

NEW STRATEGIES FOR THE USE OF TOPICAL PRODUCTS IN THE TREATMENT OF ANDROGENETIC ALOPECIA

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Abstract: The progressive thinning of the strands, follicular miniaturization and the gradual loss of hair caused by androgenetic alopecia (AAG) can be related to several factors, with genetic and hormonal factors standing out as the ones that most increase the risk of predisposition to AAG. It affects both men and women, being more prevalent in men and is also the most common type of alopecia that affects both sexes. This dermatological change has a major negative impact on the social and psychological well-being of patients. The main goals of AAG treatment include slowing down the progression of permanent hair loss and thinning, increasing scalp coverage and improving the quality and thickness of the hair. However, the inconvenience of using daily medications and side effects decrease patient adherence to treatment with oral medication. On the other hand, the use of topical formulations is increasingly becoming an alternative, including formulations that use specific shampoo bases, designed as a vehicle for carrying actives to the follicular pathway. This is due to the positive action of its surfactants in breaking the sebum barriers of the scalp, demonstrating promising results for the management of AGA, since the bioavailability of the actives via the follicular route is extremely important for the treatment. Therefore, the objective of this study is to evaluate the general strategies for the use of topical products in the treatment of androgenetic alopecia, due to the disadvantages of oral therapies and the low rate of adherence to treatment. Having as a relevant factor to be highlighted that the application in the length of the threads does not reach physiological effectiveness in the treatment of AAG, in this way all the results presented in the available literature refer to actives conveyed through topical application on the scalp, an essential factor for the effectiveness of topical treatment.

Keywords: Androgenetic alopecia, treatment, caffeine, shampoo.

INTRODUCTION

Androgenetic alopecia (AAG) can be characterized as the progressive thinning of the hair, a phenomenon caused by the alteration of the capillary cycle, which culminates in progressive follicular miniaturization, a reflection of the shortening of the anagen phase. Consequently, the strands become increasingly thin, short and depigmented (TRUEB, 2002; KRAUSE, 2006). AAG affects men and women, being more prevalent in men and is also the most common type of alopecia that affects both sexes. Hereditary, genetic and hormonal factors are the ones that most contribute to a greater predisposition to AAG (GRIJÓ, 2020).

One of the known mechanisms correlated to hormonal factors is the action of dihydrotestosterone (DHT) on the hair follicles, causing a shortening of the anagen phase, also favoring the rapid transition of the hairs to the telogen phase, in addition to provoking the miniaturization of the hair follicles. DHT is a metabolite of testosterone, formed through a reaction catalyzed by the enzyme 5 α -reductase (FISCHER, 2007).

This dermatological change has a major negative impact on the social and psychological well-being of patients. According to data from the Brazilian Hair Society (SBC), in 2018 alone the number of people affected by baldness reached 42 million. A condition that does not only affect people of advanced age. Data indicate that young patients aged between 20 and 25 years represent 25% of data related to disorders that cause hair loss (SBC, 2017).

The main objectives of the treatment of androgenetic alopecia are: to slow down the evolution of permanent hair loss and thinning, increase the coverage of the scalp

and improve the quality and thickness of the hair. Pharmacological alternatives may vary between sexes, with finasteride and spiro lactone being the main oral medications used. Observing a greater number of therapeutic alternatives for female patients, when we refer to treatments administered orally, especially due to the limitation of the use of some drugs in male patients, due to side effects linked to feminization (SILVA, 2011).

However, the use of topical formulations is increasingly becoming a viable alternative addressed in therapy, including shampoos, lotions and hair tonics (BENNER, 2011). Demonstrating positive results for the management of AAG, since the bioavailability of the actives through the follicular route is extremely important for the treatment (MARKOVA, 2004).

The inconvenience of using daily medications and the known side effects such as decreased libido, fatigue, menstrual irregularities and characterized postural hypotension are factors that decrease patient adherence to treatment with oral medications, leading to non-adherence to therapy (BENNER, 2011). On the other hand, topical formulations allow greater adherence to treatment, due to the practicality of use.

