CONSENSUS STATEMENT ON THE MANAGEMENT OF ANDROGENETIC ALOPECIA



by

Ministry of Health Malaysia
Academy of Medicine Malaysia
Persatuan Dermatologi Malaysia
(Dermatological Society of Malaysia)

2003

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CONSENSUS ON MANAGEMENT OF ANDROGENETIC ALOPECIA

Summary

Androgenetic alopecia is a common disorder in Malaysia. It is estimated that at least 50% of men develop androgenetic alopecia or male pattern hair loss at some point in their lives. Androgenetic alopecia has important psychosocial impact fects on patients. This translates into a significant economic impact in the household health expenditure. It is important that doctors including family practitioners be involved and trained in the diagnosis and treatment of androgenetic alopecia. This will help educate the public on the misinformation and myths being propagated and marketed by non-medical sources.

The basic pathophysiology of androgenetic alopecia involves the miniaturization of scalp hair follicles in site-specific areas due to a genetic predisposition being translated by a hormonal mechanism. Current evidence indicates that dihydrotestosterone(DHT) is the hormonal messenger.

Currently, the only pharmacological agents that are scientifically proven effective are oral Finasteride and topical Minoxidil. Surgical treatment is an option for selected patients.

Except for surgery, currently available pharmacological treatments are suppressive and not curative. Supporting the patients emotionally and ensuring that they understand the limitation of these treatments remains an important component of the management of androgenetic alopecia.

Definition

Androgenetic Alopecia (AGA) is a genetically determined pattern of baldness mediated by increased follicular androgen sensitivity leading to follicular minituarization with characteristic and progressive pattern of baldness in males and females.

Clinical Features

In both sexes the essential feature is replacement of terminal hair by progressively finer and shorter vellus hair in a frontovertical distribution. The onset may be any time after puberty and may be clinically apparent by age 17 in normal Caucasian males and 25-30 years in normal Caucasian females. In our Asian context, the prevalence of AGA. in Chinese is less common than in Caucasians, milder and of later onset . Japanese males for instance develop AGA. 10 years later than Caucasoids and have 1.4 times less AGA in each decade of life. In all races, the reduction in follicle size is associated with shortened anagen and increased shedding of telogen hair .

Males

The distinctive pattern as described by Hamilton and later modified by Norwood spares the posterior and lateral scalp even in the most severe cases. (see figure 1) The sequence and rate of progression can be vacariable but usually starts with bitemporal recession, balding of the vertex, then uniform balding of the frontal area which merges with the bald vertex. Eventually the frontovertical area contains only sparse vellus hairs which are finally lost.

Females

The pattern of A.G.A in women is likely to be that of a diffuse vaultal alopecia – the Ludwig pattern or 'female pattern baldness'. The progression from Ludwig I-III is usually very slow but accelerates around menopause. Abnormal androgen excess needs to be excluded in premenopausal female with Ludwig II-III baldness, Hamilton pattern IV or more. The Hamilton type of baldness is more common after menopause. In pre-menopausal women, 13% Hamilton type II-IV, while in post-menopausal women, the frequency of Hamilton type II-V increase to 37%.

Diagnosis

Males

The characteristic Hamilton-Norwood pattern of alopecia , history of increased shedding, and a strong family history makes the diagnosis easy. Other causes of hair loss have to be considered .

Females

Diagnosis may be more difficult in women with AGA. but generally before menopause the Ludwig pattern of alopecia is seen .

In difficult cases where there is no family history of AGA, together with evidence of androgenic excess eg. acne, hirsutism, a menstrual disturbance, it may be necessary to evaluate the patient over a period of weeks, perform endocrinological assessments, and even scalp biopsies (eg to exclude diffuse alopecia areata, and to prognosticate A.G.A.)

