

## REVIEW ARTICLE

# Characteristics of Androgenetic Alopecia in Asian

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Androgenetic alopecia (AGA), or pattern hair loss, is a common disorder in Asian men and women, with a reported incidence of up to 73% among general population. There are several descriptions regarding the characteristics of AGA in patients of European descent. Asian patients with AGA have different types of hair loss and family histories from Europeans, which may affect treatment response. Therefore, in this review, prevalence, hair loss patterns, familial factors, androgen receptor gene polymorphisms of Asian AGA patients, and management based on algorithmic guidelines for AGA are discussed. This review may be useful for dermatologists in clinical practice for diagnosing and designing management approaches for Asian patients with AGA. (*Ann Dermatol* 24(3) 243~252, 2012)

**-Keywords-**

Androgenetic alopecia, Asians

## INTRODUCTION

The term "androgenetic alopecia (AGA)" was introduced by Orentreich<sup>1</sup> in 1960, but the same condition in men has also been termed male pattern alopecia, common baldness, male pattern baldness, and male pattern hair loss (MPHL). Androgen dependence and hereditary factors are less obvious in affected women than in affected men, thus the term pattern hair loss, which is a much broader concept, is preferred for women. AGA is the most

common type of alopecia that occurs after puberty in both sexes. Patients typically present with progressive thinning and shortening of hair in affected areas. AGA is clearly a stressful experience for both sexes, but it may be substantially more distressing for women. In this review, Asian characteristics of prevalence, hair loss patterns, familial factors, androgen receptor (AR) gene polymorphisms, and management of AGA will be discussed.

## PREVALENCE OF AGA IN ASIAN

There are population differences in the prevalence and types of AGA. In individuals of European descent, the prevalence of AGA has been well documented by Hamilton<sup>2</sup> and Norwood<sup>3</sup>. A study of European-American men in the USA revealed a predominance for frontal baldness (Type A variant in Norwood-Hamilton classification) in 12% and a Type III or worse pattern in 16% of males aged 18~29 years old, which increased progressively to 53% in those aged 40~49 years old<sup>4</sup>. A study of 20~50 year old Norwegian men most commonly reported Type I (31%), followed by Type II (26%) and Type V or worse (20%)<sup>5</sup>.

AGA is also a common disorder in Asian people. Takashima et al.<sup>6</sup> and Kakizo<sup>7</sup> studied AGA in Japanese and found that it was minimal before the age of 40 and that, although the incidence increased with age, it remained lower than in Europeans. Japanese men develop AGA approximately one decade later than Europeans, and the prevalence is 1.4-fold lower in each decade of life<sup>6</sup>. In Korean men, the prevalence of AGA (Norwood III or above) at all ages was 14.1% and increased steadily with advancing age, but remained lower than that of Europeans: 2.3% in the third decade, 4.0% in the fourth decade, 10.8% in the fifth decade, 24.5% in the sixth decade, 34.3% in the seventh decade and 46.9% over 70 years. Type III vertex involvement was the most common type in the third decade to the seventh decade in Korean men; over 70 years, type VI was most common. A 'female

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pattern' was observed in 11.1% of cases<sup>8</sup>. In Korean women, the prevalence of AGA (Ludwig I or above) at all ages was 5.6%, and also increased steadily with advancing age: 0.2% in the third decade, 2.3% in the fourth decade, 3.8% in the fifth decade, 7.4% in the sixth decade, 11.7% in the seventh decade and 24.7% over age 70 years. Type I was the most common type up to the sixth decade; over 60 years, Type I and II were similar in prevalence. Type III was not observed<sup>8</sup>.

The age specific prevalence of AGA in Taiwanese men was compatible to that among Korean men but was lower than that among individuals of European descent<sup>9</sup>. Smoking status, current amount of cigarette smoking, and smoking intensity were statistically significant factors for AGA after controlling for age and family history<sup>9</sup>. A population-based cross sectional study was carried out in 7,056 subjects (3,519 men and 3,537 women) in Shanghai, China<sup>10</sup>. The prevalence of AGA in Chinese men was 19.9%, and the prevalence of female pattern hair loss (FPHL) in men was 0.1%. The most common type of hair loss in men was type III vertex (3.5%). The prevalence of AGA in Chinese men was lower than in European men but was similar to that in Korean men. However, over the age of 60 it approached the prevalence in European men and was higher than in Korean men. The prevalence of AGA in Chinese women was 3.1%, while MPHL in Chinese women was found in those aged over 50 years (0.4%), and the most common type was Ludwig type I (1.4%). Interestingly, the prevalence of AGA in Chinese women was lower than that in Korean women and European women, and type I was the most common type<sup>10</sup>.