It is important to emphasize that, for such formulations to be effective, it is necessary to guarantee the absorption of the actives, through conditions specially designed for this purpose. It is necessary that such substances are in the correct concentration, ideal molecular size, in addition to being conveyed in formulations with assertive physicochemical conditions, to guarantee the bioavailability of the actives in the follicular pathway. Advances in the development of innovative topical formulations with activity, efficacy and safety have been observed in the medicinal and pharmaceutical field (PHARM, 2019; DREHER et al., 2002).

Therefore, the objective of this study is to evaluate the general strategies for the use of topical products in the treatment of androgenetic alopecia.

METHOD

The methodology used in this article was exclusively a bibliographic review, using materials found on scientific platforms, such as: Scielo, Lilac's, CAPES Periodicals, Google Scholar, and relevant references such as books.

RESULT AND DISCUSSION

ABSORPTION OF ASSETS THROUGH HAIR LEATHER

One of the main functions of the epithelial tissue is physical and biological protection, in addition to allowing the control of substances that are able to enter and leave the body (CAUVILLA et al., 2015). The scalp skin is composed of the epidermis, dermis and hypodermis, being slightly thicker than the skin of other body regions, a factor that could make absorption difficult, if we did not consider the presence of follicles and attachments widely present in this region, actively contributing to the absorption of substances (WICHROWSKI, 2007; TRAUER et al., 2010). In addition, to help the absorption of actives, some factors must be taken into account as they have a direct positive impact on the absorption of certain actives: local massage to activate microcirculation, molecular size, concentration and frequency of use (LAW, 2019; HERMAN, 2012).

Vascular support directed to the hair follicle may vary between phases, and may be lower in the telogen phase, occurring in a kind of programmed angiogenesis (CRANWELL, 2016). The follicular unit is composed of the hair follicle, sebaceous glands, arrector pili muscle, in addition to other components that include epithelial cells, melanocytes, fibroblasts and numerous nerve endings

(TRUEB, 2002; PAUS, 1999; FISCHER, 1987; AHMED, 1994).

In vitro studies show the secretion of a series of cytokines, bioactive molecules and growth factors directly involved in the functioning of the hair follicle. Furthermore, in the extrinsic pathway, androgenic hormones seem to exert even more impact on the cycle, influencing the progressive shortening of the anagen phase, collaborating with the reduction of hair in this phase and with follicular miniaturization (TRUEB, 2002).

Scientific attention regarding research in the field of Androgenetic Alopecia is mainly focused on elucidating the set of molecular signals modulated by intrinsic and extrinsic influences, involved in the transition between the phases of the hair cycle.

We highlight three of them, the growth phase being anagen, where a great mitotic activity occurs, the catagen phase, where the matrix stops proliferating and detaches from the dermal papilla, and the telogen phase, where the effective hair loss occurs (ALVES, 2020); TRUEB, 2002; PAUS, 1999; FISCHER, 1987; AHMED, 1994 et al., 2019), as is the case with the hormone corticotropin, which, when released, inhibits hair growth and induces premature entry of the catagen phase into the scalp (FISCHER et al., 2020).

MAIN ASSETS WITH ALOPECIC ACTIVITY

The main approved drug of systemic action for male androgenetic alopecia is finasteride. The indication of this drug for female patients is still being discussed, without significant differences. One of the androgens responsible for hair loss is dihydrotestosterone (DHT), which is the metabolite of testosterone conversion by the 5α -reductase enzyme. Finasteride acts by inhibiting this enzyme, and consequently the production of DHT is decreased

(BARAZZETTI et al., 2019). However, in addition to its use for women not being widely indicated due to its teratogenicity, the therapy for men has shown adverse effects such as lack of libido and impaired ejaculation and erection (IAMSUMANG, 2020).

