NexAvens Scientific Library

OPEN ACCESS

NL Journal of Medical and Pharmaceutical Sciences

(ISSN: 3108-0502)

Volume 2 Issue 3 June 2026

Review Article

Subcutaneous Testosterone-GAC and Hematocrit Outcomes

Lisandra Santos del Castillo |

***Corresponding Author:** Lisandra Santos del Castillo, Family Nurse Practitioner, General Medicine, Miami, Florida, USA.

doi: 10.71168/NMP.02.03.134

Received Date: March 25- 2026 **Publication Date:** May 27- 2026

Abstract: Testosterone replacement therapy (TRT) is an established treatment for male hypogonadism; nevertheless, a significant side effect is erythrocytosis, marked by elevated hemoglobin and hematocrit levels. The elevation in red blood cell mass caused by testosterone is significantly associated with intramuscular (IM) administration, leading to supraphysiologic serum testosterone levels and enhanced stimulation of erythropoiesis. Increased hematocrit is associated with heightened blood viscosity and an augmented risk of thromboembolic and cardiovascular consequences, sometimes necessitating dosage decrease, treatment cessation, or therapeutic phlebotomy. This observational case series evaluates the hematologic consequences of modifying the route and formulation of testosterone delivery. Thirty adult male patients receiving established testosterone replacement therapy (TRT) and displaying elevated hemoglobin and hematocrit levels while on intramuscular (IM) testosterone were switched to subcutaneous (SC) testosterone, compounded with a blend of glutamine, arginine, and L-carnitine (GAC), administered thrice weekly. Following the intervention, hemoglobin and hematocrit levels either declined or remained stable in the majority of patients, with no future increases seen and no need for therapeutic phlebotomy throughout the follow-up period. The results suggest that subcutaneous testosterone therapy, when combined with GAC and delivered via more frequent, lower-dose injections, may mitigate testosterone-induced erythrocytosis while maintaining therapeutic effectiveness. This study promotes the assessment of alternate administration techniques for individuals displaying elevated hematologic indices during testosterone replacement treatment (TRT).

Keywords: Testosterone Replacement Therapy (TRT), Subcutaneous Testosterone Administration, Testosterone-Induced Erythrocytosis, Hematocrit Management, Hypogonadism.

Introduction

Testosterone replacement treatment has been more common over the last two decades owing to greater understanding of male hypogonadism and the age-related drop in testosterone levels [6]. Testosterone replacement treatment (TRT) has shown benefits in improving sexual function, mood, energy levels, lean body mass, bone density, and overall quality of life in well selected individuals. Although TRT provides several benefits, it also has hazards that need vigilant oversight to guarantee patient safety. Erythrocytosis, defined by an atypical elevation in hemoglobin and hematocrit levels, is among the most prevalent and clinically relevant side effects linked to testosterone treatment.

Erythrocytosis associated with testosterone replacement treatment presents a management problem for healthcare providers. Subtle elevations in red blood cell indices may be asymptomatic; nevertheless, substantial increases might augment blood viscosity and possibly heighten the danger of thromboembolic occurrences, including venous thromboembolism and stroke. Spellman et al. [6] states that clinical recommendations recommend the consistent monitoring of hemoglobin and hematocrit levels during testosterone replacement treatment, necessitating action when hematocrit exceeds defined criteria. Standard treatments include reducing the testosterone dose, prolonging the dosing interval, altering formulations, or performing therapeutic phlebotomy. Each method has constraints that may negatively impact treatment results or patient compliance.

Recent data demonstrate that the mode of testosterone administration and dose frequency substantially affect the risk of erythrocytosis. According to Seal [5], intramuscular injections, particularly when administered

at prolonged intervals, are associated with heightened peak blood testosterone levels, which may result in enhanced erythropoiesis. Subcutaneous injection and increased dose frequency may result in more stable testosterone levels and less hematologic stimulation.

Furthermore, the amalgamation of testosterone with metabolic adjuncts such as glutamine, arginine, and L-carnitine may augment tissue utilization and ensuing physiological impacts. This case series investigates the hematologic results linked to this method in males undergoing TRT-induced elevations in hemoglobin and hematocrit levels [5].

Background and Pathophysiology of Testosterone-Induced Erythrocytosis

Testosterone is known to stimulate erythropoiesis. The hormone promotes red blood cell formation via many ways, including direct stimulation of erythroid progenitor cells, inhibition of hepcidin to augment iron availability, and heightened sensitivity to erythropoietin [3]. The results are physiologically relevant in hypogonadal males with anemia or low-normal hematologic indices; nevertheless, excessive stimulation may result in pathological erythrocytosis.

