

## LETTER TO THE EDITOR

COMPARITIVE EFFECTIVENESS OF FINASTERIDE vs *SERENOA REPENS* IN MALE ANDROGENETIC ALOPECIA: A TWO-YEAR STUDY

A. ROSSI<sup>1</sup>, E. MARI<sup>1</sup>, M. SCARNÒ<sup>2</sup>, V. GARELLI<sup>1</sup>, C. MAXIA<sup>1</sup>, E. SCALI<sup>1</sup>, A. IORIO<sup>1</sup>  
and M. CARLESIMO<sup>3</sup>

<sup>1</sup>Department of Dermatology and Plastic Surgery, University of Rome "Sapienza" I School, Rome, Italy; <sup>2</sup>CASPUR (Inter-University Consortium for Supercomputing), Rome, Italy; <sup>3</sup>Dermatology University of Rome "Sapienza" of Rome II School, Rome, Italy

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The objective of this open label study is to determine the effectiveness of *Serenoa repens* in treating male androgenetic alopecia (AGA), by comparing its results with finasteride. For this purpose, we enrolled 100 male patients with clinically diagnosed mild to moderate AGA. One group received *Serenoa repens* 320 mg every day for 24 months, while the other received finasteride 1 mg every day for the same period. In order to assess the efficacy of the treatments, a score index based on the comparison of the global photos taken at the beginning (T0) and at the end (T24) of the treatment, was used. The results showed that only 38% of patients treated with *Serenoa repens* had an increase in hair growth, while 68% of those treated with finasteride noted an improvement. Moreover finasteride was more effective for more than half of the patients (33 of 50, i.e. 66%), with level II and III alopecia. We can summarize our results by observing that *Serenoa repens* could lead to an improvement of androgenetic alopecia, while finasteride confirmed its efficacy. We also clinically observed, that finasteride acts in both the front area and the vertex, while *Serenoa repens* prevalently in the vertex. Obviously other studies will be necessary to clarify the mechanisms that cause the different responses of these two treatments.

Androgenetic alopecia (AGA) is a common form of scalp hair loss that affects up to 80% of elderly males (mostly over 60 years old). The onset of AGA is extremely variable and the physical aspect is characterized by progressive miniaturization of scalp hair follicles (1, 2). Even though this condition is not considered a serious pathology, it is well known that loss of hair leads to stressful events for patients, often with considerable psychosocial consequences. Genetic factors and androgens play a major role in the pathogenesis of the disease. Polymorphism of the androgen receptor genes was first identified in association with androgenetic alopecia. These facts

lead to different kinds of AGA patterns that often occur in members of the same families.

Anamnesis and clinical examination can lead to the correct diagnosis of AGA, as well as a dermoscopy that can evidence the beginning of the miniaturization of the scalp hair follicles. The presence of more than 20% vellus-like hair in the androgen dependent areas can also lead to diagnosis of initial AGA (3-6).

Minoxidil and finasteride are commonly used in treating AGA, both of which have FDA approval; dutasteride, a type I and II 5- $\alpha$ -reductase inhibitor, should also be considered and is currently in Phase

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Mailing address: Dr Elena Mari,  
Department of Dermatology and Plastic Surgery,  
University of Rome "Sapienza",  
CASPUR V.le del Policlinico 155, 00100 Rome, Italy  
Tel.: +39 06 49976963  
Fax: +39 06 49976963  
e-mail: elenamari4@virgilio.it

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III of trials. The greatest efficacy is achieved by a combination of medical treatment and hair transplant surgery (1, 6-9).

Finasteride, a synthetic azo-steroid, is a highly selective 5- $\alpha$  reductase type II inhibitor which acts by avoiding the conversion of testosterone to DHT. Biodisponibility of the drug is 80% and the biggest plasmatic concentration is present after 2 hours, while the pharmacological half-life is about 6-8 hours. It is eliminated by urine (40%) and by faeces (10-12).