In Singapore, Tang et al.<sup>11</sup> reported a prevalence of 63% for Norwood type I to VII. The prevalence increased with age from 32% among young adults aged 17 to 26 years to almost 100% for those in their eighties. In Thailand, Pathomvanich et al.<sup>12</sup> conducted a randomized study including 1,124 Asian men (local Thai and Chinese) between the ages of 18 and 90. The prevalence of baldness was reported as 38.52%; this figure approached that of Europeans, rather than the one fourth to one third reported in previous studies of Asians<sup>6</sup>. The prevalence increased with age, affecting 11% of young adults aged over 20 years and reaching 61.78% at 70 years of age. There are, however, two limitations of this survey. First, the small number of men included over 80 years of age (31 men) might have affected the results when compared to the Norwood study of the same age group. In addition, there were two Asian subgroups involved in this study, Thai and Chinese.

According to these studies mentioned, the prevalence of

AGA in Chinese and Korean men was similar to, but significantly lower than, the prevalence in Thailand. The highest prevalence among the Asian groups studied was the 63% observed in Singapore; this discrepancy may be attributed to the diverse populations residing in the country or the inclusion of the almost normal Norwood type I in the Singapore study. In contrast, type II was the most common pattern among Indian males until the sixth decade, followed by type III Vertex after the sixth decade. The type A variant was only seen in 1% of Indian males, and FPHL was only observed in 0.2% of Indian males. These results suggest a less extensive balding pattern in Indian male population than in other Asian populations<sup>13</sup>. In summary, Asian men with AGA have different characteristics from those of men of European descent. There are similar increases in prevalence with age among all the Asian groups studied. This high prevalence in older men suggests that this form of hair loss may be a normal consequence of aging. However, particularly in younger men, hair loss can have significant psychosocial manifestations, and can in turn have a significant economic impacts on household health expenditures<sup>14</sup>. The wide variation in prevalence rates in the current Asian studies would require a more standardized protocol.

## AR GENE POLYMORPHISM IN AGA

Balding scalps are characterized by high levels of the potent androgen dihydrotestosterone (DHT) and increased expression of the androgen receptor gene. Most AGA patients have an androgen dependent trait, although it is thought to be under the control of multiple genes, such as genes for the AR, insulin-like growth factor-1, and DHT regulations<sup>15,16</sup>. The human AR gene is on the X chromosome at Xq11-12. The AR is a structurally conserved member of the nuclear receptor superfamily. The amino terminal domain is required for transcriptional activation and contains a region of polyglutamine that is encoded by CAG trinucleotide repeats. In humans, the number of CAG repeats is polymorphic. Expansion of CAG repeats in the AR has clinical implications for human disease<sup>17</sup>. A low number of CAG repeats in the AR gene implies increased risk factors for coronary heart disease<sup>18</sup> and prostate cancer<sup>19</sup>. In recent studies, neurotrophic factors, especially brain-derived nerve factor, were found to have potential importance mediating the effects of androgens on hair follicles, serving as negative regulatory control signals<sup>20</sup>. These findings suggest that other regulatory signals may affect the pathogenesis of AGA, as well as AR gene polymorphisms.

