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A Single Centre Study to Describe the Changes in Serum Testosterone Concentration Following Application of Testosterone Gel in Post-Menopausal Women With Hypoactive Sexual Desire Disorder (HSSD) Already Receiving This as Part of Usual Care in Conjunction With Oestrogen-Containing Hormone Replacement Treatment (HRT)

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ABSTRACT

Introduction: Hypoactive Sexual Desire Disorder (HSDD) is characterized by a long-term decrease in sexual desire (low-libido) causing personal distress. HSDD predominantly affects post-menopausal women or following oophorectomy. Despite the clear indication that testosterone action could overcome the symptoms of HSDD by elevating testosterone levels, there is little research concerning this. For decades many post-menopausal women have been prescribed off-label testosterone, an approved therapy for men, at a modified dose. The purpose of this study was to conduct an exploratory pharmacokinetic analysis in post-menopausal women with low sexual desire consistent with HSDD already established on treatment with Testosterone gel (Testogel 16.2 mg/g Gel in Pump, Besins Healthcare (UK) Ltd.).

Methods: Twenty-four women applying Testogel 16.2 mg/g via pump once every 3 or 4 days and had been prescribed Testogel 16.2 mg/g for at least 6 months were included. All were additionally taking oestrogen-based hormone replacement therapy (HRT). They attended for a testosterone day curve with Testogel 16.2 mg/g at the dose of 20.25 mg applied after an initial blood test. Samples were taken 2-hourly for 10 h and at 24 h post-Testogel 16.2 mg/g application. Testosterone was measured by mass spectrometry. The Female Sexual Functioning Index (FSFI) was completed by the women. Pharmacokinetic parameters of maximum concentration (Cmax), average concentration (Cavg), time to Cmax (Tmax), Area under curve (AUC) and half-life ($t_{1/2}$) were determined with and without adjustment for baseline testosterone.

Results: Mean age of the women was 53.7 ± 6.8 years, and the mean BMI was 27.4 ± 4.3 kg/m^2. Mean blood pressure was 126/75 mmHg. The unadjusted median Cmax testosterone concentration was 6.25 nmol/L (range 1.3–26.1), and Cavg was 4.51 nmol/L (range 0.93–20.21). AUC testosterone varied substantially from 35.9 to 458 nmol.h/L (median 121.8). The baseline-

adjusted median Cmax was 3.55 nmol/L and the Cavg was 1.64 nmol/L. There was considerable variability between individuals in both measured Cmax in testosterone through the day (1.3−26.1 nmol/L) The AUC testosterone ranged from 39.45 to 181.8 nmol.h/L. FSFI median score was 26.5/36 (25%−75% interquartile range 18−30) with the highest domain scores for sexual satisfaction and arousal (4.2/6) and slightly lower scores for orgasm and desire (4.0/6), and no reported issues regarding pain on intercourse. All women subjectively reported an improvement in sexual function with Testogel 16.2 mg/g. No symptoms of hyperandrogenism were reported.

Conclusion: We found considerable variation in all parameters relating to testosterone pharmacokinetics in women applying 20.25 mg testosterone gel in a 3 or 4-day regime. All women described clinical benefit prior to the study, with no reports of androgen-related side-effects. Progression to a daily licensed topical formulation of testosterone, where this is not available, would be a positive step for women's health.

1 | Introduction

Naturally occurring testosterone in pre-menopausal women is predominantly produced by the ovaries, either via direct ovarian production or derived from ovary-produced hormones. Healthy young women produce approximately 300 microg of testosterone per day, of which about half is derived from the ovaries [1]. Testosterone levels are found to gradually decrease with age, particularly in menopausal women [1]. The circulating levels of (dehydroepiandrosterone) DHEA, androstenedione, and total and free testosterone are highest during the third decade of life and decline in the remaining reproductive years. Around the age of 50, free and total testosterone levels decrease by about 50% [2]. In women, positive associations have been identified between testosterone levels and sexual function [3].