Finasteride does not alter the link between DHT and its receptor and does not have any affinity for the androgen receptor. Administration of a daily dose of 1 mg reduces concentrations of scalp DHT and serum DHT by 64% and 68%, respectively (13-15). The treatment is well tolerated and side effects regarding sexual dysfunction (decreased libido, impotence, ejaculatory disorders and decreased ejaculate volume) are rare and reversible after the suspension of the treatment (14,16).

*Serenoa repens* is a plant of the Arecaceae's family, also known even as *Sabal serrulata*. Used in therapy for AGA, it acts as a competitive, non-selective inhibitor of 5- $\alpha$  reductase of types I and II.

In this study we report certain considerations on the efficacy of finasteride and of *Serenoa repens* when applied on a sample of 100 patients affected by mild to moderate AGA.

## MATERIALS AND METHODS

A sample of 100 patients was used to assess the effectiveness of the two treatments. Men aged between 20 and 40 years, in good health conditions affected by mild to moderate AGA (using the Hamilton classification, modified in order to evaluate the quantity of the hair in the vertex and in the anterior region), were eligible for enrollment the study. Principal exclusion criteria included significant abnormalities on screening physical examination or laboratory evaluation; surgical alteration of scalp hair loss; topical minoxidil use in the previous year; use of drugs with androgenic or antiandrogenic properties in the past; or alopecia as a result of other causes. Men were instructed not to alter their hairstyle or dye their hair during the study.

The patients were randomly divided in two groups (of equal size): the first characterized by the use of finasteride (1 mg/die), the second treated with *Serenoa repens* (320

mg/die, dry extract from the plant). Both groups were followed for 24 months.

Measurement of hair density was made by assessment of standardized global photographs that captured hair density in the vertex and in the anterior regions. A description of the preparation of the patient for each photographic view is as follows: (1) vertex scalp: hair was combed away from the vertex-like spokes of a wheel; (2) anterior scalp: hair was center-parted and combed away from the part for assessment of part width and ease of seeing scalp through hair. All the photos were registered, using a macro-photograph 20-70X (Trichoscan Dermoscope Fotofinder®), before the treatment (T0) and at 24 months (T24). The effectiveness of the treatments was evaluated with a score, for each patient, comparing photographs taken at baseline and at T24, then rated the paired photographs separately based on a 7-point scale: -3 = greatly decreased, -2 = moderately decreased, -1 = slightly decreased, 0 = no change, 1 = slightly increased, 2 = moderately increased, 3 = greatly increased; these photos were examined by the same three experts (two dermatologists experienced in assessment of changes in scalp hair growth and one junior dermatologist).

A first statistical analysis was made in order to verify if the two samples were characterized by significantly different initial levels of AGA; for this purpose the distribution of the patients at T0 according to their levels in the Hamilton's classification was firstly considered. Secondly, the non-parametric test of Wilcoxon-Mann-Whitney (also known as the Mann-Whitney's test U) was considered. This test is usually used to verify if a not continuous variable (the score) observed in two samples derives from the same population (i.e. if the samples are significantly different or not).

Lastly, the distribution of the scores at the end of the treatment (T24) was considered; the Mann-Whitney's test U was used again to verify whether the two groups were characterized by significantly different results. For this purpose the *chi-square* test was used and applied on the cross tabulation table built by considering the Hamilton level at T0 and the scores at T24 (for each sample). It should be observed that, in this case, the patients were grouped in the following modalities: improved (when their final score was greater than 0), stable (with a final score of 0) and worsened (with a final score less than 0). This analysis was carried out to verify the existence of a dependence between the final score and the initial grade of AGA.

## RESULTS

The two groups of patients were well distributed according to their initial grades of AGA (using the

Hamilton classification). This consideration derives from the results in Table I and by observing the value of the Mann-Whitney's test U. This is equal to 1301, with a value of  $z$ , in the two tails case, equal to 0.71. In this case it is possible to accept the null hypothesis that the two samples were taken from the same population (the  $p$ -value is 0.48).

