1 experienced minimal pain with pellet insertion. During use, he did not experience adverse effects such as cellulitis, site infection, or extrusion. He decided to switch back to weekly IM testosterone cypionate injections at his original dose due to the wide range of testosterone levels seen with subdermal testosterone pellets.

Highlights

- Pellets are a reasonable form of testosterone for masculinizing gender affirmation.
- There is concern for erythrocytosis in patients using testosterone pellets.
- Providers can trend testosterone level to find the appropriate pellet dose.
- Goal time interval between pellet insertions is 3 to 6 months.
- Pellet decay rate may correlate positively with dose and negatively with BMI.

Clinical Relevance

Testosterone pellet use in the transgender male population has not been widely documented. Nonetheless, it may be an appropriate option for individuals that want a long-acting testosterone formulation.

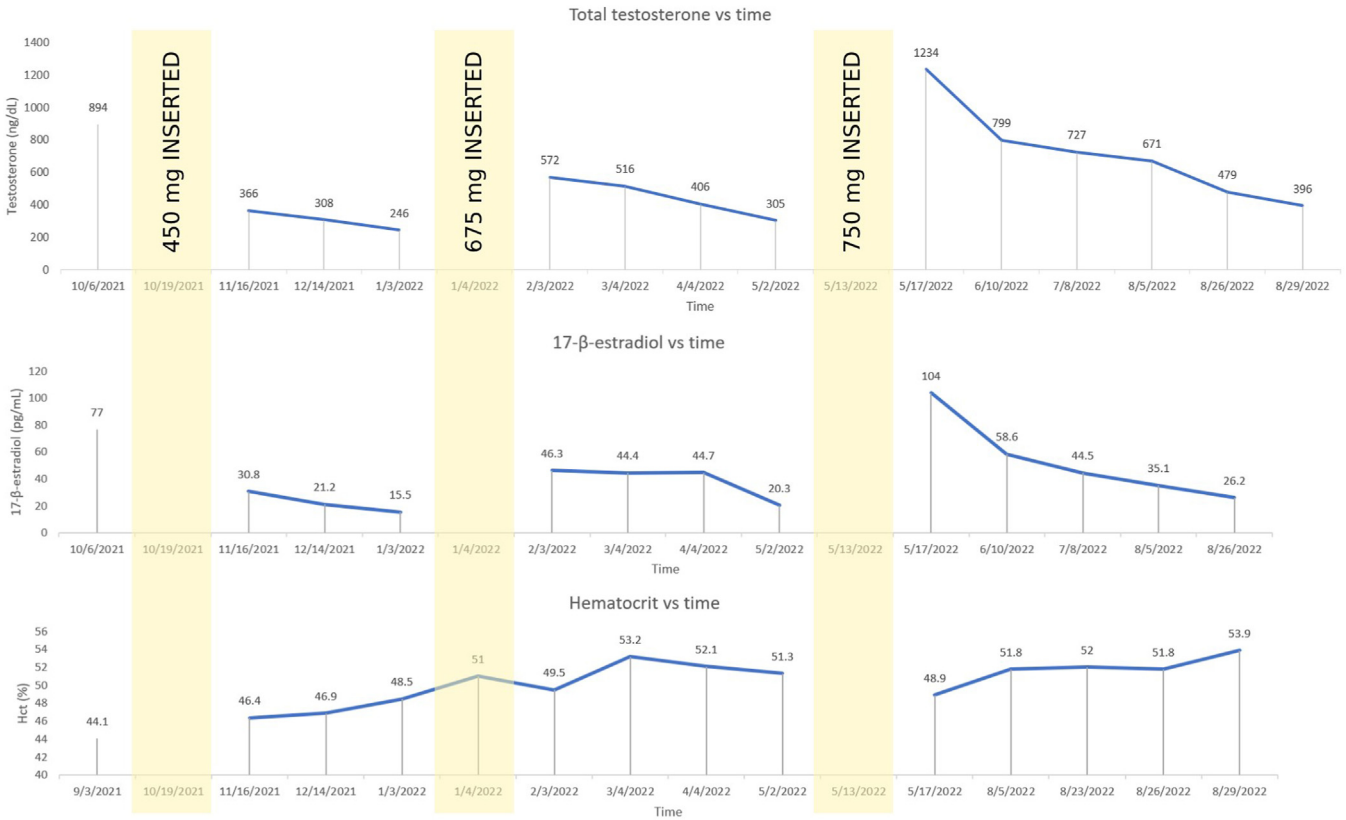

Fig. 1. Patient 1: Testosterone, 17-β-estradiol, and hematocrit vs time.