The ubiquity of the AR gene Stu I restriction site, and the

higher incidence of shorter triplet repeat haplotypes in bald men, suggests that these markers are very close to a functional variant that is a necessary component of the polygenic determination of male pattern baldness. A meta-analysis study by Zhuo et al.<sup>21</sup> suggests that the G allele of the AR Stu I polymorphism might be a potential risk factor for AGA, especially in subjects of European descent. Functional mutations in or near the AR gene may explain the high reported levels of expression of this gene in the balding scalp<sup>22</sup>. Shorter CAG repeat lengths may be associated with the development of androgen mediated skin disorders such as AGA, hirsutism, and acne in men and women<sup>23</sup>. These findings suggest that the CAG repeat length in AR may affect androgen mediated gene expression in hair follicles and sebaceous glands in men and women with androgenic skin disorders<sup>14,23</sup>. Interestingly, when the number of triplet repeats (CAG+GGC) was plotted against degree of symptom improvement after treatment with finasteride, a broad correlation between these variables was observed<sup>24</sup>. The smaller the repeat number, the greater the improvement with finasteride. The group of patients with shorter repeat regions in the AR gene responded better to finasteride than did those with longer repeat regions, although patients with shorter repeats tended to have severe initial symptoms. The determination of such polymorphisms is thought to be useful in drug choice for AGA patients<sup>24</sup>. Jung et al.<sup>25</sup> compared CAG repeat numbers within the AR genes of 64 male Korean AGA patients with those of 40 normal male controls in a preliminary study. There was no significant difference in the number of CAG repeats between the Korean AGA patients and controls. There were no correlations between CAG repeat numbers and age of onset or severity of AGA in Korean AGA patients. These results suggests that AR receptor CAG polymorphisms in the Korean male population might not play a major role in AGA susceptibility. Nevertheless, a more extensive study to clarify whether there are real population-based differences in AR gene polymorphisms is needed. Recently, advanced genetic studies of AGA have been published. Hayes et al.<sup>26</sup> reported that the gene locus of E211A is significantly lower in proportion in the vertex and vertex balding group and frontal balding group compared with the no balding group. Therefore, the AR-E211A allele, in linkage with the functional repeat sequences, is associated with a lower risk of metastatic prostate cancer and a lower risk of alopecia. Moreover, a study using genome-wide linkage study revealed a locus associated with AGA on chromosome 3q26<sup>27</sup>. Hillmer et al.<sup>28</sup> investigated the signatures of genetic variants of AR and their relationships to the AGA risk

haplotype. Haplotype homozygosity suggested that the AGA risk haplotype was driven to high frequency by positive selection in Europeans, although a low meiotic recombination rate contributed to high haplotype homozygosity. Further, they detected high levels of population differentiation and a series of fixed derived alleles along an extended region centromeric to AR in the Asian HapMap sample.

## **RACIAL DIFFERENCES IN PATTERNS OF HAIR LOSS IN AGA AND THE BASP CLASSIFICATION FOR AGA**

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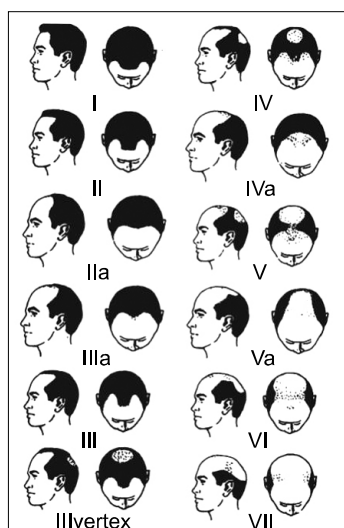
Asian men with AGA display different characteristics compared with men of other ethnicity. However, there is an increase in prevalence with age among all the Asian groups studied similar to that observed in other ethnic population<sup>8-12,29</sup>. The reason for this increase rate in the prevalence of AGA compared to Europeans remains unknown, but a transition toward a more Western diet and lifestyle may play a role.

There are also populational differences in the patterns of hair loss in AGA. In a previous study, FPHL was observed in 11.1% of Korean males with AGA<sup>8</sup>. In a Chinese study, MPHL was found in 13 of 108 (12%) women with AGA, all of whom were over 50 years of age<sup>10</sup>. In an Indian study, although it was possible to classify 80% of cases of AGA and II (28%) and III (15%) were the most common types of AGA, 27 patients of 150 male subjects (18%) did not fit into specific patterns according to the Norwood Hamilton classification<sup>30</sup>. In addition, the type 'a' variant was noted in 20% of patients, clearly indicating the limitations of the existing classifications. There is considerable overlap in types IV, V and VI in the Norwood classification, with the 'a' variants further confusing the picture<sup>30</sup>.