From Table II it can be observed that 68% of patients treated with finasteride had a score greater than 0, while these were 38% when *Serenoa repens* was used; therefore this treatment led to an improvement of clinical condition, but finasteride resulted more effective.

The result of the Mann-Whitney's test U when it considered the final score for the two samples

(874.5, with a value of  $z$ , in the two tails case, of 2.84), shows that these were not comparable (it is possible to refuse the null hypothesis because the associated  $p$ -value was less than 0.05). However, it is interesting to observe that neither treatment was effective in 10% of patients and that *Serenoa repens* stabilize the AGA in 52% of the cases.

Tables IIIa and IIIb show that there was a significant dependency between the initial level of AGA and the final scores; the value of the  $\chi^2$ -square index was 6.09 (with a  $p$ -value of 0.013) for the treatment with finasteride 1 mg/die, and 8.00 (with a  $p$ -value of 0.004) for those patients treated with *Serenoa repens* 320 mg/die. From these tables it can also be derived that finasteride was more effective

**Table I.** Distribution of patients according to the treatment (Finasteride 1 mg/die and *Serenoa Repens* 320 mg/die) by considering the values of the Hamilton classification the beginning of the treatment (T0).

Value of Hamilton classification at T0	Treatment	
	Finasteride 1mg/die	<i>Serenoa Repens</i> 320mg/die
<b>I</b>	8 (16%)	7 (14%)
<b>II</b>	21(42%)	19 (38%)
<b>III</b>	12 (24%)	16 (32%)
<b>IIIv</b>	7 (14%)	7(14%)
<b>IV</b>	2 (4%)	0 (0%)
<b>IVv</b>	0 (0%)	1 (2%)
<b>Totale</b>	<b>50 (100%)</b>	<b>50 (100%)</b>

Column percentages are in parenthesis.

**Table II.** Distribution of patients for treatment (Finasteride 1 mg/die and Serenoa Repens 320 mg/die) according to their scores at the end of the treatment (T24).

Score at the end of the treatment (T24)	Treatment	
	Finasteride 1mg/die	Serenoa Repens 320mg/die
-1	5 (10%)	5 (10%)
0	11(22%)	26 (52%)
1	30 (60%)	19 (38%)
2	3 (6%)	0(0%)
3	1 (2%)	0 (0%)
<b>Totale</b>	<b>50 (100%)</b>	<b>50 (100%)</b>

Column percentages are in parenthesis.

for 66% of patients (33 of 50) with an initial classification of AGA in levels II and III; for these the most probable result was an improvement at the end of the treatment (22 of 33, i.e. 66%). Concerning the sample treated with Serenoa repens, the majority of the patients was classified at the beginning of the treatment in II and III (35 of 50, i.e. 70%), but for those the most probable result was the stabilization of the AGA (21 of 35, i.e. 60%). In both groups all the patients remained in the study and no side effects were observed.

## DISCUSSION

Androgenetic alopecia is a progressive condition

and although the current available treatments are effective in arresting progression of the disease, they allow only partial regrowth of hair. Early treatment achieves the best desirable outcome. Topical minoxidil and oral finasteride are commonly used and have FDA approval for the treatment of male androgenetic alopecia (17-19). A selective inhibition of 5-alpha reductase increases anagen phase, modifying and improving the progressive course (3, 4). Extract of *Serenoa repens* is the most popular among the botanically derived 5-alpha inhibitors. Despite lack of proper clinical trials to support their efficacy, these products are popular among patients. In literature there are few articles that underline the importance of *Serenoa repens*.

**Table IIIa.** Distribution of patients treated with Finasteride 1 mg/die according to their classification at T0 (on the Hamilton levels) and their score at the end of the treatment.