Assessment of severity

The following features indicate a more severe disease :

1. Early age of onset of hair thinning.
2. Family history of AGA in parents, siblings, aunts, uncles and grandparents on both sides of the family.
3. Pattern and distribution of hair thinning /loss:

i) Hamilton-Norwood classification for male pattern hair loss (Refer fig. 1)

Mild : pattern I and II
Moderate : pattern IIa to IV
Severe : pattern IV a to VII

ii) Ludwig classification for female pattern hair loss (Refer fig. 2).

Mild : Ludwig I
Moderate : Ludwig II
Severe : Ludwig III

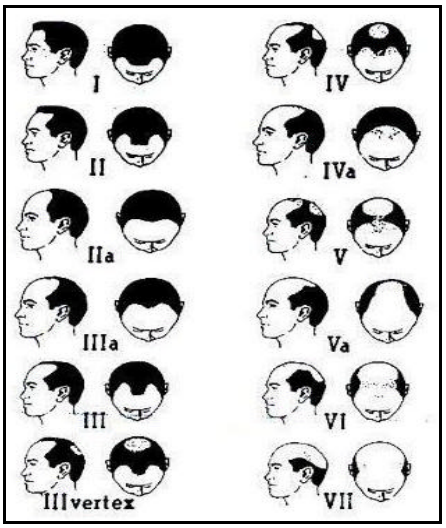


Figure 1. Hamilton-Norwood patterns of hair loss[10]

Figure 2. Ludwig pattern of androgenetic alopecia in women.

iii) Savin classification of hair density is another method of assessing severity of AGA in female patients(fig.3)

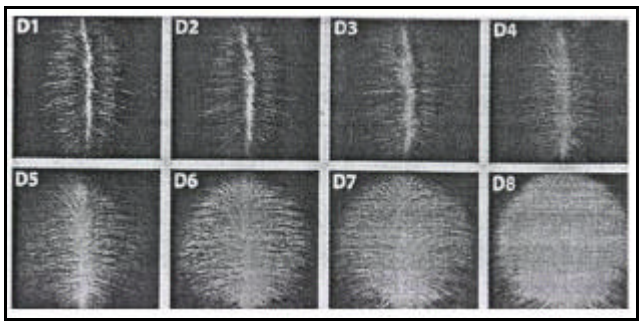


Figure 3. Savin hair density scale.

Investigations

This is a clinical diagnosis based on recognizing a pattern of alopecia and a family history of AGA. If there is any doubt in diagnosis investigations may be done to includfe out other causes of alopecia. The investigations include :

?? Microscopic examination of hair shaft and bulbs(clip test).
About 25 to 30 hairs are cut above the scalp surface and examined on a wet microscopic slide.

?? Hair pull test
About 60 hairs are pulled with constant traction and the bulbs of extracted hairs examined. Normally there should be less then 6 club hairs extracted.

?? Hair pluck test
Abruptly extract hairs from scalp with rubber tipped needle holder and examine the roots. In telogen effluvium > 20% telogen hairs noted.

?? Blood examination to exclude any systemic disorder
Full Blood Count
VDRL
Serum iron, serum, Ferritin, Total Iron Binding Capacity
Thyroid function test
Anti Nuclear Factor

?? Scalp biopsy
This is done if the diagnosis of AGA remains questionable. It helps in distinguishing AGA from telogen effluvium, alopecia areata and a concomitant primary scarring alopecia.

MANAGEMENT

Goals of Therapy
1. To slow down further hair thinning
2. To increase hair coverage of the scalp
3. To assist patients to function normally in society as it may have marked psychological impact

People concerned about their androgenetic alopecia have 4 options
1. Do nothing
2. Get aesthetic aids
3. Seek medical treatment
4. Seek surgical treatment

MEDICAL TREATMENT

Generally, with medical treatment, reduction in hair loss is usually seen in 3-6 months and visible hair regrowth in 6-12 months. Continuous treatment is needed to maintain benefit. All the medical treatments available are not curative. Ensuring that patients understand the limitations of these treatments is an important aspect in the management of androgenetic alopecia.

