CLINICAL EVALUATION OF A TRICHOLOGICAL PHYTOEXTRACT PRODUCT IN ANDROGENETIC ALOPECIA

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ABSTRACT

Androgenetic alopecia (AGA: male or female pattern baldness) is the most common form of alopecia. It affects men and women of all ages, as well as their psychological well-being. Minoxidil and finasteride are drugs which have shown some, even if debated, beneficial effect in treating AGA but their potent systemic pharmacological action and the long treatment duration influences their risk-benefit ratio.

We deemed interesting to clinically evaluate a product for scalp application, with a peculiar composition based on extracts from 9 officinal plants (Ricapil®). These substances act to increase the nutritional capillary blood inflow at epidermal level, where hair follicles are located

The study was carried out in two different centers with the same protocol and the results in 46 subjects with AGA (40 males, 6 females), treated for at least 3 months, were available for statistical analysis of the results. The parameters evaluated were: objective and microscopic examination of the hair, AGA stage rated by the Hamilton and Ludwig scale, at baseline, every month and at the end of treatment.

Out of 46 completed subjects, 25 (54%) showed clinical signs of hair follicle reactivation (anagen phase), with an initial or an appreciable regrowth of terminal hair (χ^2 test: 0,007). The local tolerability, its cosmetic characteristics and the practicality of use of Ricapil® resulted also very good.

INTRODUCTION

Alopecia (hair loss) has many causes but androgenetic alopecia (AGA) is the most frequent form. Synonymous for AGA are common baldness, male pattern alopecia, and female pattern alopecia. Man is not the only primate species in which baldness is a natural phenomenon associated with sexual maturity. The orangutan and the chimpanzee both show some degree of baldness when they reach maturity.

Studies in these animals have clearly demonstrated that common baldness is a physiological process in genetically predisposed individuals whether simian or human. Terminal follicles are progressively transformed into "vellus" follicles that are a "miniaturization" process. AGA is therefore a hereditary thinning of the hair induced by androgens in genetically susceptible men and women. Over time, the growth phase of the hair cycle becomes shorter and hair follicles become smaller, producing shorter, finer hair that cover scalp poorly.

Male pattern alopecia or baldness involves recession of the hairline in the frontal region of the scalp or loss of the hair at the vertex. It is usually associated with increasing age in men. Alopecia

may also be associated with systemic disorders, severe emotional and physical stress or skin disorders or be due to nutritional deficiencies.

Hamilton and Norwood provided the adopted classification of AGA, describing different subtypes. From the natural prepubertal scalp pattern (type I), the progression of hair loss is to type II in 96% of men and 79% of women after puberty. The patterns type V to type VIII take place in 58% of men aged over 50 years with the extent of baldness tending to increase to the age of 70 years. About 25% of women develop type IV scalps by the age of 50 years after which there is not further increase in balding. Approximately 30% of white men are affected by the age of 30 years, at least are affected at 50 years, and 80% are affected at 70 years. The negative effects of hair loss include self-perception of body image and can influence others' perception of the balding individuals with the result to deeply influence in many subjects their quality of life.

Several pharmacological treatment options have been studied: potent topical corticosteroids, topical dithranol and minoxidil, although their efficacy is discussed. The 5α-reductase inhibitor finasteride has been shown to be of benefit in men with male pattern alopecia, but it is restricted to be used in males. Furthermore minoxidil and finasteride must be used continuously as any benefit will be lost after stopping the treatment, exposing the subjects also to adverse events due to their potent pharmacological action.

The development of Ricapil® formulation is due to the researches of a well reputed Chinese dermatologist, Zhao Zhang Guang and it is an example of the olistic approach of Chinese traditional medicine. Illness - patients' conditions - use of natural Chinese herbal plants are strictly linked. This product is intended for scalp application and contains substances extracted from 9 officinal plants: *Carthamus Tinctorius, Prunus Persica, Zingiber Officinalis, Panax Ginseng, Salvia Officinalis, Cuscuta Epithimum, Carum Petroselinum, Angelica Archangelica, Capsicum Annuum*. The aim of these components is to oppose to hair loss and then to increase terminal hair production by providing, through an enhanced local microcirculation, nutrients essential for hair follicle activity and for exit from the resting phase.