Value of Hamilton classification at T0	Score at the end of the treatment (T24)			
	Worsened	Stable	Improved	Total
I	1	2	5	8
II	1	4	16	21
III	3	3	6	12
IIIv	0	2	5	7
IV	0	0	2	2
Total	5	11	34	50

Chi-square index= 6.09, p-value= 0.013

**Table IIIb.** Distribution of patients treated with Serenoa Repens 320 mg/die according to their classification at T0 (on the Hamilton levels) and their score at the end of the treatment.

Value of Hamilton classification at T0	Score at the end of the treatment (T24)			
	Worsened	Stable	Improved	Total
I	1	1	5	7
II	2	11	6	19
III	2	10	4	16
IIIv	0	3	4	7
IVv	0	1	0	1
Total	5	26	19	50

Chi-square index= 8.0, p-value= 0.004

In 2002, topical use of *Serenoa repens* was mentioned as treatment for AGA in a 24-year-old-woman (20). In the same year Prager proposed a randomized, double blind, placebo controlled trial to determine the effectiveness of Sr, demonstrating its effect (2). Murugusundram subsequently investigated the possible role of Sr in AGA (1). Based on this poor biological background present in literature we evaluated the effect of two 5 alpha-inhibitors: one synthetic, finasteride, and one vegetal, *Serenoa repens*, in the treatment of male androgenetic alopecia.

*Serenoa repens* is constituted by phytosterols and flavonoid that have antiandrogenic activity through two ways: the first one is direct and regards the DHT and androstenediol cytoplasmatic receptors; the second one is indirect and acts through the inhibition of 5-alpha reductase type I and II. It should be observed that the extract of *Serenoa repens* is composed of saturated fatty acid (lauric and miristic acid) and monounsaturated fatty acid (oleic acid). The latter inhibits the 5-alpha reductase of type I, while lauric acid inhibits 5-alpha reductase of type I and II (15-17).

Furthermore *Serenoa* activates the oestrogen receptors, particularly betasitosterina (present in the plant) which has wild oestrogenic activity, which, through adenilciclasia activation, can stimulate the matrix mitosis, by contributing to the anagen maintenance and to the catagen normalization. Obviously, because of the vegetal nature of the extract, it is necessary to have substances that have fixed and constant concentration (18). From the patient's point of view, *Serenoa repens* is a non-invasive approach to AGA, with no side effects.

We observed that 68% of patients treated with finasteride had a score greater than 0, while these are 38% when *Serenoa repens* was used. Moreover, finasteride is more related to a clinical improvement, while *Serenoa repens* is able to stabilize the hair loss.

Both treatments in this study showed some peculiar characteristics; *Serenoa* lead to an improvement, stabilizing the disorder, only in the vertex. Finasteride resulted more useful in all areas, as confirmed from other recent studies (21). The minor effect of Sr respect to finasteride and the different therapeutical areas of action could probably be explained by the lower affinity of Sr for 5-alpha

reductase than finasteride.

In our study the results of the treatments seemed to be correlated with the initial grade of AGA, with greater efficacy in patients with level II and III of the Hamilton classification.

Both therapies lead to good results and were well tolerated (without side effects in our population). Side effects are said to be uncommon. The most common side effect, that can be observed is mild stomach discomfort which can be alleviated by taking the medication after food. Like other 5-alpha reductase inhibitors, SR may reduce PSA levels by 50% after 6 - 12 months of treatment. There is therefore a risk of missing early detection of prostate cancer in self-medicating patients with *Serenoa repens* (1).

In our opinion, *Serenoa repens* could be considered as a valid approach in treating low or moderate AGA, and a good alternative for patients in whom finasteride or other topical therapies cannot be used. Sr resulted able to stabilize hair loss without having any side effects. However, further studies will be necessary to explain the mechanisms that lead to a different response of the two treatments and to support the claims of Sr efficacy.

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