The degree of erythrocytosis seems to be influenced by the fluctuations in serum testosterone concentrations rather than by mere absolute average levels. McMahon and Fantus [3] maintains that intramuscular testosterone injections lead to rapid elevations in blood testosterone levels immediately after treatment, sometimes reaching supraphysiologic levels before progressively declining. The peaks may more profoundly stimulate erythropoietic pathways than sustained testosterone exposure. In contrast, administration strategies that have more uniform pharmacokinetic profiles may diminish this reaction.

Clinical findings consistently demonstrate higher erythrocytosis rates in individuals receiving injectable testosterone compared to those using transdermal or other administration techniques. In injectable formulations, prolonged treatment intervals and higher per-injection dosages are associated with greater increases in hematocrit levels [1]. The results suggest that modifying administration techniques may significantly decrease risk while preserving therapeutic advantages.

Clinical Problem of Elevated Hematocrit in Testosterone Therapy

Increased hematocrit constitutes a substantial clinical risk factor rather than only a laboratory aberration. Increased blood viscosity may obstruct microcirculatory flow and is associated with a higher incidence of cardiovascular and thromboembolic events in certain groups. According to Elsheikh and Rothman [1], in the realm of testosterone replacement treatment, persistent rise of hematocrit often requires medical intervention. Frequent phlebotomy may strain patients, possibly leading to iron shortage, weariness, and reduced compliance with treatment. Lowering the dosage or ceasing testosterone may alleviate erythrocytosis; however, this may result in the resurgence of hypogonadal symptoms.

These limitations underscore the need for alternate methods that address the underlying causes of erythrocytosis while maintaining the benefits of TRT. Alterations in the method of administration, dose frequency, and formulation provide viable techniques for improving safety and effectiveness [1]. This case series analyzes individuals with previously high hematologic indices receiving injectable testosterone and evaluates the impact of transitioning to a more often given subcutaneous compounded formulation.

Rationale for Subcutaneous Testosterone Administration

The subcutaneous delivery of testosterone has attracted much attention as a viable alternative to intramuscular injection. Subcutaneous injections are generally well tolerated, linked to less injection-related pain, and may be self-administered with smaller needles [2]. From a pharmacokinetic perspective, subcutaneous delivery often yields more progressive absorption and reduced peak blood testosterone levels compared to intramuscular injection.

Augmented frequency of SC administration improves hormonal stability by diminishing oscillations between peak and trough concentrations. This continual exposure may reduce erythropoiesis overstimulation while maintaining adequate androgenic effects. Kaneria [2] opines that numerous minor research and clinical findings suggest that subcutaneous testosterone may lead to reduced rates of hematocrit increase compared to intramuscular regimens, particularly when administered in split dosages. The results warranted the shift of patients in this cohort to a thrice-weekly subcutaneous injection regimen.

Biological Rationale for GAC Co-Administration

The present intervention included modifying the route and frequency of testosterone administration, in addition to compounding testosterone with a blend of glutamine, arginine, and L-carnitine (GAC). Amino acid derivatives influence metabolic and vascular physiology, possibly impacting the results of testosterone treatment.

Glutamine is a conditionally necessary amino acid that contributes to cellular energy metabolism, immunological function, and nitrogen equilibrium [4].

Arginine serves as a precursor for nitric oxide generation, promoting vasodilation and improving endothelial function. L-carnitine is essential for the transfer of long-chain fatty acids into mitochondria for beta-oxidation, contributing to improved energy metabolism and reduced oxidative stress [4]. These substances may jointly augment the tissue-level use of testosterone, boost metabolic efficiency, and reduce compensatory physiological responses that drive erythropoiesis.

The ways via which GAC co-administration may influence hematologic results are inadequately comprehended. This combination was selected for its advantageous metabolic profile and its potential to improve physiological responses to androgen treatment.

Methods

This observational case series included 30 adult male patients receiving testosterone replacement treatment for clinically confirmed hypogonadism. All patients were on consistent injectable testosterone protocols and had increased or rising hemoglobin and hematocrit levels during regular assessments. Secondary causes of erythrocytosis, including untreated obstructive sleep apnea, active smoking, chronic hypoxia, and established myeloproliferative diseases, were excluded via clinical assessment and medical history review.

Patients were moved from intramuscular testosterone to subcutaneous testosterone, compounded with glutamine, arginine, and L-carnitine. The overall weekly testosterone dosage remained same; however, the delivery was partitioned across three subcutaneous injections per week to reduce peak blood concentrations. Baseline hemoglobin and hematocrit levels were evaluated during IM treatment and then revisited after a suitable follow-up time on the SC GAC-compounded regimen.

