Clinical investigation of the effects of a topical lotion and shampoo containing low molecular weight synthetic thymus peptides on women with chronic telogen effluvium and initial AGA following a six month-period of treatment

Published 2009
in Journal of Plastic Dermatology
(issue 5, Nr. 3, September – December 2009)

Official Organ of the International-Italian Society of
Plastic-Aesthetic and Oncologic Dermatology (ISPLAD)

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SUMMARY

Clinical investigation of the effects of topical lotion and shampoo containing synthetic thymus peptides on androgenetic alopecia and chronic telogen effluvium on women after a six month-period treatment

The aim of the paper has been to study during a period of six months, of the efficacy and the tolerability of both the lotion and shampoo (Timosint®/Thymuskin®) containing synthetic low molecular weight thymus peptides (GKL02 Factor), in the initial phases of androgenetic alopecia (AGA), and chronic Telogen Effluvium (TE). Ten women (mean age 31.3 yrs) with AGA (Ludwig 1) and 105 female subjects (mean age 39.96 yrs) with chronic TE have been enrolled; the treatment schedule was as follows

- *lotion: twice a day application in the first 15 days and then once a day in the following 22 weeks for a total period of treatment of 24 weeks.*
- *shampoo: two or three times/week during the study period of 24 weeks.*

All the subjects underwent pull test, evaluation of symptoms (dandruff, seborrhoea, redness, pruritis). Tolerability and cosmetic acceptance/tolerance were evaluated at the beginning of the treatment and after 30, 90 and 180 days. In AGA patients the improvement of pull test has been continuous becoming negative in study population after 180gg (p = 0,002). Symptoms were reduced in all patients. In chronic TE, pull test become negative in 88% (72 cases out of 82) (p<0,0001) with a mean symptoms' improvement of 88%. In both groups the tolerability was referred as positive in 100% of cases and no side effects were recorded. The cosmetic acceptance/tolerance was also referred as positive in 96% of the cases. In conclusion, synthetic thymus peptides showed significant efficacy and tolerability in the clinical treatment of initial AGA and chronic TE in women after a six month-treatment.

KEY WORDS: Androgenetic alopecia and Telogen Effluvium (TE) in women, Synthetic Thymus peptides, Therapy

INTRODUCTION

Chronic telogen effluvium (TE) and androgenetic alopecia (AGA) [4-6] require a lengthy period of treatment. These two dermatological conditions require patients to undergo treatment for many months (TE) or years (AGA). A dermatologist must, therefore, make it clear to patients that continual daily applications are needed in order to obtain results and keep the condition under control. In a previous study we assessed the clinical effects of synthetic thymus peptides on the above mentioned conditions for a period of three months.[7] Based on the positive results achieved it was considered beneficial to extend the trial (beyond the

set period) in order to confirm the product's effectiveness and tolerability. We are therefore now publishing the results achieved for chronic TE and initial female AGA after a period of 6 months.
From a clinical point of view, previous topical treatments using thymus extracts to treat hair follicle problems have yielded positive results[8-10]. These treatments, however, were carried out with peptides of animal origin and the unavoidable associated risks are now no longer acceptable.
Thymus peptides used in this study were obtained using laboratory techniques (GKL02 FACTOR). Their low molecular weight ensures absorption and biological effectiveness.

Aim

The aim of this study was to evaluate the effects of a synthetic thymus-peptides based lotion and shampoo (Timosint®/Thymuskin®), especially in relation to its effectiveness and tolerability, in the treatment of chronic TE and the initial phases of female AGA after a six month period of treatment.

Materials and methods

Subjects enrolled in the study

Two groups of female patients were enrolled in the study:
The first group included 10 patients with initial AGA whilst the second group included 105 patients with chronic TE and the test product was used for a total of 180 days.

Inclusion criteria

- Female patients aged between 16 and 70;
- Patients affected by chronic TE (more than 6 months) or initial AGA;
- All specific topical medication and/or cosmetic treatments to be interrupted at least 30 days beforehand.

Exclusion criteria

- Male patients
- Patients aged <16 and >70;
- Patients who are pregnant or breast feeding;
- Patients suffering from serious systemic illnesses;
- Patients undergoing treatment with drugs and/or specific cosmetic treatments;
- Patients with a known allergy to one of the product ingredients.