Males

Currently there are two drugs are approved by the FDA(US) and the Malaysian DCA for treatment of androgenetic alopecia. i.e. topical minoxidil and oral finasteride. Drug treatment does not benefit men who have severe hair loss (grade VI-VII).

1. **Topical Minoxidil solution 2%, 5%**

   Dosage: 1 ml bd

   Mechanism of action is unknown.

   Main benefit appears to be prolongation of the anagen phase and hair shaft diameter, irrespective of the underlying cause. Efficacy varies in different studies.

   In one study, 2% minoxidil arrested progression of hair loss and regrowth of hair in about 90% of men; 60% had a medium to dense growth of hair. However, another author criticized the study design and considered the figures overestimated. In his experience, only 15% have medium growth while 50% have their hair loss delayed and 35% continued to lose hair. On stopping, all new hairs shed within 3-6 months.

   It is well established that 5% minoxidil is more effective than the 2% solution. In a study of men 18 to 49 years old, hair counts were 45% higher in those receiving 5% minoxidil than those receiving 2% minoxidil.

2. **Oral Finasteride**

   Dosage : 1 mg daily

   Mechanism: potent 5? -reductase type 2 inhibitor.

   In clinical trials over a 2 year period of men 18-41 years, the following results were obtained:

   At 1 year, 48% regrew hair (slight in 30%, moderate in 16%, greatly in 2%), 51% had hair loss stabilized, and 1% had progressive hair loss.

   At 2 years, 66% regrew (moderate to greatly in 32%, slight in 34%), 33% had hair loss stabilized, and 1% lose hair. The number of responding hairs is established after 1 year and continued treatment increases the length, diameter, and pigmentation of these hairs so that the coverage of the scalp increases. If successful, treatment should be continued indefinitely. On stopping finasteride, the regrown hair persists, but the balding process resumes. 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.

Side effects : Finasteride is generally well tolerated. Side effects, which usually have been mild, generally have not required discontinuation of therapy.

The following adverse experiences have been reported in postmarketing use: ejaculation disorder; breast tenderness and enlargement; hypersensitivity reactions including rash, pruritus, urticaria, and swelling of the lips and face; and testicular pain.

Females

1. **Topical minoxidil 2%, 5%**
   Dosage: 1 ml bd
   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. A new study involving 500 women is ongoing.

   Hypertrichosis occurs in 3-5% women using 2% minoxidil and is higher among those who use the 5% solution. It occurs on the face and resolves within 1-6 months after stopping the drug. However, the hypertrichosis diminishes or disappears after about 1 year, even with continued use of minoxidil.

2. **Finasteride**
   This is contraindicated in women who are or may become pregnant because 5?-reductase inhibitors may cause abnormalities of the external genitalia of male foetuses. Currently there is no proven benefit in women. A placebo controlled study done in postmenopausal women with androgenetic alopecia given finasteride 1 mg daily over 1 year showed no significant benefit.

SURGICAL MANAGEMENT

Despite advances in medical therapy, hair transplantation remains the only means of *permanent* hair restoration in androgenetic alopecia.

Indications

Both male and female patients with severe androgenetic alopecia.

Contraindications

Systemic diseases such as hypertension, cardiac disease, and diabetes mellitus have to be brought under reasonable control before hair transplantation.
Local diseases such as cutaneous lupus erythematosus, morphoea, alopecia areata, and scalp folliculitis have to be quiescent for at least 6 months before hair transplantation.

Pre-operative assessment

This will include an interview to provide information to the prospective patient and decide on realistic goals, patient selection to exclude any cardiopulmonary disease, idiosyncratic drug reactions, allergies, bleeding diathesis, or psychiatric disease, and performing certain routine laboratory tests such as a VDRL, HIV antibody test, Hepatitis C and B profile. The cost and timing of the graft has to be discussed and photographs taken pre-operatively.

