Efficacy of human chorionic gonadotropin hormone in restoring spermatogenesis in men using non-prescribed androgens: a retrospective analysis of real-world data

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Objective: To study the efficacy of human chorionic gonadotropin (hCG) in restoring spermatogenesis in men using non-prescribed androgens who are unwilling to discontinue their use.
Design: Retrospective analysis.
Patients: Nineteen men attending a harm reduction clinic in the Netherlands from April 2023 to July 2024, who had been using androgens for at least three months and were treated with hCG without ceasing androgen use.
Exposure: Continuous use of non-prescribed androgens and hCG therapy administered as part of a harm reduction strategy.
Main Outcome Measures: Change in total sperm count (TSC) and total motile sperm counts (TMSC) from baseline to after three to six months of hCG treatment.
Results: The mean TSC increased significantly from 18.0 million to 146.9 million after hCG treatment and TMSC increased from 1.1 million at baseline to 66.9 million post-treatment. The number of men with a normal TMSC increased from 5% to 58%. No statistically significant predictors of TSC change were identified through regression analysis.
Conclusion: Human chorionic gonadotropin appears to be effective in improving spermatogenesis in the majority of men who continue non-prescribed androgen use, whereas some men remain oligospermic or azoospermic. These findings support the cautious inclusion of hCG in harm reduction strategies, while emphasizing the need for further research and individualized counseling. (F S Rep® 2025;■:■–■. ©2025 by American Society for Reproductive Medicine.)

Key Words: Anabolic steroids, androgen use, harm reduction, infertility, azoospermia

Anabolic androgenic steroids, commonly referred to as androgens, are used by a growing group of amateur strength athletes (1). These athletes obtain androgens through illicit web shops or local dealers, using them for non-medical purposes, typically to enhance their appearance, performance, and strength. The primary androgens utilized by athletes include testosterone, drostanolone, and boldenone, with many others accessible on the black market (2). Characteristically, androgens are administered in cycles lasting several weeks or months, during which multiple androgens are combined in high doses. This is followed by a recovery phase where no androgens are used. In contrast, the blast-and-cruise method involves athletes maintaining a relatively low dose of testosterone between cycles to prevent muscle loss and withdrawal symptoms (3).

A well-known effect of androgen use is the complete suppression of gonadotropins, leading to the inhibition of endogenous testosterone production

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and spermatogenesis (4). In our prospective study of 100 men using androgens, three-quarters of the participants had a total sperm count (TSC) below 40 million at the end of the cycle, and one-quarter exhibited azoospermia (2). The time required for spermatogenesis to recover to baseline levels after the end of a cycle was approximately one year, provided the athlete ceased androgen use entirely. Recovery of spermatogenesis may be prolonged when men undergo multiple consecutive cycles or begin a new cycle before full recovery is achieved.

In practice, we encounter men with low fertility who use androgens but also wish to have children. Based on the literature, there is ample justification to encourage these athletes to cease androgen use for an extended period and wait for the spontaneous recovery of spermatogenesis. The real challenge arises, however, when the athlete is unwilling or unable to quit androgens because of withdrawal symptoms such as fatigue, depressive symptoms, and low libido. These symptoms are typically the result of androgen-induced hypogonadism, the duration of which appears to be partially dependent on the cumulative prior use of androgens (5, 6). Men who adopt the blast-and-cruise method, particularly those involved in bodybuilding competitions, may be especially hesitant to take a prolonged break from androgen use, even if it would be necessary to start a family.

Athletes who use androgens often tend to self-medicate symptoms or side effects (7), with human chorionic gonadotropin (hCG) frequently recommended in bodybuilding forums to restore endogenous testosterone production and fertility. As an analogue to luteinizing hormone (LH), hCG stimulates Leydig cells, elevating intratesticular testosterone levels and supporting spermatogenesis. Clinically, hCG is indicated for restoring fertility in men with hypogonadotropic hypogonadism (8) and has been proposed for restoring fertility in androgen users (9).