These results are buoyed by the amelioration of local nutrients and oxygen availability at epidermal level sustained by a better scalp microcirculation. The product exerts also a regulatory influence on sebaceous glands function. The epidemiologic relevance of AGA with its rebounds on individuals' quality of life requires disposing of an effective and risking free approach for the treatment. Thus, given our professional specialization in Chinese traditional medicine and psychosomatic dermatology, we found interesting to carry out a direct clinical experience with this peculiar natural association.

MATERIALS AND METHODS

The study was aimed to determine if this unique formulation is able to induce a detectable effect against not only hair loss but also in favor of hair follicle reactivation (anagen phase) and its terminal hair production. Statistical analysis on response to treatment was performed using chi-square test.

The study was carried out in an open fashion in two different centers, Bologna and Milan, according to the same protocol. The formulation has been applied once a day on the scalp, gently massaging. The dose was equal to a nut and the total amount of doses used per day was related with the extension of alopecic areas to be treated (1-2 to a max of 3-4) in each individual.

In our cases the minimum treatment period was three months, the longest twelve months. The subjects have been evaluated by the investigators before and after treatment, with controls every month. The clinical evaluations consisted in macroscopic and microscopic examination of the hair, rating of AGA stage by Hamilton (males) and Ludwig (female) scales. An evaluation of product tolerability and its cosmetic and practicality properties was also done.

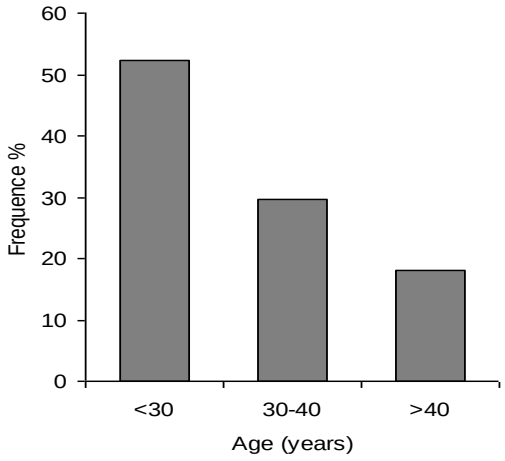
Inclusion criteria foresaw the presence of AGA, an interruption of at least 6 months of any other

therapy, local or systemic. In each subject has been carried out a careful anamnesis of the hair loss, followed by the microscopic examination of the hair to evaluate both terminal hair and follicle conditions. In each subjects routinely hematochimic tests have been performed to exclude any systemic interference exerted by product application on the scalp. Were excluded from the study pregnant or breast feeding women, subjects with systemic pathologies influencing their general conditions or treated with drugs known to interfere with hair, e.g. antineoplastic ones, as well as subjects not reliable in terms of product use and at risk for protocol violations.

RESULTS AND DISCUSSION

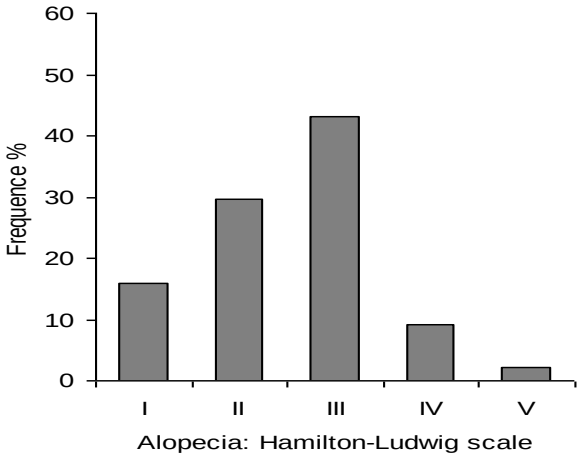
As a whole, 46 subjects have been completed, 40 males and 6 females, treated for at least three months, 30 in Bologna and 16 in Milan. Distribution by age is shown in Figure 1.