Methods of hair restorative surgery

i.) Hair transplantation in women
ii.) Alopecia reduction (AR)

Complications of hair transplant
These include ingrown hairs and foreign body reactions, infection, cobblestoning, graft depression, epidermal cysts, bleeding, headaches, scarring, keloid and hypertrophic scar, 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.

Final results
It is impossible to predict precisely how many hairs will appear in any given graft. The average number is between 10 and 18 hairs per standard round graft, 36 per minigraft, and 1 or 2 per micrograft. After 46 months, the skin surface of the grafts has usually blended in perfectly with the surrounding scalp. In some, the grafts may be a shade lighter in colour until they are "aged" by sun exposure.

AESTHETIC AIDS
In women with extensive hair loss, wigs are usually necessary. Small interwoven wigs (weaved in with existing terminal hair) may be satisfactory in some men and women. However, continued hair growth tends to lift up the interwoven wigs and frequent readjustments necessary may be expensive.

EVOLVING THERAPY
Although finasteride-minoxidil combination has not been widely tested in humans, results in animal model suggested that combination therapy leads to better results than one treatment regimen alone. Further studies are needed to determine the benefit of this combination therapy in human beings.

Other 5a reductase receptor (5aR) inhibitors currently undergoing clinical trials include Turosteride (a type II 5aR inhibitor similar to finasteride) , FK143 and GI 198745 which inhibit both type I and II 5aR enzymes.

Oral androgen receptor antagonists such as cyproterone acetate, progesterone, flutamide, spironolactone, aldactone & cimetidine are not registered for treating AGA. However off-label use for managing AGA in women is widely practiced and recommended by some authority on hair loss. However, there are no large studies showing their efficacy and they have considerable side-effects. Topical progesterone does not benefit AGA but RU58841, another topical antiandrogen which has not been marketed, has shown promising results in macaque AGA. Topical antiandrogen, if effective, will be a good treatment option for AGA particularly in women.

Gene therapy for hair loss and grey hair using a liposome-containing topical cream to deliver entrapped DNA selectively to hair follicles is currently being investigated. Research is focused on the development of a cream that could permanently restrict androgen receptor expression within hair follicles.

EDUCATION AND COUNSELLING

Hair is a persons 'crowning glory' it has been said. It is often associated with image of a person, rightly or wrongly. The problem must be taken in perspective, and as different people are affected differently when they loose hair, an emphatic approach is important.

Research has shown that most men(and women) regard hair loss as unwanted, distressing experience that diminishes their body image. Nevertheless, studies also indicate that balding men actively cope and generally retain the integrity of their personality function.