Dosage and administration

This product, whose amino acid composition is listed in Table 1, was applied in doses of 2 ml twice a day for 15 days, then 2ml once a day for 22 weeks for a total of 24 weeks (6 months). Patients were instructed to wash their scalp 2-3 times a week with a non medicated shampoo (Timosint®/Thymuskin® shampoo with synthetic thymus-peptides).

Evaluation parameters

The clinical evaluation was carried out using a form filled in by a specialist doctor at time of patient's enrolment, then after 30 days (T1), after 90 days (T2) and after 180 days (T3). The following parameters were assessed:
Pull Test:
assessment was based on the following scale:
Score 1 = neg (1-2 hairs); Score 2 = pos + (3-4 hairs); Score 3 = pos ++ (5-6 hairs); Score 4 = pos +++ (>6 hairs) and was carried out at time of enrolment, after 30 days (T1), after 90 days (T2) and after 180 days (T3). Significance of Pull Test improvement was assessed using Wilcoxon's non-parametric test for paired data.

Dandruff, Seborrhoea, Redness and Pruritis:
The following score system was used for the evaluation:
score 1 = neg, score 2 = pos +, score 3 = pos ++ score 4 = pos +++ with the purpose of highlighting improvement in % after 30 days (T1), 90 days (T2) and 180 days (T3) of treatment.

Amino Acid
Aspartic acid (Asp)
Threonine (Thr)
Serine (Ser)
Glutamic acid (Glu)
Proline (Pro)
Glycine (Gly)
Alanine (Ala)
Cysteine (Cys)
Valine (Val)
Methionine (Met)
Isoleucine (Ile)
Leucine (Leu)
Tyrosine (Tyr)
Phenylalanine (Phe)
Histidine (His)
Lysine (Lys)
Arginine (Arg)

Table 1:
Amino acid composition of GKL02 FACTOR.

The patients were considered to have:
a) improved if they passed to a lower score;
b) no change if they maintained the same score;
c) worse if they passed to a higher score.
A doctor's opinion on Effectiveness and Tolerability after 30 days (TI), 90 days (T2) and 180 days (T3) was also requested. This evaluation was based on the following opinion scale: Neg (poor): Pos + (fair). Pos ++ (good): Pos +++ (excellent).

Mean age 31.3 years

Age	number	%
16-30	6	60%
31-45	2	20%
46-60	2	20%
>60	0	0%
Total	10	100%

Table 2:
Patients with AGA

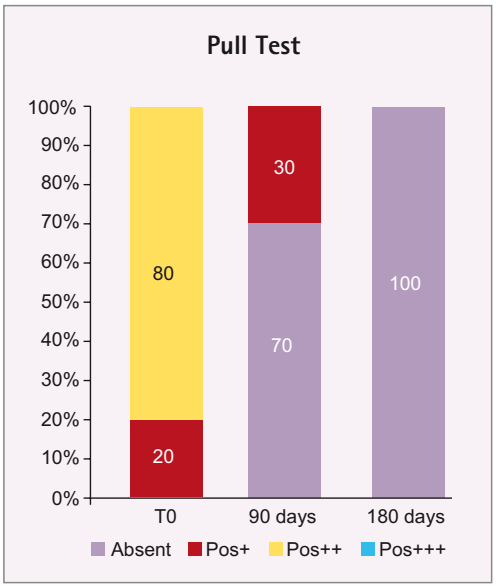

Figure 1. AGA
% of patients in which the Pull Test was found to be: absent: pos +; pos ++; pos+++ at T0, 90 days and 180 days. Improvement between T0 and 180 days, was statistically significant: p = 0.002

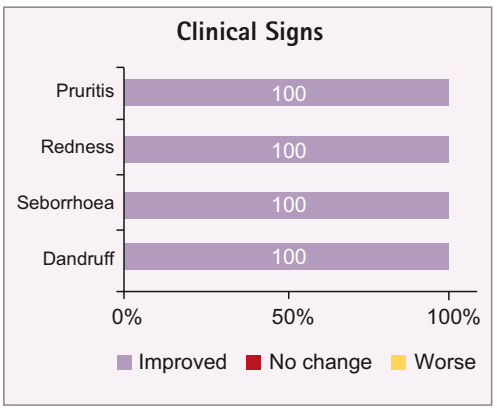

Figure 2. AGA
Patients (%) improved, no change or worse after 180 days (T3) of treatment.

