Fractionated Testosterone Gel Replacement Therapy in Clinical Practice: A Real-World Exploratory Clinical Experience

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INTRODUCTION

Testosterone replacement therapy (TRT) with transdermal gel is widely used in men with hypogonadism. Guidelines recommend once-daily application with monitoring of serum testosterone at peak levels. However, real-world clinical experience suggests that peak–trough fluctuations in some patients, potentially affecting hormonal stability and treatment tolerability. The impact of dose fractionation remains unclear.

OBJECTIVES

To compare hormonal profiles and biochemical safety parameters between once-daily and twice-daily (fractionated) testosterone gel administration in hypogonadal men receiving the same total daily dose.

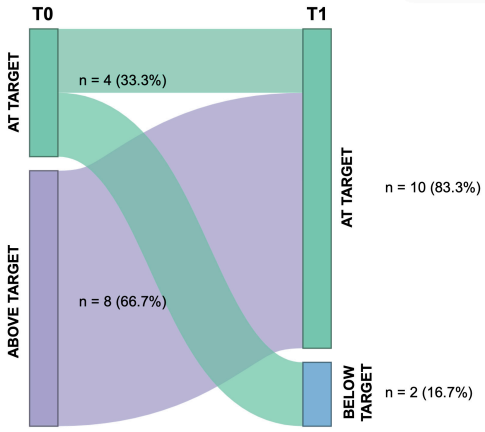
MATERIALS AND METHODS

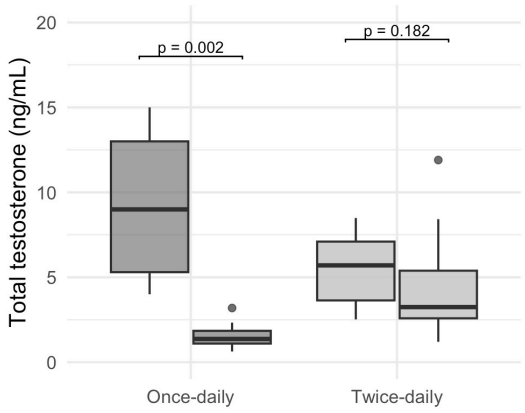
We retrospectively identified hypogonadal men treated with 2% testosterone gel who transitioned from once-daily to twice-daily dosing, maintaining the same total daily dose. Eligible patients had serum total testosterone (TT) measurements available at both peak (3 hours post-application) and nadir (pre-dose). Hormonal and laboratory parameters under the two regimens were compared.

RESULTS

Twelve patients met inclusion criteria. Fractionated dosing was associated with lower peak TT levels [9.0 (5.3 – 13.0) vs. 5.7 (3.6 – 7.1) ng/mL, paired difference −3.6 ng/mL (95% CI: −4.9 to −1.8)] and higher nadir TT levels [1.4 (1.1 – 1.8) vs. 3.2 (2.6 – 5.4) ng/mL, paired difference 2.6 ng/mL (95% CI: 1.2 to 5.1)], resulting in a reduced difference between peak-to-pre-dose difference within the observed sampling window. The proportion of patients achieving target TT levels at peak increased (33% vs. 83%). Calculated free testosterone showed a similar pattern. No clinically relevant differences were observed in luteinizing hormone, prostate-specific antigen, haematocrit, or haemoglobin.

	TRT One-daily dose	TRT Twice-daily dose	HL paired difference (95% CI)	p
TT (ng/mL) at peak	9.0 (5.3 – 13.0)	5.7 (3.6 – 7.1)	-3.6 [-4.9 to -1.8]	0.002
cFT (ng/L) at peak	93.6 (87.9 – 97.2)	78.7 (59.1 – 92.8)	-16.7 [-37.9 to -1.2]	0.048
TT (ng/mL) at nadir	1.4 (1.1 – 1.8)	3.2 (2.6 – 5.4)	2.6 [1.2 to 5.1]	0.005
cFT (ng/L) at nadir	27.9 (21.1 – 34.5)	88.3 (76.4 – 158.3)	87.6 [40.7 to 159.8]	0.018
LH (IU/L)	2.6 (0.4 – 12.2)	1.2 (0 – 2.9)	-	0.374
PSA (mcg/l)	0.9 (0.6 – 1.1)	0.8 (0.5 – 1.0)	-	0.120
HCT (%)	47.0 (44.0 – 48.0)	47.8 (46.0 – 48.1)	-	0.753
Hb (g/dl)	16 (15.8 – 16.7)	16.2 (15.8 – 16.4)	-	0.720





DISCUSSION AND CONCLUSIONS

In this real-world cohort, fractionated testosterone gel administration was associated with a higher proportion of patients achieving biochemical targets and with a reduced peak-to-pre-dose difference within the observed sampling window, without short-term biochemical safety signals. These findings should be considered hypothesis-generating.

BIBLIOGRAPHY

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