Patient 2 was a 20-year-old transgender male who presented for discussion of his testosterone therapy. His past medical history included asthma treated with albuterol, attention-deficit/hyperactivity disorder on no medications, bipolar disorder managed with olanzapine, and GAD managed with escitalopram. The patient had no history of OSA and had never used tobacco products.

Prior to presentation, Patient 2 had been on testosterone gel (5 g or 81 mg daily) for gender affirmation. However, daily administration of gel was difficult to keep up with, and the patient was not seeing adequate masculinizing changes. After approximately 1 year on gel, he switched to weekly testosterone injections. On injections, Patient 2 experienced anticipated effects of testosterone therapy, including increased skin oiliness and cessation of menses, but had pain with injections and struggled to self-administer the medication. Patient 2 had not undergone any gender-affirming surgeries. He decided to try pellets so that he would not have to self-administer testosterone.

On physical exam, vital signs included a blood pressure of 97/64, pulse of 75, and oxygen saturation of 98%. The patient had a BMI of 18.3 kg/m^2.

Prior to pellet insertion, Patient 2 was on weekly testosterone cypionate 0.25 mL (50 mg) IM injections. Total testosterone in Patient 2 was 803 ng/dL 4 weeks prior to testosterone pellet insertion (Fig. 2). Insertion of testosterone pellets was performed in a clinic setting using 75 mg pellets. The procedure mirrored that of Patient 1.

The patient received subdermal testosterone pellets for a period of 34.5 weeks. Initially, 225 mg of testosterone was inserted at the provider's discretion given the patient's lower BMI. After 9.5 weeks, testosterone levels fell to 236 ng/dL; 450 mg was implanted just prior to 11 weeks. Testosterone rose to 589 ng/dL by 5 weeks and dropped to 198 ng/dL by 18 weeks. Mean serum testosterone on 450 mg was 454 ng/dL. At 19 weeks, 600 mg was inserted; after 4.5 weeks, testosterone was 746 ng/dL 17-β-estradiol was not consistently measured. The lowest hematocrit (40.7%) was measured 9.5 weeks after insertion of 225 mg; the highest hematocrit (44.2%) was seen 11 weeks after insertion of 450 mg.

Patient 2 had minimal pain with pellet insertion. During treatment with pellets, he did not experience adverse effects such as cellulitis, site infection, or extrusion. Patient 1 remains on testosterone pellets at a dose of 600 mg.

Discussion

Herein we present 2 transgender men who were treated with subdermal testosterone pellets to promote gender affirmation.

Testosterone pellets are advantageous in their infrequent dosing and low likelihood of drug transfer. Both patients sought a long-acting testosterone formulation so use of testosterone pellets was an appropriate choice. Current food and drug administration (FDA) guidelines advise implantation of 150 to 450 mg every 3 to 6 months in hypogonadal cisgender men, though use of up to 1050 mg has been described.[2,3] Although no specific dosing guidelines for transgender men exist, the common practice has been insertion of 450 mg with subsequent dose adjustments based on achieved total testosterone levels.

Previous studies have found that total testosterone decreased to <300 ng/dL by approximately 19 weeks in cisgender men receiving 450 to 675 mg of testosterone pellets and by approximately 16 weeks in transgender men receiving 750 mg of testosterone pellets.[4-6] In this report, insertion of 450 mg of testosterone pellets resulted in total testosterone levels below 300 ng/dL within 11 weeks for Patient 1 and within 18.5 weeks for Patient 2. In comparison to other testosterone formulations, pellets show lower daily changes in testosterone levels. Total testosterone across a 24-hour period has been estimated to change by approximately 200 ng/dL on 50 mg of gel and close to 300 ng/dL on biweekly 200 mg IM injections.[7] Pellet rate of decay was calculated to determine approximate daily decreases in total testosterone by