Hypoactive Sexual Desire Disorder (HSDD) is characterized by a long-term decrease in sexual desire (low libido), causing personal distress [2]. HSDD predominantly affects post-menopausal women or those who undergo oophorectomy. Despite the observational evidence that testosterone supplementation can overcome the symptoms of HSDD by elevating testosterone levels, there is a paucity of clinical trial evidence.

Since the 1970s, testosterone has been given to post-menopausal women who suffer from low libido and low energy. Testosterone therapy has proven beneficial, resulting in a self-reported increase in satisfaction from sexual encounters, increased intensity of sexual desire, and a better sexual response to stimuli in the post-menopausal population [4]. Testosterone therapy is associated with benefits such as improvements in mood, well-being, libido, sexual arousal, and satisfaction [4, 5].

The primary intention of this study was not to define optimal dosing or establish efficacy, but rather to describe real-world pharmacokinetic exposure in post-menopausal women already receiving testosterone gel as part of routine clinical care.

This study was exploratory and descriptive in nature, and no formal power calculation was performed. Statistical comparisons were undertaken on an exploratory basis to identify potential patterns rather than to formally test predefined hypotheses.

We determined the blood levels of testosterone in post-menopausal women treated with Testogel 16.2 mg/g for the aforementioned symptoms over a period of 24 h post-application of Testogel 16.2 mg/g in natural menopause women or those with previous oophorectomy receiving testosterone for low sexual desire consistent with HSDD, slowing of cognition, and diminished vitality.

2 | Methods

Ethics approval was granted by the Research Ethics Committee, Health Research Authority, NHS (23/LO/0912). In a group of post-menopausal women applying Testogel 16.2 mg/g at the dose of 20.25 mg every 3 days or every 4 days as part of their usual care together with oestrogen ± progestogen hormone replacement therapy (HRT), we measured serum testosterone and free androgen index (FAI).

Recruited patients were already established on Testogel 16.2 mg/g treatment. A total of 27 patients were enrolled, but only 24 presented for serial blood tests. Eleven patients were taking combined HRT. The doses of oestrogen ranged from 0.05 to 3.0 mg/day, whilst progesterone doses ranged up to 100 mg/day. Ten patients were on the intrauterine device (IUD) or pessary (Supporting Information S1: Table 1). Twelve patients were on the 3-day dosing regime and nine patients were on the 4-day dosing regime, with the remaining three patients on the alternate 3/4-day dosing regimen. The dose intervals (3 or 4 days) were selected by the participants, not by the researchers. Testogel was applied concurrently with the ingestion or application of estrogen-containing HRT. The application sites were the same as described in the Testogel pump product information sheet: the manufacturer advises applying one pump actuation of gel evenly onto clean, dry, intact skin over the upper arm [6]. Participants applied the gel at approximately the same time on the days of use, first thing in the morning. A fixed amount of gel was applied to the upper arms or shoulders using the Testogel pump. This provides a fixed dose actuation. No fasting or meal restrictions were enforced.

All patients invited to join the study were attending the Endocrinology clinic at a single endocrinology centre in the United Kingdom. All had clinically confirmed post-menopausal status via clinical history, last menstruation date and endocrine testing and were already being prescribed Testogel 16.2 mg/g by their general practitioners. They were aged between 40 and 65 years old. Serum LH and FSH were elevated (> 40 iu/L) in all women. Pre-Testogel, all had normal levels of circulating testosterone (< 1.6 nmol/L).

All of the participants were given a diary card in relation to Testogel administration for the 2 weeks prior to the day curve. Participants were closely monitored to ensure that they applied the Testogel as prescribed and that they applied the Testogel on the day of attendance for the day curve after the first blood sample was taken.

The participants attended for a testosterone day curve with Testosterone gel applied after an initial blood test. Samples were taken 2-hourly for 10 h and then at 24 h post-gel application. Testosterone was quantified using Shimadzu NEXUS UHPLC with 8060 NX Mass Spectrometry. The limit of quantitation (LOQ) for the assay was < 0.2 nmol/L, ensuring sensitivity suitable for detection in female samples. Internal quality control was performed at four concentration levels (0.6, 1.8, 5.4 and 31 nmol/L), with coefficients of variation (CV %) consistently below 4%. Circulating free testosterone was estimated using the Vermeulen equation [7] using the calculator at ISSAM [8].