Figure 1. Distribution by age



Males were affected by AGA of grade I-IV according the Hamilton scale, females by AGA I-II according to the Ludwig scale (Figure 2). Out of the 46 subjects 7 suffered from AGA from 5-12 years. Out of 46 subjects 35 used other topical treatments in the past, 6 (17%) with partially satisfactory results, 29 (83%) with unsatisfactory results. In the present study, efficacy evaluations were changes from baseline *vs*. the different control monthly evaluations. The chosen objective and subjective parameters have been summarized, as far as the effects of the treatment are concerned, in a global evaluation as follows:

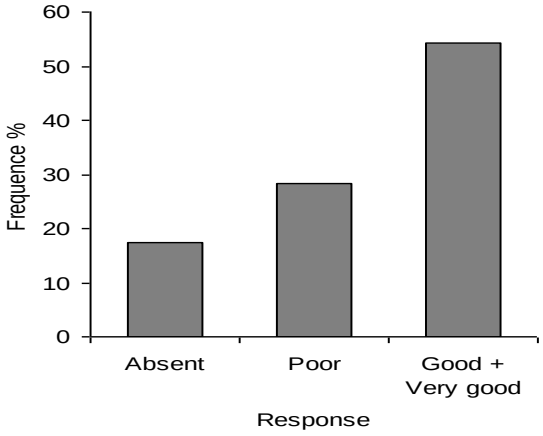
Figure 2. Degree of alopecia.



1. Not valuable regrowth (= negative result/absent)
2. Appearance of fine vellus (= first stimulation result on inactive follicles/poor)
3. Initial regrowth of terminal hair (= good)
4. Regrowth of terminal hair (= very good)

The analysis was performed grouping good and very good responses because were both signs of hair follicle reactivation besides a truly appreciable terminal hair regrowth (Figure 3).

Figure 3. Response to treatment



The results of the χ^2 test are reported in Table 1.

Table 1. Chi-square test for response

Response	Observed N	Expected N	Residual
Absent	8	15,3	-7,3
Poor	13	15,3	-2,3
Good+Very good	25	15,3	9,7
Total	46		
	Response		
Chi-Square	9,957[a]		
Df	2		
Asymp. Sig.	0,007		

CONCLUSIONS

In our clinical experience in AGA, out of 46 completed subjects 25 (54%) showed clear signs of hair follicles in anagen phase and terminal hair appreciable regrowth after 52 years. We compared these results with other reported in literature. In a randomized, placebo-controlled study in AGA with topical minoxidil 5%, 2% and placebo, the change from baseline in nonvellus hair count was, after 16 weeks: 37%, 34%, 20% respectively. After 48 years results were 28%, 22% and 9% respectively. Similar results are reported in a placebo controlled study with minoxidil in AGA in men. The value of placebo then can be reasonably placed between 9% and 20% of subjects, according to these data. In another study with a new antiandrogen for topical use, in the placebo group there was no evidence of benefit while the percentage of hair in anagen phase changed from 76% to 87% (+ 14,5%) after 9 months of treatment with the drug. In our study we found that there is a significant difference between the subjects with hair follicle reactivation and terminal hair regrowth, in comparison with either the poorly either with the non responders groups.

In conclusion, our results observed with the scalp application of Ricapil® (54%) can be considered for positive effects on hair follicles, in line with the data reported for a drug and well above the results seen with placebo. It is to underline how our results are even more positive than the ones reported for minoxidil, at a 5% concentration.

Furthermore 7/25 subjects (28%) reported positive results within the 4th month, 12/25 (48%) within the 5th month and 20/25 (80%) within the 8th month of product's use. These observations, together with a very good tolerability and product cosmetic and practicality favorable characteristics, lead us to the conclusion that this formulation with 9 officinal plants branded as Ricapil® can be proposed as an interesting and promising, besides natural, option for subjects with AGA. We know that to this formulation has recently been applied the "Crackle Technology", able to enhance the speed of interaction between substances and the epidermal strata, where hair follicle is located. This technology determines also a scalp mechanical microstimulation. This should warrant even more favorable results than the ones we observed.

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