In the Netherlands, people who use androgens have the option to visit a harm reduction clinic that specializes in promoting safer androgen use and monitoring health. It offers services such as blood analysis and cardiac ultrasound to detect early signs of organ damage. Healthcare providers in this clinic adhere to harm reduction principles (10, 11), meaning they respect the athlete's decision to use androgens and approach them without moral judgment. When side effects of androgen use arise, such as hypertension, dyslipidemia, or gynecomastia, treatments are provided using antihypertensives, lipid-lowering drugs, and anti-estrogens, respectively. In cases in which an athlete uses androgens and wishes to have children but is unwilling to cease their use, hCG is prescribed on the basis of the aforementioned presumed efficacy.

In this retrospective analysis, we aimed to address the research question of whether hCG is effective in restoring fertility in men who use non-prescribed androgens. We hypothesized that hCG would improve spermatogenesis in the majority of these men. While the methodology has inherent limitations, this analysis provides the first clinical data on the efficacy of this hormone treatment in the real-world context of continued androgen use. The findings may offer valuable insights to guide future harm reduction practices for this group of athletes.

MATERIALS AND METHODS

The retrospective analysis included all cases from the founding of the clinic in April 2023 until July 2024, when this analysis was conducted. Cases were eligible for inclusion if they met the following criteria: the individual and their partner expressed an active desire to have children during treatment or intended to start trying to conceive within one year of commencing treatment; they had been using androgens for at least three months at the time of the initial clinic visit and had not recently, i.e., in the past 3 months, used hCG; they were unwilling to cease androgen use in an effort to restore fertility or had failed to do so successfully before; and they consented to treatment with hCG. The hCG treatment typically involved Ovitrelle, a single-dose injection pen containing 250 mcg of recombinant hCG, equivalent to 6,500 IU, which could be administered in multiple smaller doses (increments of 10 mcg = 260 IU). The standard treatment protocol consisted of three injections of 520–1,040 IU per week, although variations on this protocol were possible on the basis of patient-specific factors such as cost considerations, past experience with hCG (e.g., side effects), urgency of achieving conception, and patient preferences. Besides hCG treatment, athletes were advised to stop the use of high-dose androgen cycles and transition to a maintenance dose of 125–150 mg of a testosterone ester (usually enanthate) per week, which the athletes obtained through their usual underground channels. This approach aimed to mitigate withdrawal symptoms while minimizing suppression of spermatogenesis. None of the men reported use of other anabolic steroids. Sperm analysis was performed at baseline and then again after 3 to 6 months, with the specific timing depending largely on the athlete's schedule.

Data from the case files were de-identified for this analysis, so informed consent was not required. Additionally, approval by an institutional review board was not necessary, because this study involved retrospective analysis of anonymized data, without any direct patient intervention or potential harm to participants. In addition to demographic information, records included medical history, current medication use, and details of past androgen use, especially the duration of non-stop androgen use before the hCG treatment. Semen samples were collected during a clinic visit through masturbation in a designated room. Before semen collection, the ejaculation container was weighed and recorded, and this was repeated after ejaculation so that the ejaculation weight, and therefore volume, could be calculated assuming a semen density of 1 g/mL (12). Sperm parameters were determined after liquefaction using the FDA and CE approved automated sperm quality analyzer, SQA-iO, manufactured by Medical Electronic Systems. The TSC was calculated by multiplying the semen volume by the sperm concentration. Motility was included in the analysis as total motile sperm count (TMSC), which provides a more comprehensive measure of fertility potential. Morphology was excluded because of subjectivity and inter-observer variability.

In the analysis, descriptive statistics were calculated for key parameters, followed by a paired t-test to assess the significance of TSC and TMSC changes before and after

treatment. Subsequently, a linear regression analysis was conducted to explore the potential predictors of changes in TSC and TMSC. The regression model included age, duration of prior androgen use, weeks between analyses, and weekly hCG dose as independent variables. R-squared values, regression equations, and p-values were reported to determine the strength and significance of these relationships.