The tester asked for patients' opinion with regards to cosmetic acceptance based on: hair thickness and how satisfied they were with the lotion and shampoo using the following scale:
Neg (poor): Pos + (fair)
Pos ++ (good)
Pos +++ (excellent).

When the treatment came to an end patients were asked:
a) for a final opinion on the effectiveness of treatment (excellent, good, fair and poor)
b) their opinion of this treatment compared to previous ones (better, the same or worse).

Results

Group of patients with AGA
Table 2 provides a summary of women enrolled and suffering from AGA.

Pull Test
The Pull Test showed improvement was continuous until all patients were back to normal after 180 days (T3) of treatment, 3 patients that were positive after 90 days become negative after 180 days. Statistical analysis between T0 and T3 was significant: p = 0.002 (Figure 1).

Dandruff (D), Seborrhoea (S), Redness (E), Pruritis (P) assessed at T3 (180 days) provided the following results (Figure 2):

D = improved 100%
S = improved 100%
E = improved 100%
P = improved 100%

Figure 3. AGA
Tester's opinion after treatment was over.

Effectiveness and Tolerability

With regards to the product's effectiveness after 180 days of treatment the tester's opinion was as follows: a) excellent in 50% of patients: b) good in 50% of patients (Figure 3).
With regards to product tolerability the tester's opinion was as follows: a) excellent in 60% of patients: b) good in 40% of patients (Figure 4). No side effects were recorded.

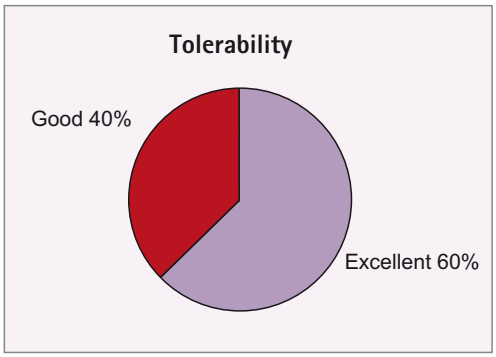

Figure 4. AGA
Tester's opinion after treatment was over.

Cosmetic acceptance

Patient satisfaction with cosmetic treatment was unvaryingly positive. Patient evaluation on how satisfied they were with the lotion, shampoo and hair thickness are summarised in Figure 5

Patients' final opinion

Patients said the product was good in 50% of cases and excellent in the other 50% of cases. This lotion and shampoo were considered to be better than those from previous cosmetic treatments in 100% of cases.

Group of patients with telogen effluvium

Table 3 provides a summary of women enrolled suffering from TE.

Table 3:
Patients with TE

Mean age 39.96 years

Age	number	%
16-30	32	30.48%
31-45	39	37.14%
46-60	22	20.95%
>60	12	11.43%
Total	105	100%

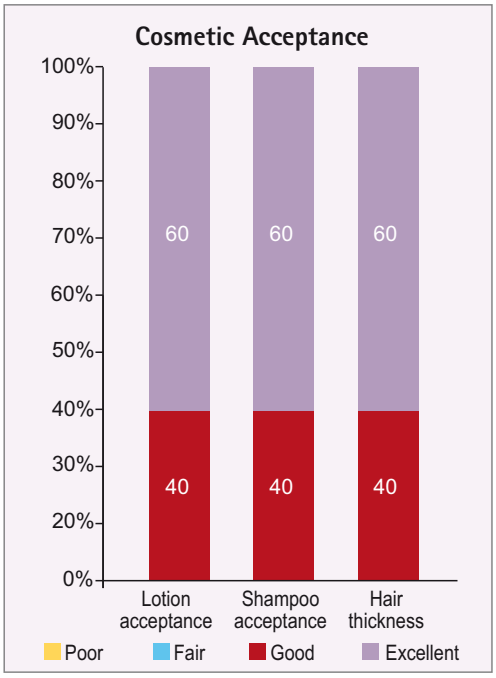

Figure 5. AGA
Patient's opinion (%) on: how satisfied they were with lotion, shampoo and hair thickness