Given that sampling was limited to 24 h post-application and that participants were established on long-term testosterone therapy, half-life estimates represent apparent half-lives derived from the post-Tmax segment and may be influenced by ongoing transdermal absorption rather than true terminal elimination.

The Female Sexual Functioning Index (FSFI) [9] was completed by each of the women.

2.1 | Statistical Analysis

Descriptives were analysed as mean, standard deviation, median and interquartile ranges as appropriate. The maximum concentration (Cmax) of testosterone and time to Cmax (Tmax) were determined by direct review of data. Testosterone concentrations at respective time intervals were utilised to calculate area under the curve (AUC) using the linear trapezoid method. Half-life ($t_{1/2}$) was calculated by running a log-linear regression of ln (concentration) versus post Tmax segment where there were at least 3 concentration time points following Tmax. Average testosterone concentration (Cavg) was calculated by dividing AUC by 24. Pharmacokinetic parameters were calculated using two complementary approaches. Unadjusted analyses represent total circulating testosterone concentrations and constitute the primary descriptive pharmacokinetic (PK) assessment. In addition, a secondary exploratory analysis was performed in which baseline (0 h) testosterone concentrations were subtracted ('zero-clamped') to estimate incremental exposure following the observed dosing episode. This approach was used to account for variable baseline concentrations resulting from prior intermittent dosing and should be interpreted as descriptive rather than as a conventional steady-state PK analysis.

Correlations between non-parametric variables were assessed using Spearman's rho, whilst comparisons between non-parametric variable ranks were assessed using Kruskal–Wallis and post-hoc tests.

3 | Results

The baseline data of the study population is shown in Table 1. The mean age of the women was 53.7 years, and the mean BMI was 27.4 kg/m^2. Mean blood pressure was 126/75 mmHg. The baseline testosterone did not show statistically significant correlations with any of the lipid parameters.

The key pharmacokinetic parameters of Cmax, Tmax, Cavg and $AUC_{0\text{-}24}$ with and without adjustment for baseline testosterone are shown in Table 2. The unadjusted parameters were consistently greater than when adjusted for baseline testosterone levels. However, Cmax and Tmax in both analyses showed wide variability, whilst the unadjusted Cavg and AUC values showed a wider spread compared to the adjusted model. The median Cavg values for unadjusted and adjusted models were 4.51 nmol/L (range 0.93–202.21) and 1.64 nmol/L (0.0–7.58), whilst the AUC_{0-24} were 108.35 and 39.45 nmol.h/L, respectively. The mean $t_{1/2}$ was 88.15 h with a large range. The 0 minimum values in the adjusted model resulted from one participant having lower than baseline testosterone day curve measurements.

TABLE 1 | Baseline characteristics of the study population.

Variable	*n*	Mean	SD	Median	IQR	Min	Max
Age (years)	24	54.04	6.71	54.5	48.5–57.25	44.0	67.0
Height (cm)	19	163.74	7.8	163	158.5–166.6	152	181.3
Weight (kg)	22	73.86	10.38	73.5	65.62–80.1	56.4	95.1
BMI (kg/m^2)	19	27.83	3.99	28.11	25.21–30.57	20.37	33.87
Systolic BP (mmHg)	24	125.58	14.69	127.5	118.0–135.25	93.0	155.0
Diastolic BP (mmHg)	24	74.04	10.99	76.5	66.5–81.5	53	93
HbA1c (mmol/mol)	18	37.5	6.08	35.5	34.25–39.0	28.0	55.0
Total Cholesterol (mmol/L)	18	5.13	0.96	5.1	4.6–5.76	3.7	7.6
HDL-C (mmol/L)	18	1.68	0.4	1.6	1.36–2.03	1.06	2.4
LDL-C (mmol/L)	18	2.72	0.95	2.66	2.05–3.18	1.12	5.12
Triglycerides (mmom/L)	18	1.64	0.91	1.3	1.02–2.06	0.63	4.1
Non-HDL-C (mmol/L)	18	3.41	1.18	3.55	2.55–4.07	0.8	6.3
CHR	18	3.22	1.0	3.05	2.65–3.82	1.8	5.8
Baseline Free Testosterone (nmol/L)	24	0.03	0.03	0.02	0.01–0.03	0.0	
Baseline Total Testosterone (nmol/L)	24	3.0	3.85	2.0	1.18–3.42	0.8	19.7