RESULTS

A total of 19 men were eligible for this analysis, with a mean age of 33 years (standard deviation [SD] 6.2 years) and a mean duration of prior non-stop androgen use of 43 months (SD 35 months). The sperm test results per case are summarized in Table 1. At the first sperm analysis, 15 men had azoospermia, 3 had oligozoospermia, and 1 had a normal TMSC, that is, >15 million. The mean TSC and TMSC at the first analysis were 18.0 (SD 18.1) and 1.1 million (SD 3.7), respectively. Treatment with hCG was initiated, with a mean dose of 2,273 IU per week (SD 1,167 IU). The second sperm analysis was conducted after a median duration of 17 weeks (interquartile range 8 weeks). Both TSC and TMSC improved in 16 (84%) and 17 (89%) out of 19 cases, respectively, with mean TSC increasing to 146.9 million (SD 207, $P=.008$), and the mean TMSC increasing to 66.8 million (SD 126, $P=.011$). Following treatment, 11 men (58%) achieved a normalized TMSC, whereas 6 remained oligozoospermic and 2 azoospermic (Fig. 1). At the time of manuscript preparation, six pregnancies were reported among the cases included in this study.

Linear regression analysis was performed to explore the factors potentially influencing the observed change in TSC and TMSC after hCG treatment. The analysis included age, duration of prior androgen use, weeks between the analyses, and the weekly hCG dose as independent variables. None of the factors were statistically significant predictors of the change in TSC and TMSC ($P>.05$ for all variables), although time between analysis was marginally close to significance (coefficient 3.59 with $P=.08$ for TMC; coefficient 1.18 with $P=.10$ for TSMC).

DISCUSSION

The results of this retrospective analysis indicate that hCG is highly effective in restoring spermatogenesis in the majority of men with low sperm counts because of non-prescribed androgen use and who wish to continue their use. The observed mean increase in TMSC (from 1.1 million to 66.8 million over approximately 4–5 months) was substantial and statistically significant ($P=.011$), despite the small sample size. Although the analysis did not structurally include data on conception rates after treatment, the reported pregnancies underscore the clinical relevance of hCG treatment in this population.

The hCG treatment was not equally effective in all men, with TSCs ranging from 3.8 to 770.3 million after several months of therapy, with two men remaining azoospermic. Longer treatment duration appeared to correlate with higher TSCs, but this relationship was not statistically significant. It is known that TSC may continue to rise for up to one year after initiating hCG treatment, as demonstrated by Kohn et al. (2017) in a cohort of 66 men with infertility after testosterone use (13). This may especially hold true if exogenous testosterone is continued. Additionally, older age and the duration of prior testosterone therapy may be linked to slower sperm count recovery (14), whilst our regression analysis did not find these to be significant predictors. Factors such as testicle size and low body mass index may also serve as predictors (15), but these were not assessed in our cases. Despite these considerations, individual response to treatment is likely influenced by other factors, including genetic variability and overall health status.

Interestingly, the hCG dose did not significantly influence changes in TMSC (coefficient 0.011, $P=.21$), consistent with the understanding that even minimal doses of hCG are sufficient to normalize intratesticular testosterone concentrations (16, 17). Once these concentrations are normalized, further dosage increases may boost endogenous testosterone production, but not significantly enhance spermatogenesis, because higher-than-normal intratesticular testosterone levels are unlikely to yield additional benefits. This finding suggests that the effectiveness of fertility restoration depends more on the consistent administration of hCG rather than the dosage itself. In our cases we recommended continuing hCG treatment until conception was achieved and extending it several months into gestation, given the general risk of spontaneous abortion. Prolonging treatment in this manner helps ensure stable fertility during the critical early stages of pregnancy, because a decline in sperm count would likely follow the discontinuation of hCG therapy.

Our findings thus support the use of hCG as a viable option for men using androgens who wish to restore fertility without discontinuing androgen use, which is of significant practical importance for urological, endocrinological, and fertility clinics. Limited data exist on the concurrent use of hCG and testosterone for fertility preservation. Avila et al. (2010) and Hsieh et al. (2013) demonstrated that hCG can preserve spermatogenesis in men undergoing testosterone replacement therapy (18, 19). However, these studies did not specifically address the restoration of suppressed spermatogenesis after prolonged androgen use. Karila et al. (2004) provided some indirect evidence, reporting that men self-administering hCG during androgen use had a mean TSC of 33 million, with only 6% exhibiting azoospermia (20). Our findings align with these studies while extending their applicability to real-world harm reduction settings.