Another drug approved by the FDA and indicated for the treatment of androgenetic alopecia is minoxidil. The drug works by promoting smooth muscle relaxation, however, its mechanism of action has not yet been very well elucidated. The effect on hair growth is mainly due to its metabolite, minoxidil sulfate, occurring through the action of the sulfotransferase enzyme located in the hair follicles (SUCHONWANIT, 2019), presenting some side effects such as contact dermatitis, skin irritation, sweating and headache, generally well tolerated (NANTES et al., 2018).

In order to avoid high exposure to side effects caused by the use of oral medications, to ensure the efficacy and safety of the patient for the treatment of androgenetic alopecia in both sexes, several studies involving the search for topical alternatives have been discussed, with the aim to locally inhibit 5α -reductase and improve blood circulation in the scalp (DHARIWALA, 2019).

What has been showing significant results for the treatment of androgenetic alopecia is caffeine, a methylxanthine from the family of alkaloids. The main mechanism of this active is the blocking of the phosphodiesterase enzyme inhibitor, the enzyme responsible for converting ATP into cAMP, so that it stimulates cellular metabolism, which can neutralize the miniaturization of the hair follicle, induced by testosterone and dihydrotestosterone DHT (BUSSOLETI, 2011). In addition to numerous beneficial effects associated with properties of other components present in coffee extract,

such as chlorogenic acid and polyphenols, including antioxidant and protective effects on epithelial cells (TOCI, 2006; DAGLIA et al., 2000).

In addition, it is known that caffeine can also have an exfoliating effect, which stimulates cell renewal, favoring blood circulation, promoting greater absorption and greater effectiveness with the treatment (FERREIRA, 2018), and stratum corneum, which occurs in about 2 minutes, making the use of the active even more promising (FISCHER, 2007).

FORMULATIONS

Although the term dermocosmetics is not recognized by regulatory agencies, ANVISA recognizes it as 2nd degree cosmetics, that is, products that have specific indications. For such products, information about safety and efficacy is required, in addition to the method of use, and they are subject to specific legal requirements for this class (ROCHA et al., 2015).

Although basic shampoo formulations are used only for the purpose of cleaning the hair and scalp, strategic formulations specially designed for the purpose of favoring the penetration of substances into the scalp, work as excellent vehicles for the absorption of actives (MOLDOVAN, 2012).

Current formulations have adaptations according to their function, quality and purpose for which they will be used. Surfactants are composite cleaning agents, with affinity for both fatty chains and polar groups, making them soluble in water to remove dirt. In this way, specific surface-active agents provide better absorption of the actives in dermocosmetics, as they favor the rupture of the sebum layers and residues that could compromise the penetration of the actives in the scalp (TRUEB, 2005).

It is known that the search for topical

actives for the treatment of androgenetic alopecia becomes increasingly promising and that the benefits of using shampoo formulations, provided they are specially designed for this purpose, are revealed as excellent alternatives for optimizing the absorption of actives on the scalp. Studies show that after 6 months of shampoo application, as a vehicle for caffeine absorption, a slowdown in the progression of baldness and a significant reduction in hair loss were observed in patients with androgenetic alopecia (FERREIRA et al., 2018).

CONCLUSION

Considering that androgenetic alopecia affects a considerable percentage of the population in both sexes and that it can lead to a negative psychological impact, the search for effective and safe topical alternatives becomes extremely necessary, since the available therapeutic arsenal has the capacity to promote side effects, which can make adherence to treatment difficult. In this way, actives conveyed through topical formulations, such as shampoos scientifically designed for this purpose, may have promising effects in patients affected by this condition, making this represent an important advance in the treatment, in addition to providing a new alternative for patients who have difficulty adherence to other therapies.

The physiological characteristics of the scalp favor topical treatment for the bioavailability of actives via the follicular, provided that the physical-chemical characteristics of the molecules used, concentration of actives and form of application are observed, always associated with scalp massage to favor the activation of local microcirculation. In addition, another important factor to be highlighted is that the application in the length of the threads

does not reach physiological effectiveness in the treatment of AGA, thus, all the results presented in the available literature refer to actives conveyed through topical application on the scalp, a factor essential for the effectiveness of topical treatment.

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