Abbreviations: BMI = body mass index, BP = blood pressure, HbA1c = glycated haemoglobin, HDL = HDL-cholesterol, CHR = cholesterol/HDL-cholesterol ratio, LDL = LDL-cholesterol, non-HDL = non-HDL cholesterol, TC = total cholesterol, TG = triglycerides.

TABLE 2 | Key pharmacokinetic parameter values for testosterone baseline, unadjusted and adjusted models.

Parameter	*N*	Mean	SD	Median	IQR	Min	Max
Unadjusted Cmax (nmol/L)	24	8.05	6.05	6.25	3.55–10.10	1.3	26.1
Unadjusted Tmax (h)	24	9.08	8.36	8.0	4.00–10.00	0.0	24.0
Unadjusted Cavg (nmol/L)	24	5.41	3.95	4.51	2.60–6.75	0.93	20.21
Unadjusted AUC (nmol·h/L)	24	129.92	94.89	108.35	62.4–162.3	22.4	485.0
Unadjusted t½ (h)	15	88.15	56.15	87.57	45.2–121.6	13.52	270.41
Baseline-adj Cmax (nmol/L)	24	5.04	5.0	3.55	1.20–6.85	0.0	21.3
Baseline-adj Tmax (h)	24	9.08	8.36	8.0	4.00–10.00	0.0	24.0
Baseline-adj Cavg (nmol/L)	24	2.68	2.58	1.64	0.60–3.55	0.0	7.58
Baseline-adj AUC (nmol·h/L)	24	64.22	61.89	39.45	14.4–84.9	0.0	181.8
Baseline-adj t½ (h)	15	34.83	44.35	17.62	8.9–42.6	2.52	150.36

Although median testosterone showed a smooth, slightly increasing profile through the day curve period, there was considerable variability between individuals in both measured Cmax in testosterone through the day (1.3−26.1 nmol/L and also in AUC_{0-24} testosterone (108.35– 485.0 nmol.h/L) (Figure 1a,b).

Similar patterns were seen for estimated free testosterone (Supporting Information S2: Figure 1a and 1b and Supporting Information S1: Table 2).

The AUC_{0-24} values of free testosterone as per the dosing regime are shown in Figure 2. There was a significant effect of dosing regimen on free testosterone AUC_{0-24} values (Kruskal–Wallis $H = 6.92$, $p = 0.03$). Pairwise comparisons revealed that the 4 days regime had greater AUC_{0-24} values compared to the 3 days regime ($p = 0.04$). In contrast, there were no significant differences in baseline-adjusted AUC_{0-24} rank values between dose regimens (Kruskal−Wallis H 1.60, $p = 0.45$).

There was no correlation between BMI and AUC_{0-24} total testosterone values (Spearman rank correlation $p = -0.19$, $p = 0.43$, $n = 19$), or AUC_{0-24} free testosterone values (Spearman rank correlation rho = −0.09, $p = 0.71$, $n = 19$).

FSFI median score was 26.5/36 (25%−75% interquartile range 18−30) with the highest domain scores for: sexual satisfaction and arousal (4.2/6) and slightly lower scores for orgasm and desire (4.0/6) and no reported issues re pain on intercourse.

There was no correlation between lipid parameters and unadjusted total or free testosterone AUC values, as shown in Table 3 below.

4 | Discussion

In the present study, we investigated the pharmacokinetic profile of a commercially available testosterone gel in postmenopausal women, administered in three dosing regimens, at a single endocrinology centre.