Various classification methods have been proposed for describing AGA. In 1950, Beek<sup>31</sup> published a classification system, based on 1,000 males of European descent, which used two evolutionary aspects: frontal and frontovertical baldness. In the following year, the first systematic classification of AGA was established by Hamilton<sup>2</sup>, who sub-classified patterns of baldness based on frontoparietal, frontal recession, and vertex thinning, then evaluated a large group of men and women for the presence of specific patterns of hair loss from the prenatal period through the tenth decade of life. In 1975, Norwood<sup>3</sup> refined Hamilton's classification by emphasizing temporofrontal or vertex only subcategories of hair loss into seven types with a type A variant and reported the incidence of male pattern baldness at various ages in 1,000 adult male

subjects of European descent. An additional pattern was introduced as the Norwood-Hamilton classification in a clinical trial of finasteride in MPHL<sup>32</sup>. Olsen<sup>33,34</sup> proposed assigning separate designations (temporal, frontal, mid and vertex) to areas of the scalp that bald at different rates in different individuals with MPHL. Ludwig<sup>35</sup> presented quite a different picture of hair loss in women from that described by Hamilton<sup>2</sup>. He emphasized preservation of the frontal fringe despite progressive centrifugal loss over the top of the scalp and arbitrarily designated three gradations of hair loss. Olsen<sup>36</sup> proposed that frontal accentuation (or the “Christmas tree” pattern) should be considered an additional pattern of hair loss in women, which helps to distinguish AGA from potential hair loss mimics in women. Presently, the Norwood-Hamilton classification<sup>32</sup> for MPHL and the Ludwig classification<sup>35</sup> for female AGA are the most commonly used classification methods for assessing AGA worldwide.

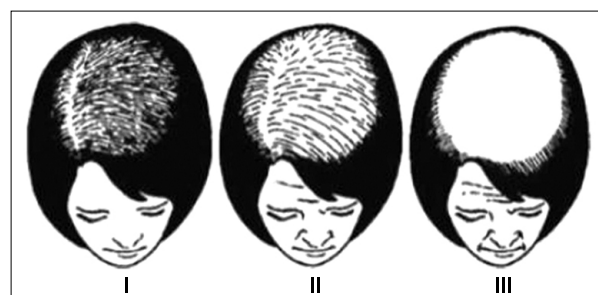
Each of these existing classifications has substantial limitations in clinical setting. The Norwood-Hamilton classification (Fig. 1)<sup>3</sup> is very detailed and is less stepwise classifications in its descriptions, making it difficult to memorize for common use. It does not list some non-typical types of baldness, such as FPHL in men. Additionally, many women with MPHL cannot be classified using the Ludwig classification system (Fig. 2)<sup>35</sup>. For most of these classification systems, clinicians must use different classification systems for each gender in order to correctly classify patterns<sup>34</sup>.



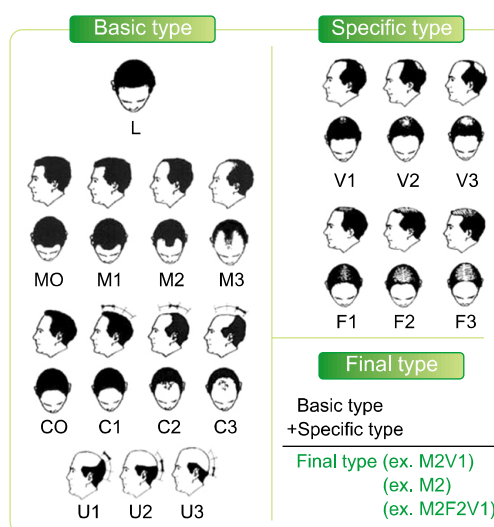
**Fig. 1.** The Norwood-Hamilton classification of male balding defines two major patterns and several less common types. Thinning starts in both temples as well as the crown/vertex and slowly progresses to encompass the entire top of the scalp (cited from Ref. 3).

