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Minoxidil 1 mg Orally *versus* Minoxidil 5% Solution Topically for the Treatment of Female Pattern Hair Loss: A Randomized Clinical Trial

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48 **Conflict of interest:** Rodney Sinclair is director and stockholder of Samson
49 Medical PTY LTD that holds patents on the use of oral minoxidil to treat hair
50 loss. The other authors have no conflict of interest to declare.

51

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58 **Keywords:** Female pattern hair loss, androgenetic alopecia, minoxidil, oral,
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64 **Abbreviation list**

65 TM – Topical minoxidil;

66 FDA – Food and Drug Administration;

67 FPHL – Female pattern hair loss;

68 OM – Oral minoxidil;

69 UNESP – Universidade Estadual Paulista;

70 WAA-QoL – Women's Androgenetic Alopecia Quality of Life Questionnaire;

71 CI 95% – confidence interval;

72 bpm – beats *per* minute (heart rate)

73

74 Topical minoxidil (TM) is the only FDA-approved drug for treatment of female
75 pattern hair loss (FPHL). Premature discontinuation of treatment commonly
76 occurs due to lack of perceived efficacy, adverse effects or altered hair texture.
77 Low-dose oral minoxidil (OM) has been reported as effective for FPHL (0.25–
78 1.25mg/day).^{1,2} To date, no study has compared the relative efficacy of OM
79 and TM in the treatment of FPHL.

80 We performed a 24-week, randomized, open, comparative study of 1mg OM
81 *versus* TM 5% solution for the treatment of FPHL, at a dermatology clinic
82 (UNESP-Botucatu, São Paulo, Brazil).

83 Women between 18 and 65 years old with FPHL (Sinclair's Stage II-IV) were
84 randomly assigned to receive 1mg OM or TM 5% solution (1ml), once daily, for
85 24 weeks.

86 The primary endpoint was the change in total hair density in a target area
87 (parietal) from the baseline to week 24. Blinded analysis of the trichoscopic
88 images was performed using TrichoLAB Hair-to-Hair Matching technology (Bad
89 Birmbach, Germany). Secondary outcomes were: change in terminal hair
90 density; global photographic evaluation (three board-certified dermatologists);
91 quality-of-life evaluation using the Women's Androgenetic Alopecia Quality of
92 Life Questionnaire (WAA-QoL); and Sinclair's hair-shedding score (six-point
93 scale).³

94 Outcomes were compared according to time and to the groups (over time) by
95 linear mixed-effects models. Intention to treat analysis was performed. The
96 sample size was calculated to detect a difference greater than 20% in hair
97 density between the groups (alpha: 0.01, power: 0.9).

98 Fifty-two participants were enrolled (table 1). Baseline characteristics were
99 similar between the groups ($p \geq 0.05$). Fifty participants completed the trial.
100 Dropouts were not related to treatment side effects. The main outcomes are
101 presented in table 2. After 24 weeks of treatment the total hair density increased
102 by 12% (CI 95% 8.0-16.1%) in women taking OM and 7.2% (CI 95% 1.5-12.9%)
103 in women applying TM, with no difference between them ($p=0.10$).

104 Adverse events are shown in table 2. Scalp pruritus affected 19% of
105 participants in the TM group. Pretibial edema occurred in 4% participants in the
106 OM group. Hypertrichosis was more commonly with OM: 27% *versus* 4%,
107 although it was mild and well tolerated. Three participants did not take any
108 action to reduce the hair and five managed it with waxing. There was no
109 difference between the groups regarding the variation of mean blood pressure
110 over time. The mean heart rate at rest increased 6.5% in the OM group without
111 tachycardia; there was no change in the TM group. No hypotension-related
112 events occurred. No adverse events in OM group required cessation of
113 medication.

114 Our results reveal that low dose OM provides improvement of FPHL that does
115 not differ from TM 5% solution, with a safe profile and well tolerated adverse
116 effects.