Ideally, discontinuing androgens should remain the primary recommendation, because this not only allows for the spontaneous restoration of fertility but also enables the recovery of endogenous testosterone production and mitigates other negative health effects of androgen use. However, the reality is that some men are determined to continue using androgens, even after extensive counseling. In such cases, it is crucial for healthcare practitioners to adopt harm reduction principles and take a pragmatic approach. A recommendation of how to treat subfertile men using androgens with hCG is displayed in Figure 2. Refusing to offer hCG treatment in this context may result in persistently low fertility. Consequently, couples may seek help from fertility clinics, where

TABLE 1

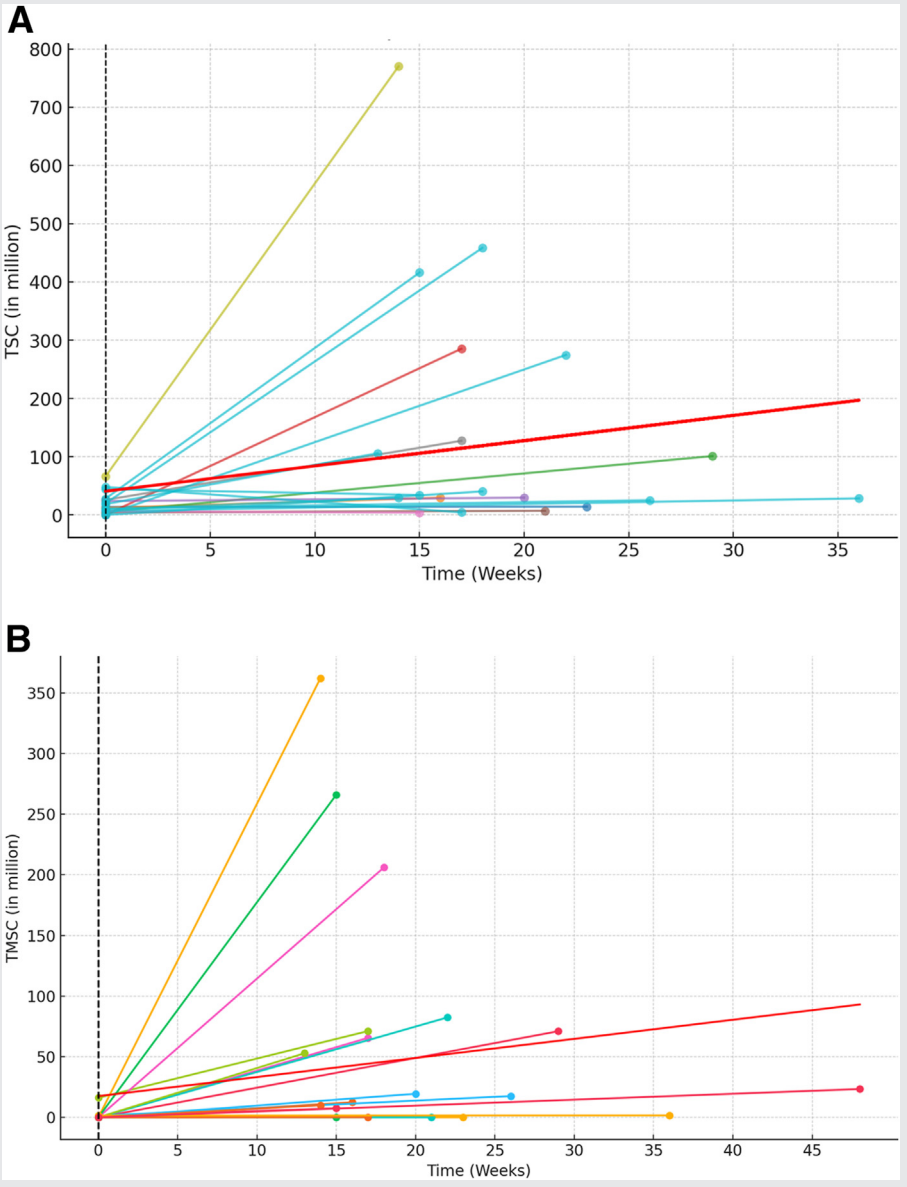
All cases who started hCG while continuing androgen use.

