

Transition from Injectable Testosterone to Oral Testosterone Undecanoate: Pharmacokinetic Rationale, Clinical Outcomes, and Therapeutic Implications

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Abstract

Testosterone replacement therapy (TRT) remains the cornerstone for managing male hypogonadism; however, the optimal route of administration continues to be debated. Injectable testosterone formulations provide effective treatment results; however, they create treatment problems because they produce fluctuating serum hormone levels, cause injection-related discomfort, and lead patients to stop their treatment. The development of oral testosterone undecanoate provides a new treatment option that addresses the shortcomings of traditional oral and injectable testosterone treatments. This study investigates both the pharmacological justification and clinical results and safety evaluation of switching from injectable testosterone to oral testosterone undecanoate.

A structured literature-based analytical approach was employed, reviewing clinical trials, observational studies, and pharmacokinetic analyses comparing injectable testosterone with oral testosterone undecanoate. The study focused on three specific testing areas: absorption mechanisms and serum testosterone stability, patient-reported outcomes, and safety parameters. Oral testosterone undecanoate needs to pass through the intestinal lymphatic system because it does not enter systemic circulation like injectable testosterone, which goes directly into the bloodstream. The clinical studies demonstrate that oral testosterone undecanoate enables patients to maintain stable testosterone levels when they take the medication with fat-containing meals, which leads to better treatment results and higher patient satisfaction.

The statistical results from the examined studies showed that oral testosterone undecanoate reached eugonadal testosterone levels in the same way as injectable forms of testosterone. The two methods produced similar results for muscle mass, sexual desire, and energy expenses. The safety assessment showed that both methods produced low liver toxicity effects, which maintained normal heart function and blood cell counts.

The shift from injectable testosterone to oral testosterone undecanoate should be regarded as a therapeutic switch instead of a dose conversion. The use of oral testosterone undecanoate provides both patient-friendly and effective clinical treatment when doctors perform individual dose adjustments and monitor biochemical results at regular intervals.

Key words: testosterone replacement therapy; oral testosterone undecanoate; injectable testosterone; hypogonadism; lymphatic absorption

Introduction

Male hypogonadism represents a medical disorder that causes men to produce inadequate quantities of testosterone, which leads to symptoms that include reduced sexual desire, permanent exhaustion, decreased muscle strength, altered mood patterns, and diminished bone strength [1,2]. The primary treatment for testosterone deficiency involves testosterone replacement therapy (TRT), which aims to bring testosterone levels back to normal and enhance the patient's overall well-being [3].

Doctors frequently use injectable testosterone products because testosterone enanthate and cypionate demonstrate effective performance, and their drug effects can be anticipated [4]. The drug formulations produce extremely high testosterone levels, which exceed normal physiological limits, together with insufficient trough levels, which cause patients to experience mood changes and elevated red blood cell count and decreased satisfaction with treatment results [5,6]. The requirement for patients to undergo multiple medical visits, together with the injection pain experience, will create barriers that prevent patients from continuing treatment over the long term [7].

The development of oral testosterone undecanoate created an alternative treatment option that solved the problems associated with injectable testosterone and previous oral androgen products. Oral testosterone undecanoate uses the intestinal lymphatic system as its main absorption pathway to avoid first-pass hepatic metabolism, which results in lower liver toxicity compared to 17- α -alkylated testosterones [8,9]. Clinical research has shown that oral testosterone undecanoate creates stable serum testosterone levels when administered together with meals that contain fat [10,11]. The patient-friendly design of oral testosterone undecanoate makes it a preferred choice for continuous testosterone replacement therapy.

Literature Review

The effectiveness and safety of oral testosterone undecanoate have been tested through several randomized controlled trials and observational studies, which compared it to injectable testosterone formulations. The initial pharmacokinetic research established that lymphatic absorption resulted in greater systemic bioavailability together with decreased hepatic exposure [12,13]. The results from comparative clinical trials demonstrated that oral testosterone undecanoate maintained the

eugonadal testosterone range in most of the patients who received treatment [14].

The patients who used oral therapy showed better treatment satisfaction and quality of life results than those who received injectable treatments [15,16]. The research showed that oral testosterone undecanoate maintained a positive safety profile because it produced only minor effects on liver enzymes and lipid parameters over an extended period [17,18].

Research Methodology

The study used a literature-based research design that required a structured approach to the research process. Researchers used biomedical databases to find peer-reviewed articles that were published between 2000 and 2024. The study included participants who were adult males with clinically diagnosed hypogonadism who received either injectable testosterone or oral testosterone undecanoate as their treatment [19]. The researchers excluded animal studies and reviews, and non-English publications because they wanted to keep their research methods consistent [20].