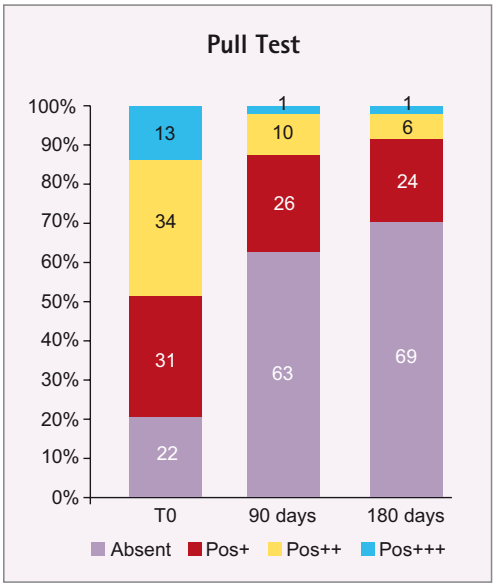

Figure 6.
Chronic Telogen effluvium
% of patients in which the Pull Test was found to be: absent; pos +; pos ++; pos+++ at T0, 90 days and 180 days. The result was: T0 to T3 p < 0.0001 highly significant

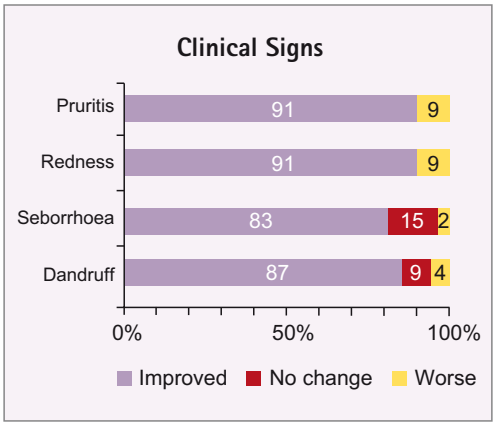

Figure 7.
Chronic Telogen effluvium
Patients (%) improved, no change or worse after 180 days (T3) of treatment

Pull Test

Pull Test showed further improvement as 7 patients who had a positive score after 90 days showed a negative score after 180 days. From a statistical point of view, Pull Test improvement between T0 and T3 was highly significant and precisely: T0 versus T3 comparison $p < 0.0001$ (Figure 6).

Figure 8.
Chronic Telogen effluvium
Tester's opinion after treatment was over.

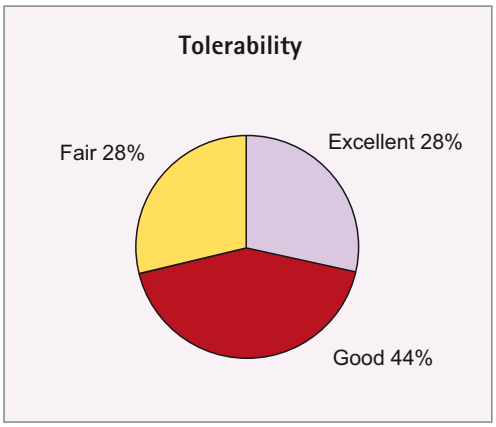

Figure 9.
Chronic Telogen effluvium
Tester's opinion after treatment was over.

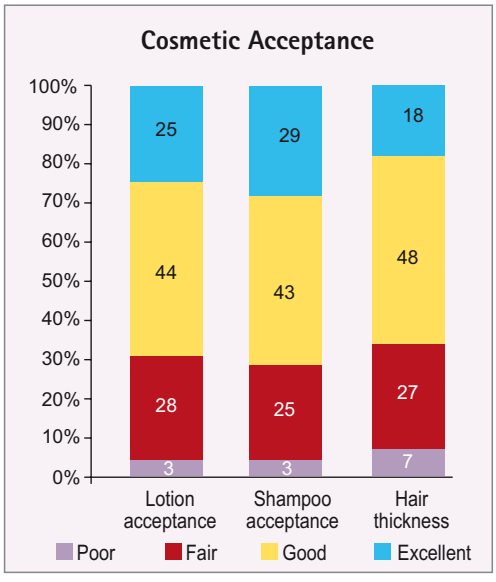

Figure 10.
Chronic Telogen effluvium
Patient's opinion (%) on: how satisfied they were with lotion, shampoo and hair thickness