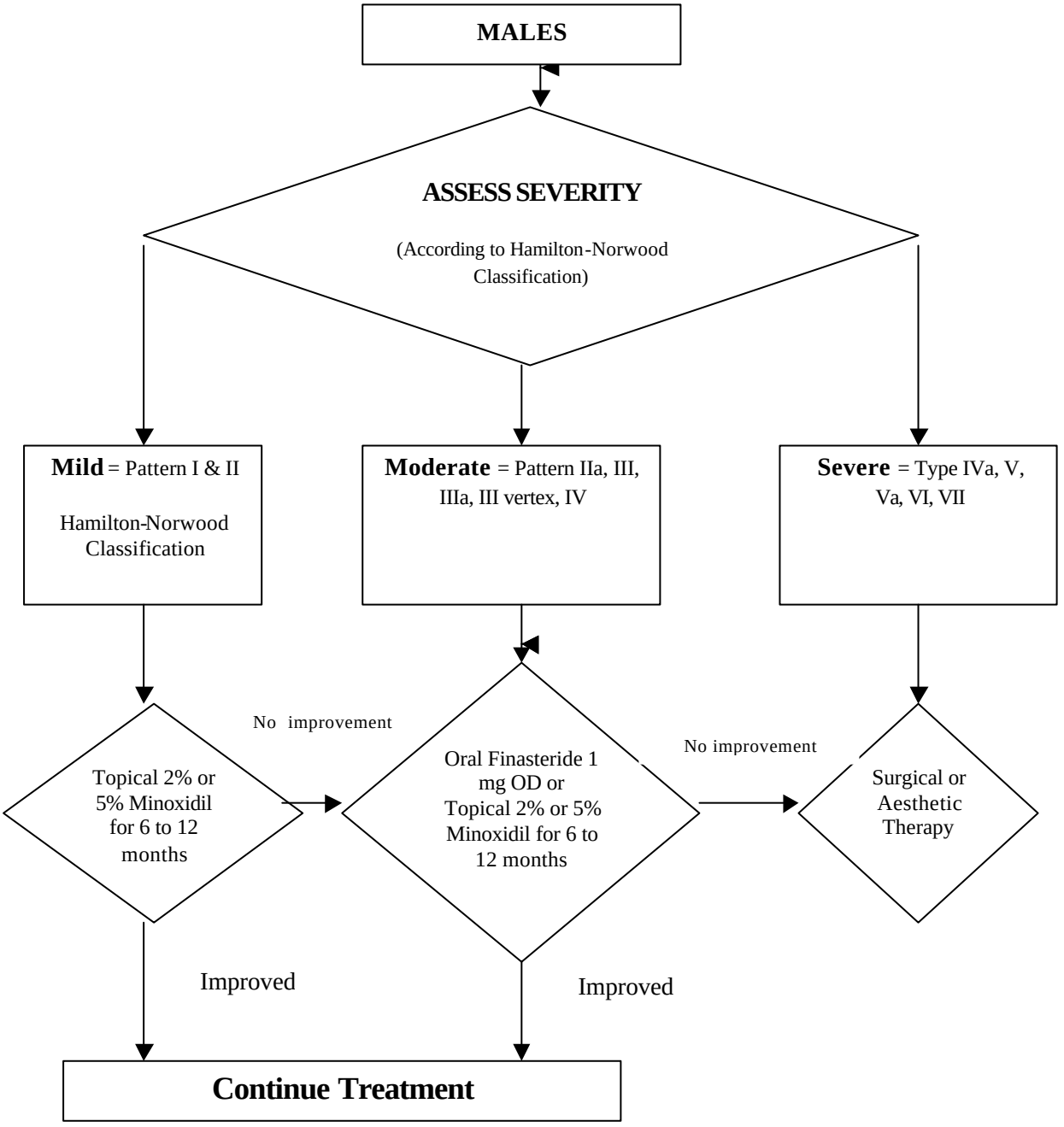
Knowledge and understanding of the genetic and physiological basis of AA, which can be acquired from their doctor or reading correct literature on the topic, may help allay misconceptions and anxiety about its occurrence, and indirectly influence the gregarity with which one might seek treatment for this condition.

Because of the psychological impact, patients may seek inappropriate and unproven therapies that are available and much publicised in non-medical settings, often at great expense to the consumer.