We have found considerable variation in all parameters relating to testosterone pharmacokinetics in women applying Testogel 16.2 mg/g. The wide dispersion in key pharmacokinetic parameters—Cmax, Tmax, AUC, and half-life reflect a significant variability in the absorption and systemic handling of testosterone in this study population.

The study is limited by its modest sample size and exploratory design and was not powered to detect between-regimen differences. Multiple statistical comparisons were performed without adjustment for multiplicity; consequently, *p* values should be interpreted descriptively and as hypothesis-generating rather than confirmatory. The findings are intended to characterise variability in real-world testosterone exposure rather than to inform definitive dosing recommendations.

Given the 2-h sampling intervals, it was possible that identification of an earlier peak concentration due to rapid early absorption may have been limited in some cases. Therefore, the reported Cmax values should be interpreted as observed rather than absolute. However, the reported AUC and Cavg values, which reflect overall exposure, are less sensitive to sampling frequency and better reflect clinically relevant testosterone levels.

This exploratory, uncontrolled study describes the real-world pharmacokinetic profile of transdermal testosterone gel in postmenopausal women already established on treatment. The absence of a control group and the modest sample size could limit the conclusions regarding optimal dosing or efficacy; rather, the data provide descriptive insight into the variability of systemic testosterone exposure under a commonly used off-label regimen.

Transdermal application has the potential to affect the kinetics of absorption through variation in skin permeability, skin reservoir effects, body composition, and site of application. Despite standard dosing, differences in application site and skin thickness contribute towards subject-level variance in dose exposure. Approximately 9%–14% of the applied testosterone dose enters systemic circulation following topical application. However, absorption rates vary between individuals due to factors including skin characteristics, application technique, and environmental conditions [10–12].

Testogel 16.2 mg/g, originally formulated as a male product, delivers 20.25 mg of testosterone per application [6]. In contrast, female-specific transdermal testosterone products deliver significantly lower doses of testosterone (i.e., AndroFeme 10 mg/mL cream) [13]. Controlled pharmacokinetic studies of female-dose transdermal testosterone in postmenopausal women demonstrate more predictable exposure and lower peak-to-trough variability

