ORIGINAL RESEARCH

Accuracy of Testosterone Concentrations in Compounded Testosterone Products

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ABSTRACT

Objective: This study aims to evaluate the accuracy of the testosterone concentrations within testosterone gels and creams manufactured by compounding pharmacies.

Methods: Ten compounding pharmacies within Toronto area were included. Pharmacies were blinded as to the nature of the study. A standardized prescription for 50 mg of compounded testosterone gel/cream applied once daily was presented to each pharmacy. Two independently compounded batches were analyzed from each pharmacy 1 month apart. Testosterone concentrations in a 5-g sachet of Androgel® 1% (Abbott) and 5-g tube of Testim®1% (Auxilium) were evaluated as controls. Samples were analyzed independently and in a blinded fashion by the Laboratory Medicine Program at the University Health Network. Measurement of testosterone concentration was performed using a modified liquid chromatography tandem mass spectrometry validated for serum testosterone.

Results: Compounded formulations included seven gels and three creams with a volume/daily dose ranging from 0.2 mL to 1.25 mL. Product cost ranged from $57.32 to $160.71 for a 30-day supply. There was significant variability both within and between pharmacies with respect to the measured concentration of testosterone in the compounded products. In contrast, the concentration of testosterone within Androgel and Testim was consistent and accurate. Collectively, only 50% (batch 1) and 30% (batch 2) of the compounding pharmacies provided a product with a testosterone concentration within ±20% of the prescribed dose. Two pharmacies compounded products with >20% of the prescribed dose. One pharmacy compounded a product with essentially no testosterone.

Conclusions: Testosterone concentrations in compounded testosterone products can be variable and potentially compromise the efficacy and safety of treatment. **Grober ED, Garbens A, Božović A, Kulasingam V, Fanipour M, and Diamandis EP. Accuracy of testosterone concentrations in compounded testosterone products. J Sex Med 2015;12:1381–1388.**

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Introduction

Testosterone deficiency is common among North American men with contemporary crude prevalence rates that suggest approximately 25% of men between the ages of 40 and 62 years are biochemically testosterone deficient [1]. With the proportion of elderly males projected to increase globally over the next decades, the incidence of testosterone deficiency is expected to rise [2].

Signs and symptoms as a consequence of testosterone deficiency commonly include decreased energy levels and vitality, weakness and fatigue, diminished libido, erectile dysfunction, mood changes, and decreased overall quality of life [3,4].

Importantly, several prospective population-based studies have linked testosterone deficiency with significant comorbid conditions including type 2 diabetes, metabolic syndrome, obesity, hypertension, chronic obstructive pulmonary disease, and osteoporosis [5–10]. Moreover, a series of recent investigations have demonstrated an association between low testosterone and increased overall mortality [11,12]. The ability of testosterone replacement therapy to modify many of these comorbid conditions is currently being investigated [9,13,14].

The goals of testosterone therapy include symptomatic improvement through the achievement of physiologic testosterone levels [3,10]. A variety of safe and efficacious products are available for testosterone replacement for symptomatic, hypogonadal men and include injectable, oral, transdermal agents (patch, gel, axillary solution) and subcutaneous pellets [10].

On a global scale, the past decade has witnessed a progressive increase in testosterone prescribing with the most dramatic increases in per capita testosterone prescribing observed in Canada and the United States [15]. The utilization of compounded pharmaceutical products has evolved concurrently with the increase in prescriptions for testosterone from large-scale commercial pharmaceutical manufacturers. The compounding pharmacies industry experienced an annual revenue growth of 5.5% to $1.8 billion in the 5 years to 2012 [16].

The growth of the compounding market has been fueled by an aging population as well as an overall increased demand for pharmaceutical therapies. More specifically, compounding offers a potential solution to drug shortages and allows for customized preparations with respect to dosing, ingredients, delivery methods, flavoring, and modification for allergy and sensitivities. In some cases, compounded medicine may be more cost effective compared with brand name medications [17].

According to Health Canada's policy on Manufacturing and Compounding Drug Products (POL-0051, 2009), the compounding of drugs by healthcare professionals (pharmacists and doctors/veterinarians) is to be regulated by the respective regulatory authorities in each province/territory [18]. In contrast, drug manufacturing of commercial pharmaceuticals is regulated at a national level by Health Canada under the Federal Food and Drugs Act and Food and Drugs Regulations [18]. Similar to Canada, the federal U.S. FDA regulates commercial pharmaceutical manufacturing, whereas state law regulates standards and licensure of pharmacies (NCSL) [19].

Despite such regulation, concerns have been raised over the accuracy and safety of medications manufactured by compounding pharmacies. A report completed by the U.S. FDA in 2006 found that in 36 samples of medication from compounding pharmacies, 12 (33%) failed to meet standards for potency and uniformity. The U.S. FDA suggested that the route cause of such concerns relates directly to the compounding process itself [20]. Within Canada, following a national investigation of diluted chemotherapeutic medicines in 2012, the Ontario Ministry of Health and Long-Term Care made a series of recommendation designed to minimizing future compounding errors within Canadian hospitals [21].

Specific to testosterone, the safety and accuracy of the active ingredients within compounded products is not well established. As such, the primary objective of the current study was to evaluate the accuracy of the testosterone concentrations within testosterone gels and creams manufactured by compounding pharmacies.

Methods

This study was approved by the Research Ethics Board at Mount Sinai Hospital.

Compounding Pharmacies

Ten randomly selected compounding pharmacies within the greater Toronto area (GTA) were presented with a standardized prescription for compounded testosterone gel or cream. All pharmacies were active members of the Association of Compounding Pharmacies of Canada and were blinded to the nature of the study. Prior to inclusion, all pharmacies confirmed their experience and comfort in compounding testosterone products.