Androgenic alopecia and dutasteride in hair mesotherapy: A short review

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ABSTRACT

Androgenic alopecia (AGA) is the most common cause of patterned hair loss in predisposed men and women. AGA is a multifactorial and polygenetic condition, affecting up to 80% of men and 40-50% of women during life. AGA is characterized by a gradual reduction of the anagen and increase in telagen phase, leading to a progressive follicle miniaturization. As a consequence, terminal hairs are converted into vellus hairs decreasing hair density. The pathophysiology of AGA is heterogeneous and highly complex. A diverse combination of genetical factors, endocrine abnormalities, circulating androgens, drugs, diet and microinflammation in hair follicles of each individual are related to this condition. However, it is well known that androgens are the major modulators of male AGA but their specific action on female AGA is still under debate. Circulating testosterone is converted by 5α-reductase in 5α-dihydrotestosterone (DHT) in the periphery, a decrease of anagen phase occur, anticipating catagen phase in a complex process involving apoptosis as probably microinflammation. In AGA treatment, mesotherapy is being used with 5α-reductase inhibitors, especially dutasteride, injected directly on scalp. Thus, this updated review summarized the injectable use of dutasteride based on data available on PubMed until March 2017. Dutasteride, a second-generation inhibitor of 5α-reductase is more potent than finasteride due to the capability of inhibit types 1 and 2 of the enzyme. The efficacy and safety of hair mesotherapy with dutasteride were reported by distinct groups and the best results were achieved when this compound was used in combination with other substances, increasing hair growth. This result could be explained by the multifactorial pathophysiology of AGA, involving hair follicle sensitivity to DHT and microinflammation. Therefore, a multi-therapeutic approach seems to be more effective in AGA management. In conclusion, more studies are needed to establish protocols and to evaluate long- term dutasteride injections.

Key words: Androgenic alopecia; Dutasteride; Mesotherapy.

INTRODUCTION

Androgenic alopecia (AGA) is the most common cause of patterned hair loss in predisposed men and women. AGA is a multifactorial and polygenetic condition, affecting 80% of Caucasian men and 40-50% of Caucasian women during life [1-3]. In Asian and African populations, the prevalence descresce to about 14% in men [4,5].

AGA is characterized by a gradual reduction of the anagen and increase in telagen phase, leading to a progressive follicle miniaturization. As a consequence, terminal hairs are converted into vellus hairs decreasing hair density. The patterned male hair loss is classified in seven degrees according to the stage, firstly described by Hamilton in the 1950s [1] and improved later by Norwood [6]. Two years later, Ludwig described the female hair loss scale [7].

Mesotherapy, that employs multiple microinjections of a mixture of compounds into the mesoderm, is a cosmetic tool used worldwide. In AGA treatment, mesotherapy is being used with 5α-reductase inhibitors, especially dutasteride, injected directly on scalp. Thus, this updated review summarized the injectable use of dutasteride based on data available on PubMed until March 2017.

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Pathophysiology of AG

The pathophysiology of AGA is heterogeneous and highly complex. A diverse combination of genetical factors, endocrine abnormalities, circulating androgens, drugs, diet and microinflammation in hair follicles of each individual are related to this condition [8-10].

Despite that the inheritance mode is unknown, several gene polymorphisms were found in AGA. Mutations in 5α-reductase, aromatase, estrogen receptor α and others have been related on literature [9,11-14]. However, the strongest association with AGA development is made when genetic alterations occur in androgenic receptors. These alterations increase androgenic receptors expression especially in frontal and vertex regions [15], explaining the patterned hair loss [16].

It is well known that androgens are the major modulators of male AGA but their specific action on female AGA is still under debate [17-19]. Circulating testosterone is converted by 5α-reductase in 5α-dihydrotestosterone (DHT) in the periphery. This reductase present 3 isoforms: types 1, 2 and 3 [20,21]. Type 1 is mainly found in the skin, especially hair follicles, sweat and sebaceous glands [22,23] whereas type 2 is predominantly located in male genitalia and prostate but is also found in the inner root sheath of hair follicles [24]. DHT, which present 10 times more affinity to androgen receptors compared to testosterone, binds to these receptors in genetically predisposed hair follicles, impairing hair cycle. The landmark decrease of anagen phase occur, anticipating catagen phase in a complex process involving apoptosis as probably microinflammation [10,25]. The involvement of hair follicle microinflammation in AGA is being reported since the 1970s. This process that occurs at least in one-third of AGA cases [10,26-29] initiates at infundibulum mediated by bacteria, UV irradiation, chemical and/or mechanical stress. Keratinocytes rapidly respond to stressors releasing interleukin-1α (IL-1α) [30,31] that was shown to inhibit hair growth in vitro [32-34]. A transcriptional cascade is activated, increasing pro-inflammatory cytokines (IL-1α, IL-1β, TNFα), chemokines (IL-8, MCPs), collagenases and others. Fibroblasts also respond to pro-inflammatory factors [35] and cellular defenses (neutrophils, T cells, Langerhans cells) are mobilized [36,37]. The inflammation usually persists and may lead to tissue remodeling via collagenases, generating a perifollicular fibrosis [10] and also to apoptosis that has been recently related to follicle miniaturization [25].