Thus, a more widely accepted, accurate, and stepwise method for classifying AGA would be of great benefit. Lee et al.<sup>37</sup> devised a new classification system, named the Basic and Specific (BASP) classification (Fig. 3), which is comprehensive and systematic regardless of population or gender. The BASP classification<sup>37</sup> was based on observed patterns of hair loss. The basic (BA) types represent the shape of the anterior hairline, and the specific types (SP) represent the density of hair on distinct areas (frontal and vertex). There are four basic types (L, M, C, and U) and two specific types (F and V). The final type is assigned according to a combination of the assigned BA and SP types.

A total of 2,213 Korean subjects, comprised of 1,768 males and 445 females, were classified according to the BASP classification<sup>37</sup>. According to the severity of the



**Fig. 2.** The Ludwig pattern of hair loss (3-point). There are three main classes, each with increasing hair loss (cited from Ref. 35).



**Fig. 3.** The BASP classification system includes four basic types (L, M, C, and U) and two specific types (V and F). The basic types represent the shape of the anterior hairline, and the specific types represent the density of hair on specific areas (frontal and vertex). The final type is decided by the combination of the basic and specific type (cited from Ref. 37).

phenotype, both the basic and specific types were subclassified into subtypes in order to generate a more stepwise and systematic classification. It is possible to describe patterns of hair loss in detail using the BASP method, and, thus estimate the further extent of hair loss and therapeutic response to a certain therapy. For both sexes, the majority of patients enrolled in the study were in the third and fourth decades of life (65.1% of males and 56.68% of females). In males, the older as well as the younger group were more likely to have little recession of the frontal hairline (classified as type M1-2) and diffuse thinning over the top of the scalp (type F1-2). The women in the study developed typical female AGA.

In men, regardless of age, 1,434 of the 1,768 males were classified as type M, accounting for 81.1% of cases. Among the subtypes and according to the severity of baldness, the majority of subjects below 50 years of age were classified as type M1, whereas most subjects over the age of 50 were classified as type M2. The incidence of Type L (9.3%) tended to decrease with age, but those of types C (5.8%) and U (3.8%) tended to increase. In women, type L showed the highest frequency in all age groups, accounting for 210 (47.2%) of 445 female subjects. Regardless of age, types M, C, and U were the next most common in order, observed in 121 women (27.2%), 111 women (25.0%), and 3 women (0.6%) of the 445 subjects, respectively. Type C0 was the second most common subtype in female subjects between the second and fourth decade of life, and its incidence decreased with age. In men, type F, which is identical to FPHL in the Ludwig classification, was observed in 42.4% (749/1,768) of male subjects, and type V was observed in 19.8% (350/1768). The grades of both types increased slightly with age. In women, type F was observed in 70.6% (314/445) of female subjects with AGA.

The BASP classification is a stepwise, systematic, and universal classification system for AGA, regardless of race or sex. It is an easily available comprehensive classification system. The BASP classification may prove particularly useful in communicating the exact amount and distribution of hair loss in those with AGA<sup>37</sup>. For these reasons, we use the basic and specific (BASP) classification in this review.

## FAMILIAL FACTORS IN AGA

Family history plays an important role in the onset of AGA, which is believed to be influenced by genetic factors. However, the exact mode of inheritance has not been well characterized. Although there are some reports regarding the prevalence of AGA in male paternal family members, reports regarding the maternal side are rare. The

AGA prevalence in male family members of patients (30.3%) was higher than those of controls (8.5%)<sup>38</sup>. AGA prevalence on the paternal side was greater than on the maternal side. However, no differences were found between paternal and maternal AGA prevalence, analyzed according to the age of onset and severity of AGA. These results suggest that AGA expression might be influenced by familial AGA prevalence and that paternal AGA prevalence has a greater effect in general on AGA expression than maternal AGA prevalence<sup>38</sup>.