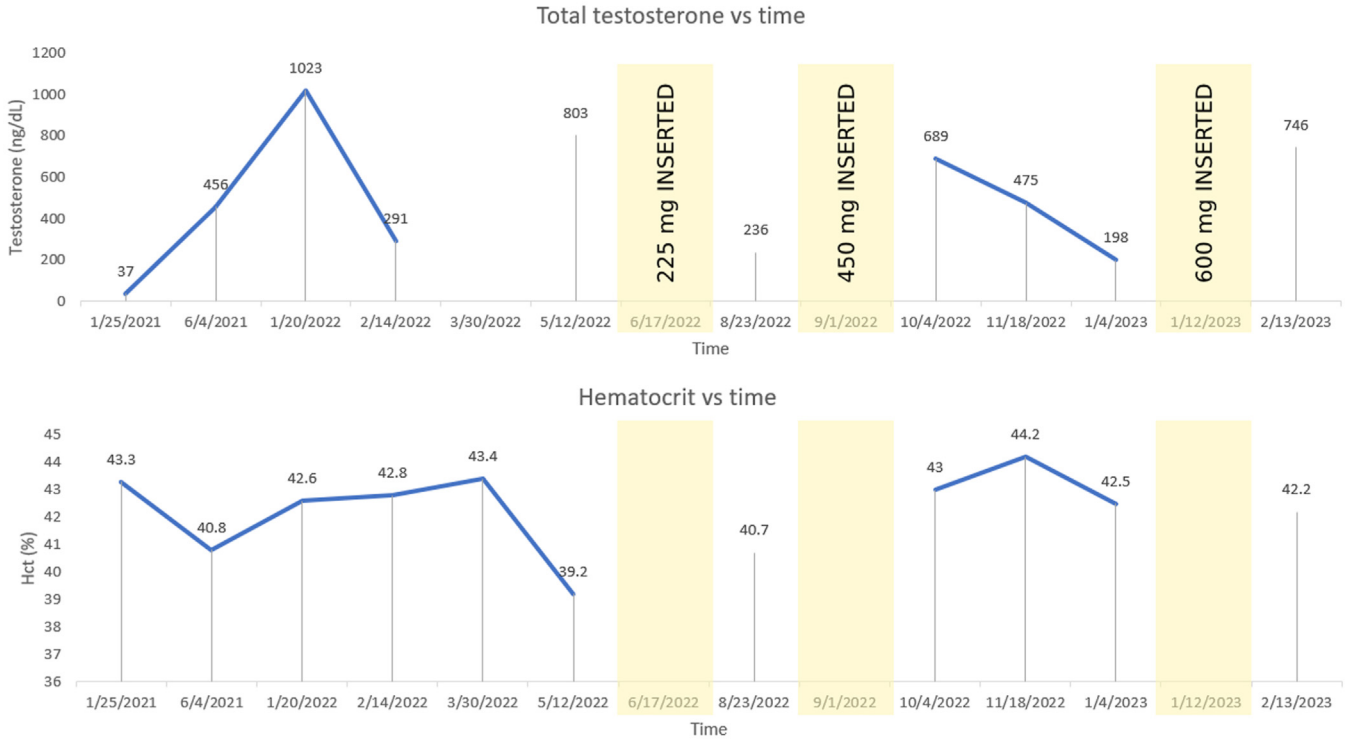

Fig. 2. Patient 2: Testosterone and hematocrit vs time.

Table 1
Testosterone Dose vs Decay Rate

Patient 1		Patient 2	
Testosterone pellet dose	Rate of decay (ng/dL/d)	Testosterone pellet dose	Rate of decay (ng/dL/d)
450	0.008 ($R^2 = 0.97$)	450	0.014 ($R^2 = 0.95$)
675	0.007 ($R^2 = 0.95$)		
750	0.009 ($R^2 = 0.91$)		

dose (Table 1). A higher rate of decay was found at higher doses.[4] In comparing the 450 mg testosterone pellet dose, lower BMI was associated with a higher rate of decay. Previous studies found faster decay in men with BMI <25 kg/m^2; this trend could potentially be due to androgen sequestration in adipose tissue.[4]

Increased hematocrit is seen regardless of exogenous testosterone formulation. Incidence of erythrocytosis (hematocrit >51%) with testosterone pellets is estimated to be 35.1% in the cisgender male population; in transgender men, a study found the rate of polycythemia to be 46.67%.[6,8] Both patients presented experienced a dose-dependent increase in hematocrit on pellets, and Patient 1 developed erythrocytosis. Although Patient 1 is a smokeless tobacco user, increases in hematocrit have not been consistently found to occur with smokeless tobacco use.[9,10]

The dose and frequency of testosterone pellet insertion required to achieve and maintain testosterone levels within the cisgender male reference interval for transgender men remains unknown, especially given the lower baseline endogenous testosterone production compared to cisgender men. There is concern for erythrocytosis in patients on this form of testosterone. A larger case series is needed to examine the relationship between BMI and dose. Because testosterone therapy is often a life-long treatment which is initiated in transgender men at an earlier age on average than their cisgender counterparts, it is necessary to assess the long-term effects of this method of testosterone administration in this population.

Despite the limited scope and retrospective nature of this case study, these patients demonstrate that pellets are a reasonable method of administration for use as testosterone treatment for transgender men. They may be presented as an option to individuals with limitations to injectable or topical formulations, though routine monitoring of total testosterone and hematocrit is necessary.

Disclosure

The authors have no multiplicity of interest to disclose.

Acknowledgment

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