Case	Age	1st analysis (TSC + TMSC in 10^6)		2nd analysis (TSC + TMSC in 10^6)		Absolute change (in 10^6)		Weeks between analyses	hCG dosage (IU per week)
1	30	0.0	0.0	285.3	65.6	+285.3	+65.6	17	3,120
2	30	0.0	0.0	274.7	82.4	+274.7	+82.7	22	1,560
3	32	0.0	0.0	40.3	23.4	+40.3	+23.4	48	1,560
4	32	5.1	0.0	101.0	71.1	+95.9	+71.1	29	1,560
5	32	4.2	0.0	7.0	0.0	+2.9	+0.0	21	4,680
6	29	6.3	0.0	3.8	0.0	–2.5	+0.0	15	1,560
7	36	9.0	0.0	29.6	10.1	+20.6	+10.1	14	3,120
8	34	6.6	1.58	28.4	1.70	+21.8	+0.12	36	780
9	47	10.8	1.40	25.2	17.6	+14.4	+16.2	26	4,680
10	37	13.6	0.0	14.2	0.71	+0.6	+0.71	23	2,340
11	25	11.9	0.0	29.6	12.4	+17.7	+12.4	16	1,820
12	29	18.5	0.0	105.8	52.9	+87.3	+52.9	13	1,560
13	34	19.9	0.0	458.3	206	+438.4	+206	18	1,560
14	25	28.0	0.0	416.0	266	+388.0	+266	15	1,560
15	28	23.7	0.0	29.6	19.5	+5.9	+19.5	20	1,560
16	29	25.7	16.2	127.2	71.2	+101.5	+55	17	2,340
17	33	44.1	0.89	34.2	7.52	–9.9	+6.63	15	4,680
18	49	48.0	0.0	4.4	0.22	–43.6		17	1,560
19	32	66.2	0.0	770.3	362	+704.1		14	1,560

The 1st analysis denotes total sperm count (TSC) and total motile sperm count (TMSC) around the intake visit. The 2nd analysis shows the results after several months of hCG therapy.

Smit. hCG for spermatogenesis in androgen use. F S Rep 2025.

FIGURE 1



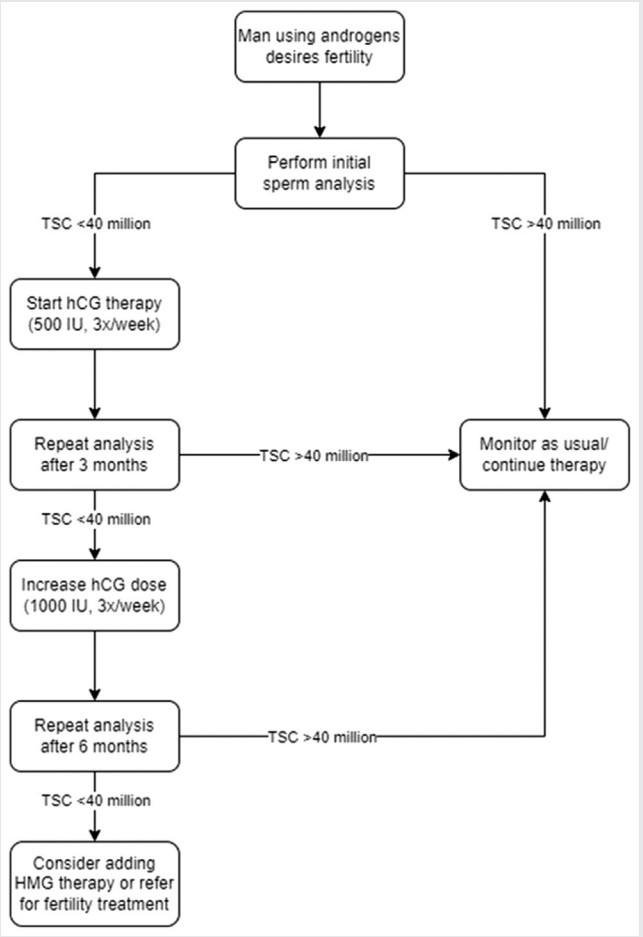
(**A**) Total sperm count (TSC) and (**B**) total motile sperm count (TMSC) over time, with time set to 0 for the first analysis and progressing to the time of the second analysis. Each line represents an individual case, showing the change in TSC from the first to the second analysis. The vertical dashed line marks the time of the first analysis and the red lines are the calculated regression lines for: a) TSC = 40.65 + 4.34 × (time in weeks), and b) TSMC = 6.83 + 5.12 × (time in weeks).