In another Korean study, a family history of baldness was present in 48.5% of men and 45.2% of women with AGA<sup>8</sup>. In a Chinese study, a family history of AGA was present in 55.8% of men and 32.4% of women with AGA<sup>10</sup>. In contrast to the Korean study, the proportion of Chinese men with a positive family history was higher, suggesting that genetic background is important for determining the prevalence of AGA in Chinese men, and confirming that subjects with positive family histories are at greater risk of developing severe AGA<sup>9</sup>. The proportion of Chinese women with positive family histories was lower, further indicating that AGA is a polygenetic hereditary disease. In a Singaporean study, a positive family history of AGA was recorded in 58.9% (151/256) of subjects. Male patients tend to be more likely to have a father or male sibling with a similar problem, whereas female patients tend to be more likely to have a mother or female sibling with AGA<sup>39</sup>. In an Indian study of 150 subjects, positive family histories were found in 127 (85%) of subjects, paternal in 101 (67%), maternal in seven (5%) and both in 19 (13%). In 23 (15%) patients, no family history could be elicited.

In a Taiwanese study, an association was detected between moderate or severe AGA and family history of AGA from paternal relatives, whereas there was no corresponding association with maternal relatives<sup>9</sup>. Moderate or severe AGA was associated with a family history of AGA among first degree and second degree relatives but not among third degree relatives after adjusting for age. In addition, family histories of AGA among paternal relatives were predictive of moderate or severe AGA after adjusting for age. These findings do not support an association between moderate or severe AGA and a family history of AGA among maternal relatives. Moreover, a family history of AGA is associated with the risk of early onset AGA. This implies that those with a family history of AGA may have a higher risk of early onset AGA and a higher risk of developing severe AGA. Most importantly, early onset AGA showed a dose dependent association with AGA grade after adjusting for age and family history. From a clinical point of view, this suggests that patients with early

onset AGA should receive early advice to prevent further deterioration<sup>9</sup>. These results of various epidemiologic familial studies suggest that AGA expression is influenced by familial AGA prevalence and, particularly, that paternal AGA prevalence has more effect on AGA expression than maternal AGA prevalence.

A recent study by Lee et al.<sup>40</sup> using the BASP classification revealed that familial factors affecting the morphology of AGA in Asians differ between males and females, and for each BASP subtype. Parental influences on anterior hairline shape in men were predominantly from the paternal side, whereas these effects were less notable in women. In patients without family histories of AGA, a higher frequency of early-onset AGA than late-onset AGA was identified in men but not in women. Basic types of hair loss had a higher degree of heritability from the paternal side of the family, regardless of the specific type. This study provides detailed information indicating that each hair loss pattern according to the BASP classification has different familial factors in Asians<sup>40</sup>. Therefore, we can provide appropriate information to patients if we obtain careful personal and familial histories of AGA.

## MANAGEMENT OF AGA IN ASIAN

### General consideration

AGA is often related to poor self-image and low self-respect. The problem must be viewed in perspective; an emphatic approach is important, as different people are affected in various ways when they lose hair. Patients should avoid hair-care products likely to injure the scalp and/or hair. Patients should maintain adequate diet, especially with adequate protein. The National Institutes of Health of the United States recommended daily allowance for protein is 0.8 g/kg<sup>41</sup>. Topical medications act only where the medication is applied; therefore, the whole area at risk of hair loss (the top of the scalp) should be treated with a given topical agent. If possible, any drugs that could negatively affect hair growth should be stopped and alternative substitutes used. Any underlying scalp disorders, such as seborrheic dermatitis or scalp psoriasis, should be treated as these conditions can affect the ability to use topical treatments for hair loss without irritation.

The typical man with MPHL who seeks treatment has significant concerns about the condition and has already engaged in considerable efforts to obtain information and at times even resorted to self-medication. Individualized consideration of attitudes, concerns, self-treating efforts, and expectations is crucial for effective management of men seeking medical treatment for MPHL<sup>42</sup>. Research has

shown that most men and women who have unwanted hair loss have distressing experiences that diminish their body image<sup>43</sup>. Because of the psychological impact of hair loss, patients may seek inappropriate and unproven therapies. However, they must also appreciate the real goals and true limitations of each form of therapy. It is important that misconceptions should also be corrected. Some patients mistakenly think that their hormone levels are too high. Others erroneously place too many restrictions on their hair and grooming (e.g., hair styling, teasing, hair spray, washing frequency, hair color or permanents)<sup>44</sup>. Knowledge and understanding of the genetic and physiological basis of AGA may help allay misconceptions and anxiety about its occurrence, and indirectly influence patient willingness to seek treatment for this condition<sup>45</sup>. Clinicians should follow the progress of their patients periodically to identify problems, utilizing photographic records of treatment results.