117 The performance of OM in hair-shedding score was superior to TM, reinforcing
118 the favorable results reported on telogen effluvium.⁴ The increase in total hair
119 density lied within the TM CI95%, however if the outcomes are taken together,
120 they suggest a trend towards a greater improvement in the OM group.
121 Confirmation of this would require larger and longer studies.

122 In conclusion, OM can be considered an option for FPHL patients with poor
123 compliance and/or intolerability of TM.^{2,4,5}

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148 **Table 1.** Main clinical and demographic data from participants.

	Oral Minoxidil 1 mg	Topical Minoxidil 5%
N	26	26
Age (years)#	40.6 (12.0)	47.3 (11.8)
BMI (kg/m ²)##	26.3 (23.4-30.7)	23.5 (22.5-29.4)
Skin phototype - n (%)		
II	7 (27)	7 (27)
III	13 (50)	11 (42)
IV-V	6 (23)	8 (31)
Race - n (%)		
European	21 (81)	19 (73)
African-American	4 (15)	4 (15)
Amerindian	- (-)	2 (8)
Asian	1 (4)	1 (4)
Baseline Sinclair scale - n (%)		
II - Mild	15 (58)	17 (65)
III - Moderate	10 (38)	8 (31)
IV - Severe	1 (4)	1 (4)
Baseline density – per mm ²		
Total hair	164.6 (48.1)	163.2 (46.0)
Terminal hair	106.5 (34.2)	113.3 (41.1)
Hair shedding score##	5 (3-5)	4 (3-5)
WAA-QoL##	68 (51-80)	60 (28-77)

149 # mean (sd); ## median (p25-p75);

150 BMI: body mass index.

151 WAA-QoL: Women's Androgenetic Alopecia Quality of Life Questionnaire.

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Table 2. Main results and adverse effects of the comparative effectiveness of oral minoxidil 1mg *versus* topical 5% minoxidil solution for twenty-four weeks in the treatment of FPHL (n=52).

	Oral Minoxidil 1mg			Topical Minoxidil 5%			p-value (time*group)
	T0	T24	p-value*	T0	T24	p-value*	
Hair density [#] – per cm ²							
Total hair	164.6 (48.1)	184.7 (57.1)	<0.01	163.2 (46.0)	176.3 (61.5)	<0.01	0.09
Terminal hair	106.5 (34.2)	112.6 (36.4)	0.03	113.3 (41.1)	116.8 (44.9)	0.09	0.17
Global photograph ^{##}							0.16
Slightly impaired	-	1 (4)	-	-	2 (8)	-	
No change	-	7 (27)	-	-	12 (46)	-	
Slightly improved	-	16 (62)	-	-	11 (42)	-	
Greatly improved	-	2 (8)	-	-	1 (4)	-	
Hair shedding score ^{###}	5 (3-5)	3 (2-3)	<0.01	4 (3-5)	4 (3-5)	0.20	<0.01
WAA-QoL ^{###}	68 (51-80)	15 (6-36)	<0.01	60 (28-77)	25 (11-41)	<0.01	0.09
Adverse effects							
Edema of the limbs ^{##}	-	1 (4)	-	-	0 (-)	-	0.99
Hypertrichosis ^{##}	-	7 (27)	-	-	1 (4)	-	0.02
Heart rate (bpm) [#]	72 (8)	77 (8)	<0.01	70 (9)	70 (8)	0.83	<0.01
MAP (mmHg) [#]	93 (9)	91 (8)	0.23	89 (11)	89 (11)	0.97	0.51
Scalp pruritus ^{##}	-	0 (-)	-	-	5 (19)	-	0.02

* T0 vs. T24 ; [#] mean (sd); ^{##} n (%); ^{###} median (p25-p75);

WAA-QoL: Women's Androgenetic Alopecia Quality of Life Questionnaire; MAP: Mean Arterial Pressure.

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