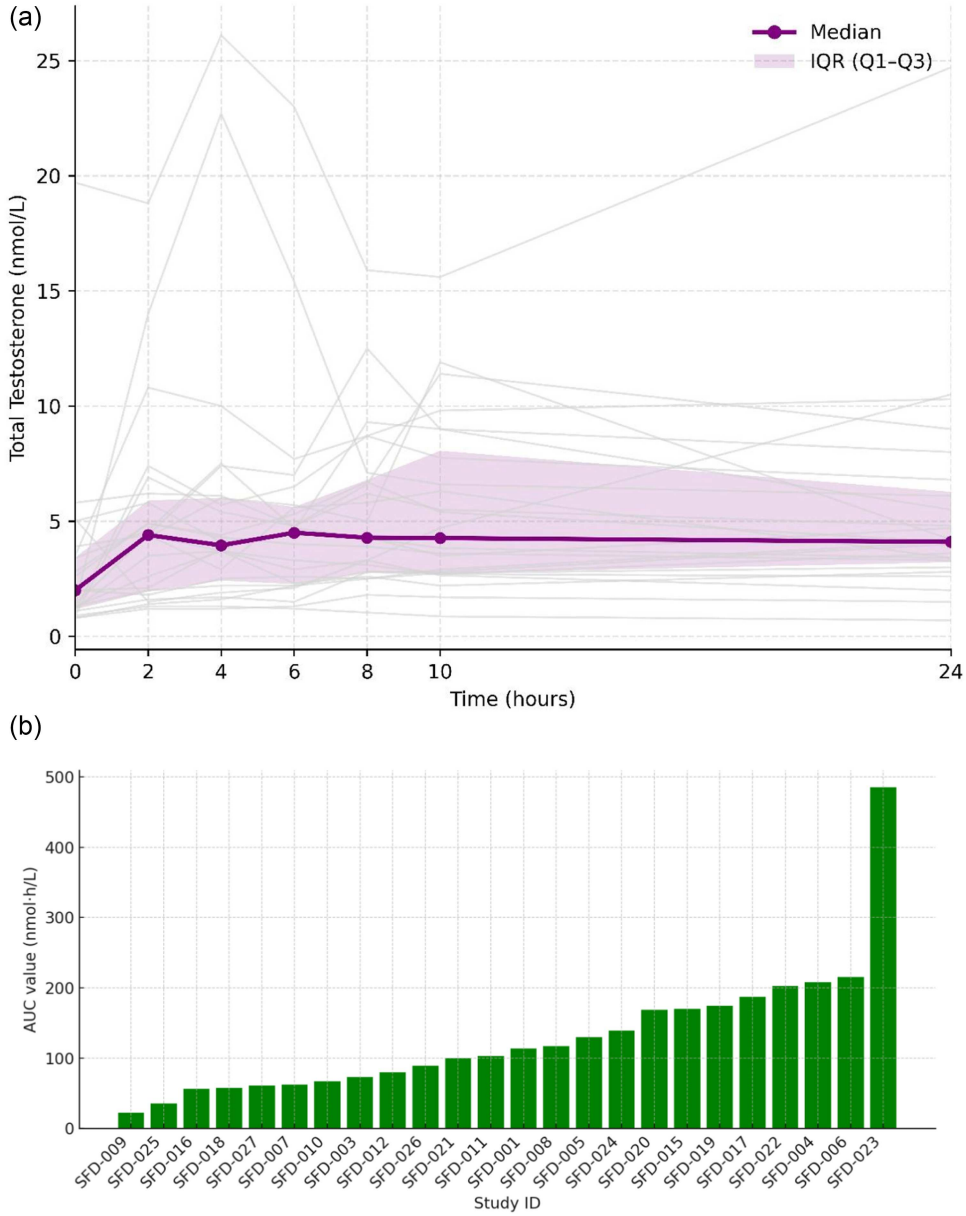

FIGURE 1 | (a) Unadjusted total testosterone day curve with median profile. Each line denotes an individual patient. (b) Unadjusted total testosterone Area Under the Curve values. Each bar denotes an individual patient. [Color figure can be viewed at wileyonlinelibrary.com]

than observed in our real-world cohort. Singh et al. reported that daily application of 4.4–13.2 mg testosterone gel produced dose-dependent increases in total and free testosterone, with concentrations declining by 24–36 h post-application, supporting once-daily dosing and physiological targeting; higher doses resulted in supraphysiological exposure [12]. Similarly, Fooladi et al. showed that daily application of a 5 mg female-specific testosterone cream achieved relatively stable 24-h concentrations within the physiological female range, whereas higher doses increased exposure [14]. In contrast, our study of intermittent 3–4-day dosing using a male-formulated gel demonstrated substantially greater inter-individual variability, higher peak concentrations, and less predictable exposure. Together, these comparisons support the view that daily female-dose formulations provide more consistent pharmacokinetics and safer titration than intermittent use of higher male-formulated products in women.

FSFI score indicated reasonable sexual function in this group of women treated with Testogel 16.2 mg/g. This mirrors previous findings in women with HSDD treated with testosterone [15, 16].

The pharmacokinetic analysis of total testosterone demonstrated notable differences between unadjusted and baseline-adjusted (0-clamped) results. Unadjusted AUC_{0-24} and Cmax values were consistently higher, reflecting the contribution of baseline testosterone with high variability (0.8−19.7 nmol/L). The fact that the participants had received Testogel 16.2 mg/g for 6 months at the time of measurement would also have contributed to this. Baseline-adjusted values (0-clamped) provided a more accurate estimate of incremental exposure due to treatment, with mean Cavg reduced from approximately 5.4 to 2.7 nmol/L. Variability (SD) was high in both approaches, reflecting inter-subject differences. Tmax values were similar

across methods, as expected, since baseline concentration affects magnitude but not the timing of peak concentrations.