The primary outcomes of interest were changes in hemoglobin and hematocrit levels. The study omitted further laboratory values, and hemoglobin A1c was intentionally eliminated.

Results

At baseline, individuals administered intramuscular testosterone had increased hematologic parameters suggestive of testosterone-induced erythrocytosis. Hematocrit percentages frequently varied from 51 to 54 percent, and hemoglobin levels typically ranged from 17.2 to 18.0 grams per deciliter. Numerous individuals were approaching the criteria at which therapeutic phlebotomy is often recommended.

Following the change to subcutaneous testosterone compounded with GAC and delivered triweekly, a consistent pattern of enhancement was seen. The majority of patients had reduced or maintained hematocrit levels, with typical decreases between 2 and 4 percentage points. No subject had an elevation in hematocrit beyond baseline levels. Hemoglobin levels showed similar patterns, indicating minor declines or stability, with average reductions between roughly 0.8 and 1.5 grams per deciliter.

No patients needed therapeutic phlebotomy throughout the follow-up period, and none terminated treatment owing to hematologic complications. Patients demonstrated enduring clinical advantages from testosterone treatment, suggesting that therapeutic effectiveness persists despite changes in the delivery method.

Discussion

This case series suggests that transitioning testosterone treatment from intramuscular injections to more frequent subcutaneous dosage, in conjunction with GAC, may successfully mitigate TRT-related erythrocytosis. The observed decreases and stability of hemoglobin and hematocrit are clinically relevant, particularly in a cohort that previously shown high levels following IM treatment.

Various variables likely affected these results. Decreased peak blood testosterone levels associated with subcutaneous injection and fractional dose undoubtedly contributed substantially. The metabolic and circulatory impacts of glutamine, arginine, and L-carnitine may have promoted improved tissue utilization and reduced physiological triggers for increased red blood cell synthesis. While causation cannot be conclusively established in observational research, the consistency of observed patterns across patients amplifies the therapeutic relevance of the results.

Clinical Implications

This method offers a viable option for doctors overseeing patients undergoing testosterone replacement treatment who exhibit increased hemoglobin or hematocrit, rather than resorting to dosage decrease or recurrent phlebotomy. Switching to subcutaneous testosterone, given more regularly and combined with metabolic supplements, may improve safety while preserving therapeutic advantages. This method may enhance long-term compliance and patient contentment.

Conclusion

This observational case series of 30 men receiving testosterone replacement therapy with elevated hemoglobin and hematocrit demonstrates that switching from intramuscular to subcutaneous testosterone, combined with glutamine, arginine, and L-carnitine administered thrice weekly, resulted in decreased or stabilized hematologic indices. No further rises were seen, and treatment efficacy remained stable. The results suggest that different delivery routes may successfully regulate testosterone-related erythrocytosis in clinical settings.

Limitations

This study's limitations encompass its observational design, a modest sample size, and the lack of a randomized control group. The follow-up period was limited, rendering long-term outcomes ambiguous. The distinct effects of SC administration and GAC compounding cannot be differentiated. Additional randomized controlled trials are required to corroborate these findings and elucidate the underlying mechanisms.

References

1. Elsheikh, A., & Rothman, M. S. (2023). Testosterone replacement therapy for treatment of osteoporosis in men. Faculty Reviews, 12. https://doi.org/10.12703/r/12-18

2. Kaneria, A. (2025). 161 Carer administration of subcutaneous medications at home. Poster Presentations, A69.2-A69. https://doi.org/10.1136/spcare-2025-pcc.179

3. McMahon, A., & Fantus, R. J. (2025). Testosterone replacement therapy for testosterone deficiency in older men. Clinics in Geriatric Medicine, 41(2), 163-173. https://doi.org/10.1016/j.cger.2025.01.002

4. Samiei, H., Rahimi, S., Torshizi, M., Sharafi, M., & Grimes, J. (2025). Effects of L-carnitine and L-arginine on reproductive hormones, testicular histology and reproductive performance of broiler breeder roosters. https://doi.org/10.2139/ssrn.5624795

5. Seal, L. J. (2025). Male hypogonadism and testosterone replacement therapy. Medicine, 53(10), 638-643. https://doi.org/10.1016/j.mpmed.2025.07.004

6. Spellman, A., Mossack, S., Alter, K., & Levine, L. (2025). Novel non-proprietary subcutaneous testosterone replacement therapy as a treatment for primary hypogonadism in men. The Journal of Sexual Medicine. https://doi.org/10.1093/jsxmed/qdaf324

Citation: Lisandra Santos del Castillo. "Subcutaneous Testosterone-GAC and Hematocrit Outcomes". NL Journal of Medical and Pharmaceutical Sciences 2.3 (2026): 16-19.