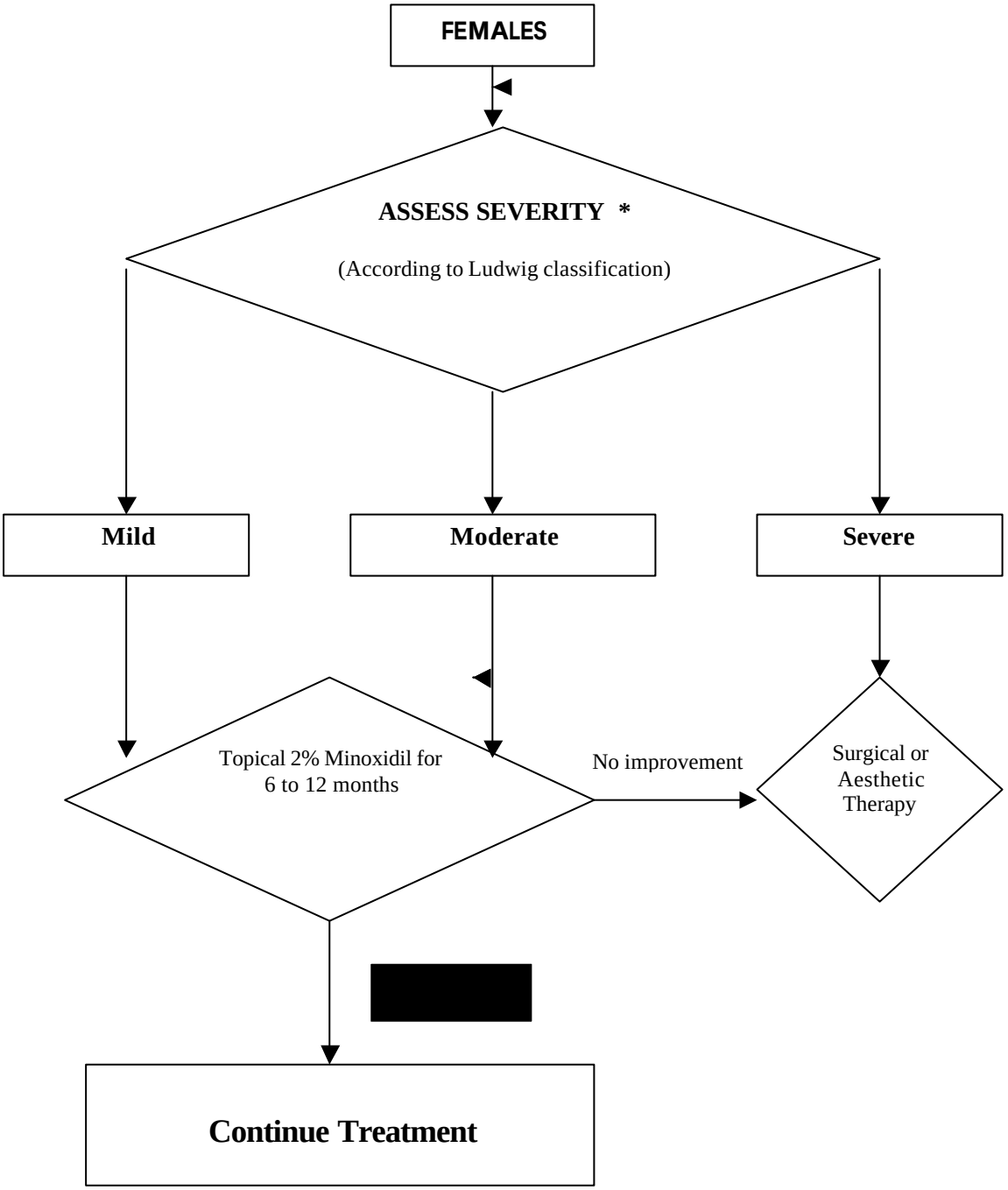
Patients must know that safe and effective treatment is available if they require it. But they must also, at the same time appreciate the real 'goals' and true 'limitations' of each form of therapy. (Refer to relevant sections in this consensus).

Misconceptions must also be corrected. Some mistakenly think they have too much hormones. Others put too much restrictions on their hair and grooming, such as hair styling, teasing, hair spray, frequency of hair wash, hair colour or permenants, which are all misconceptions.

ALGORITHM FOR MANAGEMENT OF ANDROGENETIC ALOPECIA



N.B. Some patients may opt for no treatment after counselling


FEMALES
ASSESS SEVERITY *
(According to Ludwig classification)
Mild
Moderate
Severe
Topical 2% Minoxidil for
6 to 12 months
No improvement
Surgical or
Aesthetic
Therapy
Continue Treatment

NB.

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