Diagnosis of AGA

The classic male pattern hair loss can be identified based on the Norwood scale however, a differential diagnosis is crucial to better evaluate this condition. Family history of baldness and the observation of a transition from large, thick, pigmented to thinner, shorter and nonpigmented vellus hairs are strong indicative of this condition [38]. Thrichoscopy can be useful to evaluate the alteration in hair diameter [39] and the presence of inflammation and erythema on scalp should also be considered [38]. In women, polycystic ovary syndrome, congenital adrenal hyperplasia and other disorders related to hormonal metabolism are often related do AGA [40].

The physical examination is the landmark to diagnose AGA but some laboratory exams may help in patient assessment. The analysis of testosterone metabolism and thyrotropin levels can be useful to correlate AGA with hormones disorders when suspected [38,41]. Alteration in iron metabolism and nutricional deficiencies may also be involved in AGA [38].

Dutasteride and the management of AGA

The complex pathophysiology is a challenge in AGA treatment and, for this reason, the stop of progression and further thinning are the main goal. In addition, there is only two FDA-approved therapies: finasteride, a type II 5α-reductase inhibitor that present well documented sexual adverse effects and minoxidil, a vasodilator that may present unwanted hair grow [42].

Dutasteride, a second-generation inhibitor of 5α-reductase is more potent than finasteride due to the capability of inhibit types 1 and 2 of the enzyme. This leads to a 90% reduction of DHT serum levels whereas finasteride reduces only 70% [43]. The firsts short-term studies comparing dutasteride to finasteride emerged at the 2000s [44-46]. Olsen et al showed that 24 weeks dutasteride 2.5 mg is more efficient than finasteride 5 mg in men with AGA [44]. Similarly, dutasteride 0.5 mg was also more potent than finasteride 1 mg [46].

The safe and efficacy of dutasteride was also observed in long-term studies. A six-months phase III study showed tolerability and improvement of hair growth in AGA patients receiving 0.5 mg/day dutasteride [45]. Recently, Chung and coworkers showed that dutasteride for more than 6 years was safe and increased terminal, vellus and total hair count in male AGA patients [47].
the other hand, adverse effects to those presented by finasteride (alterations on erectile, ejaculatory functions and fertility) and its long half life (4 weeks) [42] are the main factors that contribute to the reluctance on the use of dutasteride in AGA. Thus, the local administration of dutasteride by mesotherapy and a consequent reduction of systemic side effects is a relevant tool on AGA treatment [48].

Hair mesotherapy

Mesotherapy consists in intradermal injections of pharmacological substances in a specific body region with minimal or no systemic effects [49]. This minimally invasive technique was introduced by Michael Pistor in 1958 to treat asthma but the patient’s hear loss was also resolved. More than 50 years later, mesotherapy has been used in the treatment of hair loss, cellulite, wrinkles, scar reduction, melasma, and fat deposits. The combination of pharmaceuticals, vitamins, enzymes and other bioactive substances vary according to the indication since there is no standardized formulation [49,50].

Hair mesotherapy, also called mesohair, is used to treat alopecia with injections directly on affected areas of scalp of patients with AGA up to type IV on Norwood-Hamilton classification [51]. The objective is to improve local circulation and stimulate hair follicle environment by providing nutrients. There are few scientific studies showing an improvement of patterned hair loss and despite the lack of a standardized protocols, some chemicals are commonly used: finasteride, dutasteride, minoxidil, biotine, dexpanthenol and minerals.

The efficacy and safety of hair mesotherapy with dutasteride were reported by distinct groups [48,52,53]. In this regard, Abdallah and coworkers showed that a dutasteride-containing preparation (dutasteride 5 mg, D-panthenol 500 mg, biotin 20 mg and pyridoxine 200 mg in a final volume of 10 mL) increased hair count in man with hair loss. A reverse correlation between hair loss duration and scored hair improvement was also observed in this study [48]. Increased hair diameter, thickness and other aspects were also found using mesotherapy in women with alopecia but using the same dutasteride-containing preparation [52]. The main question that arose from these early studies was regarding the specific role of dutasteride on these effects since the solutions also contained several vitamins. Thus, Sobhy and colleagues recently compared mesotherapy sessions with the same dutasteride-containing solution as previous works with pure dutasteride and saline in men. A trichogram analysis showed that the best result was achieved when dutasteride was used in combination with other substances, increasing hair growth [53]. This result could be explained by the multifactorial pathophysiology of AGA, involving hair follicle sensitivity to DHT and microinflammation. Therefore, a multi-therapeutic approach seems to be more effective in AGA management.

Besides being generally safe, hair mesotherapy may present undesirable effects. Some studies reported patchy hair loss [54] and cicatricial alopecia [55] after the injections. Multifocal scalp abscesses with fat necrosis was also reported [56]. These cases underlie the possible risks of hair mesotherapy, emphasizing the importance of the professional experience and the cocktail composition.

CONCLUSION

Hair mesotherapy is being increasingly used by dermatologists and hair specialists in several countries and is a good alternative to manage AGA. Better results are achieved when dutasteride-containing solutions are used and mesotherapy are early initiated. However, more studies are needed to establish protocols and to evaluate long-term dutasteride injections.

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