### Medical treatment

A reduction in hair loss is usually seen after 3~6 months of medical treatment, and visible hair regrowth is observed after 6~12 months. Continuous treatment is needed to ensure sustained benefits. Unfortunately, available medical treatments are not curative. Ensuring that patients understand the limitations of these treatments is an important aspect of the management of AGA. Patients should be counseled that treatment for AGA will not restore hair growth to its prepubertal density and that the main aim is to prevent further progression of hair loss. Currently there are two agents, topical minoxidil and oral finasteride (only for males), approved by the United States Food and Drug Association (FDA) for the treatment of AGA.

#### 1) Male

##### (1) Topical minoxidil solution

Topical minoxidil solution is administered at a dosage of 1 ml twice daily. Its mechanism of action is unknown. However, the main benefit appears to be a prolongation of the anagen phase and hair shaft diameter, irrespective of the underlying cause of baldness. It is well established that 5% minoxidil is more effective than 2% or 3% solution. Patients should be warned that during the initial 2~8 weeks, a temporary telogen effluvium may occur in some patients, which is self-limiting and subsides when subsequent anagen regrowth begins, and should not be a cause for treatment cessation<sup>46</sup>.

A recent advancement in the use of minoxidil as a hair loss treatment is the development of a 5% topical foam. Placebo controlled, double-blind trials have demonstrated

that the hydroalcoholic foam is efficacious, safe, and well accepted cosmetically by patients<sup>14</sup>.

## (2) Oral finasteride

Oral finasteride, a potent type II 5 $\alpha$ -reductase inhibitor, should be administered at a daily dosage of 1 mg. In clinical trials over a 2-year period in men aged 18~41 years, the number of responding hairs was established after 1 year and continued treatment increased the length, diameter, and pigmentation of these hairs so that the coverage of the scalp increased over time. On stopping finasteride, the balding process resumed. An extension of the above study to 5 years showed that finasteride 1 mg/day was well tolerated, and led to durable improvements in scalp hair growth<sup>47</sup>.

Finasteride is generally well tolerated, side effects are typically mild and do not require discontinuation of therapy. Rare side effects may include some loss of libido and erectile function. At present, there is no proven benefit for finasteride in women. A placebo-controlled study in postmenopausal women with AGA given finasteride 1 mg/day over 1 year showed no significant benefit<sup>47</sup>.

## 2) Female

### (1) Topical minoxidil solution

Topical minoxidil solution is administered at a dosage of 1 ml twice daily. The 5% solution was compared with the 2% solution in 2 studies involving 493 women. On the basis of hair-count data, the 5% solution was not significantly more effective than the 2% solution<sup>48</sup>. Patients should be warned that in the initial 2~8 weeks, a temporary telogen effluvium may occur in some patients, which is self-limiting and subsides when subsequent anagen regrowth begins, and should not be a cause for treatment cessation<sup>46</sup>. Side effects include hypertrichosis which occurs in 6% of women using 2% minoxidil, and 14% among those using the 5% solution<sup>46</sup>. This occurs on the face and resolves within 1~6 months after drug discontinuation. However, hypertrichosis diminishes or disappears after about 1 year, even with continued use of minoxidil.

### (2) Oral antiandrogens

Cyproterone acetate, spironolactone and flutamide can be used as alternatives to minoxidil, but most of the antiandrogen therapies have not been rigorously studied in FPHL<sup>49</sup>. In general, better results are seen in women with hyperandrogenism. Side effects are generally greater with cyproterone acetate and spironolactone<sup>41</sup>.

## Surgical management

Despite advances in medical therapy, hair transplantation

remains the only means of permanent hair restoration in cases of severe AGA. It is contraindicated in patients with systemic diseases such as hypertension, cardiac disease, and diabetes mellitus, all of which must be controlled before hair transplantation. Local diseases such as cutaneous lupus erythematosus, morphea, alopecia areata, and scalp folliculitis must be quiescent for at least 6 months before hair transplantation. Complications of hair transplantation include ingrown hairs and foreign body reactions, infections, cobblestoning, graft depression, epidermal cysts, bleeding, headaches, scarring (keloid and hypertrophic scars), poor hair growth, arteriovenous fistula, osteomyelitis, wound dehiscence, telogen effluvium, accelerated hair loss, delayed temporary marked thinning, curly, lusterless hair, chronic mild folliculitis, and patient dissatisfaction.

