Supraphysiologic Testosterone Concentrations and Androgenic Adverse Effects After Subcutaneous Testosterone Pellet Therapy in Menopausal Women: A Case Series

Leia Verret, BSPS, Pharm.D. Candidate[1] Shannon W. Finks, Pharm.D.[1,2]

[1]The University of Tennessee Health Science Center College of Pharmacy, [2]Züp Medical Services, Memphis Tennessee

Background

- Testosterone therapy use for menopausal symptoms in women is increasing despite the absence of a U.S. Food and Drug Administration (FDA) approved formulation.
- Some patients receive compounded or subcutaneous pellet-based products.
- Subcutaneous pellets may result in prolonged and variable exposure due to unpredictable pharmacokinetics.
- This variability can lead to supraphysiologic testosterone concentrations and androgenic adverse effects.
- Despite these clinical concerns, real-world data describing affected patients from testosterone pellet therapy remains limited.

Purpose

- To characterize testosterone serum concentrations and associated adverse effects among menopausal women who received testosterone pellet therapy from external providers and subsequently presented to a pharmacist-led menopause clinic.

Methods

Study Design:

- A retrospective descriptive case series of symptomatic patients.

Population:

- 14 postmenopausal women (≥40) presenting with adverse effects after receiving testosterone pellets from external clinics.

Data Collected:

- Total and free testosterone levels, reported adverse events, and symptom resolution post intervention.

Statistical Analysis:

- Descriptive statistics and Spearman correlation analysis to evaluate the dose-response relationship.

Results

Table 1. Patient Characteristics and Hormone Concentrations

N=14	Mean	Reference Range	Percentage of patients with supraphysiologic levels	Mean fold-elevation above the ULN
Total Testosterone	204.5 ± 100.0 ng/mL	9-55 ng/mL	100%	3.7x
Free Testosterone	25.7 ± 13.5 pg/mL	1.1-5.8 pg/mL	100%	4.4x
ADEs per patient	2.0 ± 1.5	-	-	-

Figure 1. Frequency of Androgenic Adverse Events (N=14)

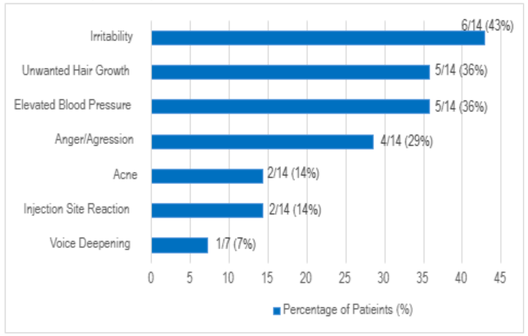
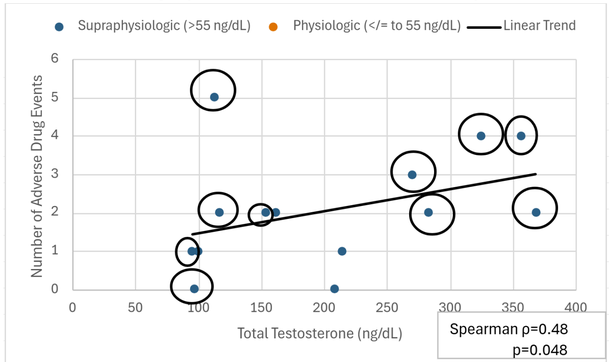


Figure 2. Total Testosterone vs. Number of Adverse Events (N=14; blue=supraphysiologic)

- The Spearman correlation revealed no significant relationship between total testosterone concentration and adverse event burden (ρ=0.478, p=0.084). Circled data points indicate resolution of symptoms after discontinuation of pellets.



Discussion

- Symptomatic postmenopausal women receiving testosterone pellet therapy exhibited markedly supraphysiologic testosterone concentrations (~3-6x physiologic range) with multiple androgenic adverse effects.
- The observed adverse effect profile (e.g., acne, hirsutism, alopecia, mood changes, voice alterations) is biologically consistent with androgen excess.
- Findings support concerns that pellet-based delivery may result in prolonged and variable systemic exposure due to unpredictable pharmacokinetics.
- This study adds to limited real-world data describing patients presenting with adverse effects following testosterone pellet therapy.
- Use of pellet-based formulations may reflect the absence of FDA-approved testosterone products for women, potentially contributing to variability in dosing and monitoring.
- Interpretation is limited by symptom-based selection, lack of a comparator group, and incomplete exposure characterization.
- Results are descriptive and hypothesis-generating but highlight a potential safety signal.
- Prospective, controlled studies are needed to better define pharmacokinetics, safety, and monitoring strategies for testosterone therapy in women.

Limitations

- Retrospective descriptive case series without a comparator group; causality between testosterone pellet therapy and adverse events cannot be established.
- Symptom-based inclusion introduces selection bias, as all patients presented with adverse effects, limiting generalizability.
- Incidence and prevalence of adverse events among all testosterone pellet users cannot be determined.
- Incomplete characterization of exposure(e.g., pellet dose, timing) and non-standardized laboratory assessment may affect interpretation.
- Findings are hypothesis-generating and should be interpreted as descriptive rather than causal.

Conclusion

- Testosterone pellet therapy in symptomatic patients was associated with consistently supraphysiologic testosterone concentrations (~3-4x above physiologic range) and clinically significant androgenic adverse effects, including neuropsychiatric symptoms
- No clear relationship between reported exposure and adverse effect burden was observed, suggesting potential interpatient variability in response and challenges in predicting toxicity.
- These findings underscore the importance of evidence-based prescribing, physiologic dosing strategies, and careful clinical monitoring when considering testosterone therapy in menopausal women.

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