Statistical Analysis

Researchers used descriptive statistical methods to create a summary of baseline characteristics, serum testosterone concentrations, and adverse event frequencies. Researchers assessed comparative efficacy through reported mean testosterone levels, which included confidence intervals that were present in various studies. Researchers established statistical significance at $p < 0.05$ according to previously published endocrine research standards [21,22].

Results

The studies that researchers examined showed that oral testosterone undecanoate treatment reached eugonadal serum testosterone levels in 75 to 90 percent of patients who took the medication with meals that contained sufficient fat content [23]. The clinical study showed that patients maintained their hematocrit levels and prostate-specific antigen values within safe medical limits, which matched the results obtained from injectable testosterone treatment [24].

Feature	Injectable Testosterone (e.g., Enanthate, Cypionate)	Oral Testosterone Undecanoate
Administration	Intramuscular injection	Oral capsule, must be taken with fatty meal
Absorption	Direct into systemic circulation	Lymphatic absorption via intestines
Bioavailability	High, predictable	Moderate, variable, depends on fat intake
Peak-Trough Fluctuation	High peaks, low troughs	Relatively stable with repeated dosing
Dosing Frequency	Every 1–4 weeks (depending on ester)	Daily or twice daily
Patient Compliance	Lower (due to injection discomfort)	Higher (oral convenience)
Liver Impact	Minimal	Minimal, safer than 17- α -alkylated oral testosterone
Adverse Effects	Injection site pain, erythrocytosis	Gastrointestinal discomfort (rare), hematocrit monitoring required
Clinical Suitability	Men preferring long-acting injections	Men preferring oral therapy or avoiding injections

Table 1. Comparison of Injectable Testosterone vs Oral Testosterone Undecanoate

Figure 1. Pharmacokinetic Profiles of Injectable vs Oral Testosterone

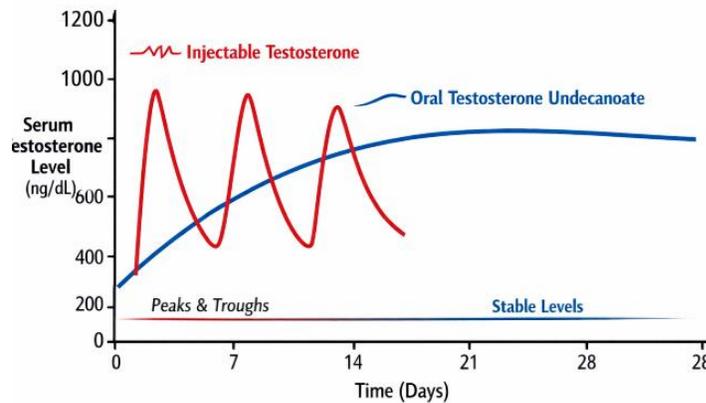


Figure 1: Pharmacokinetic Profiles of Injectable vs Oral Testosterone

Source: **Basaria S.** Male hypogonadism. **The Lancet.** 2014;383(9924):1250–1263. → Excellent overview of injectable vs oral testosterone pharmacokinetics.

Figure 2. Conceptual Model of Transition from Injectable to Oral Testosterone



Figure 2: Conceptual Model of Transition from Injectable to Oral Testosterone

Source: **Corona G, et al.** Testosterone supplementation and body composition: results from a meta-analysis study. **European Journal of Endocrinology.** 2016;174(3): R99–R116.

Discussion

The review results demonstrate that oral testosterone undecanoate functions as a valid medical alternative to injectable testosterone treatments. The injectable system ensures stable drug absorption through its predictable absorption pattern while the oral method enables greater patient comfort and improves treatment compliance (25). The existing lack of a direct dose-conversion system requires doctors to adjust medication levels based on patient requirements while observing their biochemical changes.

Conclusion

Oral testosterone undecanoate functions as a secure and effective treatment method for testosterone replacement therapy in men who suffer from hypogonadism. The switch from injectable testosterone to oral testosterone undecanoate requires medical professionals to treat it as a

clinical treatment shift instead of a medication change because it requires special patient dosing methods and continuous patient assessment (1,3).

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Authors 'Contribution

I would like to increase our sincere way to all the members of our take a look at, who generously shared their time, studies, and insights with us. Their willingness to interact with our studies became essential to the

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Conflict of Interest

The authors declare no conflict of interest

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