After 4~6 months, the skin surfaces of the grafts have usually blended in perfectly with the surrounding scalp. In some patients, the grafts may be a shade lighter in color until they are "aged" by sun exposure<sup>50-52</sup>.

## Other alternative medical therapies

Dutasteride is a dual type I and type II 5 $\alpha$ -reductase inhibitor. In clinical trials, oral dutasteride showed significantly greater efficacy than placebo according to phototrichometric hair count, subject self-assessment, and investigator and panel photographic assessment<sup>53</sup>. Dutasteride is generally well tolerated, with rare side effects that may include some loss of libido and erectile function. Dutasteride is only approved by the Korean FDA for the treatment of AGA.

Topical alfatradiol may be an alternative, though reports of its efficacy have variable results to treat AGA<sup>54</sup>. Under the influence of 17 $\alpha$ -estradiol (alfatradiol), an increased conversion of testosterone to 17 $\beta$ -estradiol and androstendione to estrone improves hair growth<sup>55</sup>. Topical alfatradiol is available in Europe, South America, and Korea. Kim et al.<sup>56</sup> reported single center, open-label, non-comparative, phase IV study of the efficacy and safety of alfatradiol (17 $\alpha$ -estradiol) solution on female pattern hair loss in Korean women. Hair counts and diameter from baseline to 4 and 8 months after treatment were significantly increased in treated patients.

Bimatoprost and latanoprost, which are prostaglandin (PG) analogues, demonstrate stimulatory effects on hair growth of eyebrows and eyelashes and pigmentation in a high numbers of patients<sup>57</sup>. Currently bimatoprost is approved as eyelash growth enhancer. It might be used for the treatment of AGA off-label. The expressions of PG receptors were examined in mouse skin hair follicles, and mRNA was identified in dermal papilla and outer root

sheath follicular structures during the anagen phase. In addition, other studies have demonstrated the ability of PG to stimulate movement from telogen to anagen in mice.

Ketoconazole might also be used for the treatment of AGA. The mechanism of ketoconazole is unknown, but may involve inhibition of inflammation, or anti-androgenic properties<sup>58</sup>. There is some evidence, both in humans and in rodents, that this agent may stimulate hair growth<sup>14</sup>. Prostaglandin analogues and ketoconazole are not approved for AGA treatment and further studies are needed to investigate the therapeutic effect on AGA.

### Other devices and non-medical aesthetic aids

Devices can be used as alternative tools for the treatment of AGA. Laser hair comb (Low-level laser therapy)<sup>59,60</sup> and Fractional photothermolysis laser<sup>61</sup> have been tried to treat AGA. However, these treatments cannot be substituted for the medical and surgical approaches previously mentioned.

Non-medical approaches can provide cosmetic relief to both men and women with thinning hair, if medical treatments are not indicated, not effective, or not desired by the patient. Non-medical aesthetic aids include wigs, hairpieces, hair extensions, and topical powder makeup. They can also be used as adjuvant tools to medical or surgical treatments<sup>41</sup>.

### CONCLUSION

Although the clinical aspects of AGA are recognized in both men and women and the role of DHT is well documented, much remains to be determined regarding the most appropriate treatments for AGA based on genetics and pathophysiology. AGA is a disconcerting experience for both sexes, but it may be substantially more distressing for women. Therefore, dermatologists should take into account the psychological well-being of patients with AGA, which can lead to the choice of an appropriate treatment. Moreover, most of the previously published studies of AGA were conducted among only patients of European descent. There are effective treatments, medical or surgical, currently available for some men and women with AGA. Compared to other populations, Asian patients with AGA have different types of hair loss and family histories, which may influence treatment response. This review of AGA in Asians may be practical for informing dermatologists regarding their approaches to understand, diagnose and treat Asian patients with AGA in clinical practice.

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