Dandruff (D), Seborrhoea (S), Redness (E), Pruritis (P)

assessed at T3 (180 days) provided the following results (Figure 7):

D = improved 87%: the same 9%: worse 4%
S = improved 83%: the same 15%: worse 2%
E = improved 91%: worse 9%
P = improved 91%: worse 9%

Effectiveness and Tolerability

The tester's opinion on product effectiveness after 180 days of treatment was positive in 92% of cases (Figure 8).
The tester's opinion on product tolerability was positive in 100% of cases (Figure 9). No side effects were recorded.

Cosmetic acceptance

Patient satisfaction with cosmetic treatment was unvaryingly positive. Patient evaluation regarding how satisfied they were with lotion, shampoo and hair thickness are summarised in Figure 10.

Patients' final opinion

Patient opinion was excellent in 41% of cases, good in 36%, fair in 16%, adequate in 4% and poor in 3%. The lotion and shampoo that were used were considered better than those used in previous cosmetic treatments in 75% of cases, the same in 23% and worse in 2% of cases.

Conclusions

The aim of this study was to evaluate a compound (Timosint®/Tymuskin®), which is based on a "functional" principle made up of synthetic low molecular weight peptides, natural substances (Vitamin E, caffeine and Urtica Dioica (stinging nettle)) and cosmetic ingredients (vegetable proteins, panthenol) over a fairly long period of time (six months). Synthetic thymus peptides (contained both in the lotion and the shampoo) are characterised by low molecular weight, are obtained synthetically and are not of animal tissue origin. The mean molecular weight of individual peptides varies from 180 to 600 Daltons and this aids transfollicular penetration after topical use[11].

The amino acid composition of these peptides is what causes the biological results. The compound acts:
a) as a pool for the synthesis of Keratins[12]
b) in the stimulation of keratinocyte growth[13]
e) in the development of immunologic homeostasis of the skin[14].

The natural "active" ingredients (caffeine-Vitamin E-Utica dioica (stinging nettle)) help improve conditions for hair growth by stimulating the production of energy needed by the hair follicle metabolism and by carrying out a "scavenger" action.

Cosmetic ingredients (vegetable extracts-panthenol and vegetable proteins) increase hair volume and make it easier to comb.

After six months of treatment an improvement in pull test was recorded: three patients with AGA and seven with chronic TE who were still positive after 90 days were back to normal after six months of treatment. We can draw the conclusion that the product's positive effects continued beyond the three month period of treatment and that this is due to the stimulating action of thymus-peptides on the growth stage of keratinocytes. Dandruff, seborrhoea, redness and pruritis symptoms continued to improve up until the end of the 6 month treatment period. These effects are the indirect result of action on the keratinocyte metabolism, on the skin inflammation process and the production of sebum. Both the lotion and the shampoo contain natural ingredients such as: tocopheryl acetate, caffeine, panthenol and vegetable extracts which can improve the cosmetic quality of hair shafts[15]. Effectiveness and tolerability were also confirmed after the 6 month period. Tolerability and cosmetic quality of these products are crucial when treatment times are unavoidably lengthy such as in these cases.

Data results confirm patient compliance was excellent regarding use of lotion and shampoo. The above mentioned cosmetic qualities of the shampoo were highly rated by patients who reported an improvement in the volume and shininess of their hair.
In conclusion, this study with low molecular weight peptides for the treatment of certain common scalp conditions such as chronic TE and initial AGA, show that a clinical response is possible both for hair loss as well as the symptoms that accompany it, such as: dandruff, seborrhoea, redness and pruritis. Therefore, the assumption made in the planning phase of the study that low molecular weight peptides have a positive effect on specific clinical conditions can now be confirmed.

The continual improvement in the pull tests highlights the fact that treatment should continue for a lengthy period of time so that the stimulus at follicle level can aid:
a) a quick recovery of the number of hairs lost due to chronic TE
b) a slowing down in the development of hair loss due to AGA

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Imprint

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The study was carried out by order of Biocure SRL.
We like to thank Biocure for the good and trustful cooperation.

Thymu skin®

GKL

...no Surrender to Hair Loss