We tested 3 dosing regimens, with Testogel 16.2 mg/g applied every 3rd day, 4th day, and alternatively. When unadjusted for baseline testosterone, those who received 4th day treatment showed significantly greater AUC values compared to those on the 3rd day regime. Whilst this finding seems counterintuitive, it serves to demonstrate in a real-world perspective, how intermittent dosing schedules may lead to day-to-day variability in testosterone kinetics.

We observed significantly greater AUC values for the 4-day regimen group compared to the 3-day group. Given that there was no significant difference in SHBG levels between the two groups, this difference was likely to inter-individual variability in absorption and elimination kinetics. First, the variability in baseline testosterone would have been driven by residual carryover exposure resulting from long-term established testosterone therapy. Differences in timing intervals since last application could influence baseline and early curve concentrations, thus increasing unadjusted AUC values. This is supported by our finding that dose regimen differences were not observed in the adjusted analysis. Second, the group sizes were somewhat modest and exposure was highly variable, making results susceptible to skew from a small number of higher-exposure individuals.

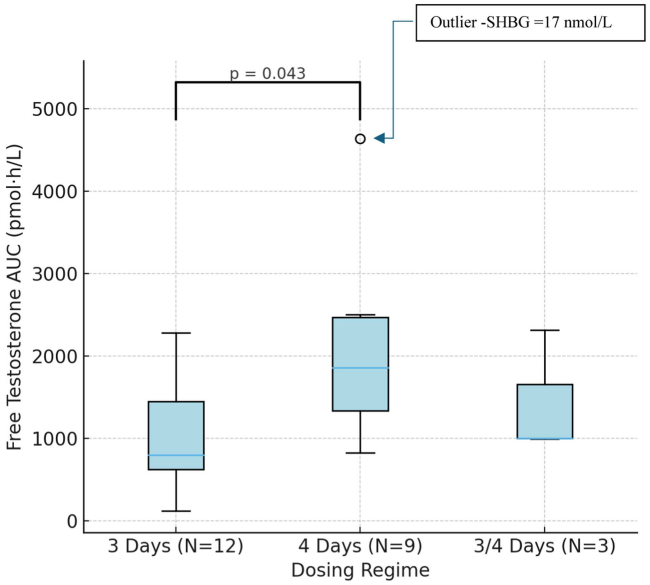

FIGURE 2 | Free Testosterone AUC by dosing regime. The outlier in the 4-day regime (case SFD-022) had relatively very low SHBG levels, resulting in a higher circulating free testosterone. [Color figure can be viewed at wileyonlinelibrary.com]

The 24-h sampling window was not designed to fully capture the terminal elimination phase of transdermal testosterone. Consequently, the reported half-life values likely reflect continued absorption from the skin reservoir rather than true systemic clearance. Furthermore, as participants were established on long-term testosterone therapy, the observed profiles represent steady-state day curves rather than single-dose pharmacokinetics.

In a single participant, testosterone concentrations during the day curve fell below baseline values. This may reflect normal analytical and biological variability at low concentrations, residual baseline exposure from previous dosing, or variability in transdermal absorption or application technique. Repeat testing was not performed, as the study was designed as a single-visit, descriptive pharmacokinetic assessment within routine clinical care.

The observed high variability in half-life and AUC with the male formulated testosterone gel used highlights important implication regarding developing more effective dosing strategies. The erratic absorption kinetics results in high inter-individual variability in testosterone exposure. Conversely, a 'female-dose' transdermal product would be expected to reduce this by delivering more consistent amounts of testosterone, thus reducing peak and trough fluctuations. Such a dosing regimen could be expected to maximise therapeutic efficacy and compliance whilst minimizing adverse effects.

Several participants exhibited supraphysiological testosterone concentrations, highlighting the risks inherent in direct adaptation of a male-formulated product for female use. Our findings should therefore not be interpreted as evidence that biochemical monitoring or physiological targeting is unnecessary. Rather, they re-affirm the current guidance for cautious dosing, regular monitoring, and maintenance of testosterone levels within the physiological female range with close monitoring for sings of supraphysiological exposure such as acne, hirsutism, lowering of the voice and dyslipidaemia.