Smit. hCG for spermatogenesis in androgen use. F S Rep 2025.

men might hesitate to disclose their androgen use because of fear of moral judgment and prejudice (21). This can lead to unnecessary and expensive medical investigations in both partners. If fertility techniques such as intrauterine insemination or in vitro fertilization are required, the female partner may need to undergo intensive hormonal treatments, which carry potential side effects and the risk of repeated disappointment and stress (22).

While our study provides valuable insights, several limitations must be acknowledged. First, the study is retrospective in nature and lacked randomization and a control group. The absence of follow-up sperm analyses prevents us from assessing the long-term sustainability of the observed improvements in TSC, particularly if hCG treatment is discontinued. We also cannot exclude the possibility of later declines in semen parameters, although there is little reason

FIGURE 2



Flowchart showing recommended clinical management of fertility in men using androgens who are unwilling to discontinue their use. Treatment should not necessarily be initiated sooner than 1 year before the man has a desire to conceive.

Smit. hCG for spermatogenesis in androgen use. F S Rep 2025.

to assume this would occur. The small sample size and the homogeneity of the study population, i.e., all participants were from a single clinic, further limit the generalizability of these findings to a broader population. In addition, our analysis did not include important factors such as the presence of varicocele and testicular size, which may have influenced the variability in response to hCG therapy. All participants in this analysis continued a maintenance dose of testosterone while using hCG, leaving it unclear whether similar results would be observed in men undergoing high-dose androgen cycles. Finally, the focus on TSC and TMSC as the primary outcome meant that other crucial parameters of sperm health, such as morphology, were not included in the analysis. The study of Karila et al. (2004), for instance, found that higher hCG dose was associated with a higher amount of morphologically abnormal spermatozoa (20). Qualitative sperm parameters are also essential to fertility and should be evaluated in future studies to provide a more comprehensive understanding of the impact of hCG therapy.

Future research should also focus on prospective, randomized controlled trials to confirm our findings and further explore the mechanisms underlying individual variability in response to hCG treatment in this particular population. Different dosing regimens should be experimented, the time to optimal effect should be assessed, as well as the combined use of hCG with other therapies, such as recombinant follicle-stimulating hormone.

CONCLUSIONS

This retrospective analysis suggests that hCG can improve spermatogenesis in the majority of men who continue to use non-prescribed androgens. However, a significant proportion remained oligospermic or azoospermic despite treatment, highlighting that hCG is not universally effective. These findings support the cautious incorporation of hCG therapy into harm reduction strategies for this population, while emphasizing the need for individualized counseling to

ensure realistic expectations. Further research is required to refine treatment protocols, explore long-term outcomes, and identify factors that influence individual responses to hCG therapy.

CRediT Authorship Contribution Statement

Diederik L. Smit: Writing – original draft, Supervision, Investigation, Formal analysis, Data curation, Conceptualization. **Tijs Verdegaal:** Writing – review & editing, Data curation. **Peter Bond:** Writing – review & editing.

Declaration of Interests

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