Regarding limitations, we did not collect data on haematocrit, liver function, acne/hirsutism scoring, as this was not a clinical trial. However, routine monitoring in the clinic has not shown

TABLE 3 | Association between lipid parameters and total and free testosterone AUC0-24 ($n = 18$).

	Total testosterone AUC_{0-24}		Free testosterone AUC_{0-24}	
Parameter	**Spearmen rho**	***p***	**Spearman rho**	***p***
TC	−0.098	0.698	0.011	0.964
HDL-C	−0.252	0.313	−0.267	0.285
CHR	0.25	0.3	0.224	0.371
LDL-C	0.191	0.448	0.135	0.593
TG	−0.034	0.893	−0.034	0.893
Non-HDL	0.065	0.806	−0.022	0.936

Abbreviations: CHR, cholesterol ratio; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; Non-HDL, Non-High Density Lipoprotein Cholesterol; TC, total cholesterol; TG, Triglycerides.

any raised haematocrit or aberrant liver function tests, nor any acne/unwanted hair growth in more than 45 women. Also, sampling was limited to 24 h post-application and therefore did not capture testosterone concentrations over the next 48–72 h which would have been informative in assessing the pharmacokinetic profile across the full 3–4 day dosing interval. Hence, this study cannot determine whether trough concentrations remain within a physiological female range throughout the dose period. Future studies should incorporate extended sampling across the entire dosing cycle to better inform dosing frequency.

It should also be noted that, although participants were treated in routine clinical practice for symptoms of low sexual desire consistent with HSDD, this study did not include formal diagnostic confirmation of HSDD using structured criteria, and FSFI scores were collected for descriptive purposes rather than diagnostic classification.

In summary, within this real-world cohort of women already established on testosterone therapy, patient-reported clinical benefit was observed despite substantial inter-individual variability in serum testosterone exposure. However, in the absence of prospective efficacy data, these descriptive findings should not be interpreted as evidence that any variability in serum testosterone is benign or that the need for specific biochemical targets should be overlooked. We have provided supportive pharmacokinetic evidence of variability in serum testosterone with the off-label male formulation of Testogel when applied in women.

As all participants were already established on testosterone therapy and pre-Testogel FSFI scores are unavailable, conclusions about clinical benefit must be interpreted cautiously. Nevertheless, given the breadth of our Cmax and $AUC_{0\text{-}24}$ distributions, our data reinforce calls for licensed, female-dose products to improve pharmacokinetic predictability and facilitate safer titration. Increasing numbers of women are being prescribed testosterone gel, hence the need stated for a daily licensed testosterone gel preparation in Europe.

In 2025, the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) approved AndroFeme for the treatment of HSDD in postmenopausal women [17]. In countries where the preparation is available, it is important to inform women of this option when considering testosterone therapy, particularly in the context of achieving more predictable and physiologically appropriate testosterone exposure.

Testosterone supplementation should only be considered in women who complain of low sexual desire after a biopsychosocial approach has excluded other causes such as relationship, psychological and medication-related HSDD [18]. It is hoped that in due course a female-specific testosterone formulation will be available more widely.

Acknowledgements

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Ethics Statements

Ethics approval was granted by the Research Ethics Committee, Health Research Authority, NHS (23/LO/0912).

Conflicts of Interest

The study was funded by Besins Healthcare, with the funding paid to the Northern Care Alliance NHS Trust, where the study was conducted. None of the co-authors received any direct payment, nor did their salary include any contribution from Besins Healthcare. The other authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.
Supplementary Figure 1a: Free testosterone day curve with median profile. Each line denotes an individual patient. **Supplementary Figure 1b:** Free testosterone Area Under the Curve values. Each bar denotes an individual patient. **Supplementary Table 1:** Hormone Replacement Therapy of study participants. This is includes the 3 individuals who did not ultimately participate in the study. **Supplementary Table 2:** Summary of pharmacokinetic parameters for free testosterone.