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## Efficacy and safety of intradermal injection of some therapeutics in treatment of androgenetic alopecia: Comparative study

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### Abstract

A fairly prevalent hair issue is androgenetic alopecia. Treatment of this type of alopecia can be challenging. The available modalities may not have the same efficacy in different patients. The invasive method as intradermal injection treatment modalities may be more effective and gives better results.

**Keywords:** Androgenetic alopecia, intradermal injection treatment, hair, dihydrotestosterone hormone

### Introduction

The most typical kind of gradual loss of hair is androgenic alopecia. It is a genetic and hormonal disorder through the action of dihydrotestosterone hormone on the hair follicle with different grades of severity, it only affects the vertex and temporal regions of men, preserving the occipital area <sup>[1]</sup>. Race and age affect the frequency and prevalence of androgenetic alopecia <sup>[2]</sup>.

It occurs by miniaturization of the hair follicles by decrease in the papillary cell numbers and papillary size results in a smaller hair follicle, anagen phase duration shortens, telogen phase lengthens, and terminal hair changes to vellus hair <sup>[3]</sup>.

### Pathophysiology

The pathological theory postulates that the activity of the 5 alpha-reductase enzymes, which takes place as two isoenzymes, results in the synthesis of dihydrotestosterone hormone (the functional type of testosterone). Type 1 which presents in the sweat and sebaceous glands, hair follicles, while type 2 mainly presents in the hair follicles <sup>[4]</sup>.

### Clinical Picture

#### A. Male pattern hair loss

In male, there is a specific pattern of hair loss, it starts at the scalp' vertex and the temples and continues until just a rim of hair at the back and side of the head is left. There are many classifications for androgenetic alopecia <sup>[5]</sup>.

#### 1) The modified Norwood-Hamilton classification: figure (1) <sup>[5]</sup>.

- **Grade I:** The hair line has little to no recession.
- **Grade II:** At the fronto-temporal hairline, a triangular, often symmetrical zones of recession were existed.
- **Grade IIa:** The hair line is 2 cm in front of the external auditory meatus (EAM) in the coronal plane.
- **Grade III:** The temples have deep, symmetrical recessions which are either bald or just sparsely haired.
- **Grade IIIa:** The hairline has retreated to a region that is between the grade IIa boundary and the EAM.
- **Grade III vertex:** The fronto-temporal hairline only recedes slightly beyond the degree

observed in grade III, with the majority of the hair losses coming from the vertex.

- **Grade IV:** There is less hair or none at all on the vertex, and the fronto-temporal recessions is worse than it was in grade III. A belt of somewhat thick hair that runs along the top divides the two regions of hair loss. On the sides of the head, this band joins the completely haired fringe.
- **Grade IVa:** Although it has not yet reached the vertex, the hairline has begun to recede beyond the EAM.
- **Grade V:** Although it is less defined, the vertex loss of hair zone is still different from the fronto-temporal area. The frontotemporal and vertex zones of hair loss are

larger, while the band of hair over the crown is smaller and sparser.

- **Grade Va:** The vertex is part of the denudation zone. Greater than grade V hair loss that cannot be separated from grades VI or VII
- **Grade VI:** There is no longer a hair bridge over the crown; instead, there are simply a few scant hairs. The degree of hair loss is larger where the fronto-temporal and vertex areas connect.
- **Grade VII:** the most severe kind of hair loss, when just a thin horseshoe-shaped ring of hair is left on the back and sides of the head<sup>[5]</sup>.

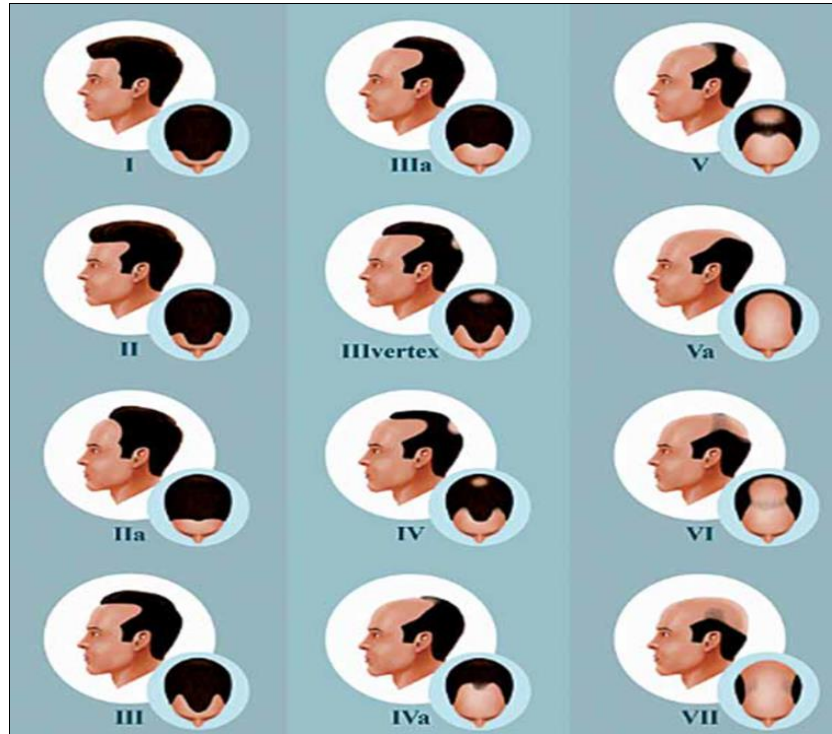


Fig 1: The modified Norwood-Hamilton classification<sup>[5]</sup>.

**B. Female pattern hair loss:**

Females are usually presented with different loss of hair patterns than males. The hair thickness and density decrease that results in a reduction in hair volume but the frontal hairline is usually preserved<sup>[6]</sup>.

There are many classifications for female-pattern loss of hair:

**1) The Ludwig classification:** figure (2)<sup>[7]</sup>.

It constitutes an extremely typical category for loss of hair in women. It comes in three grades with a frontal hairline that has been relatively preserved.

- **Grade I:** A line positioned 1-3 cm beyond the frontal hair-line limits minor crown hair loss in the front.
- **Grade II:** moderate thinning in the hair of the crown of the head in the region shown in grade I.
- **Grade III:** Over grades I and II, there is complete baldness in their regions.

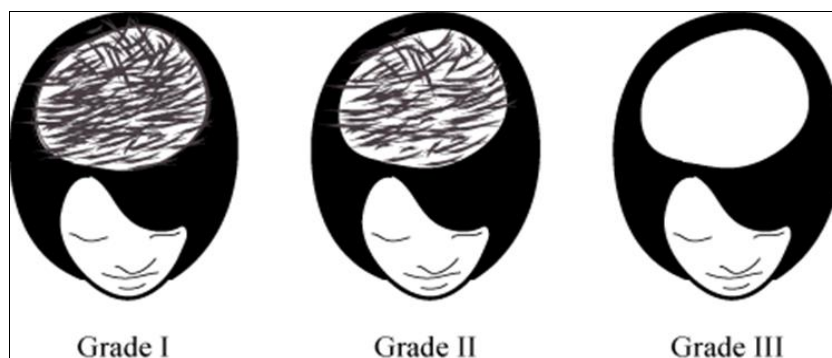


Fig 2: Ludwig's classification.<sup>(7)</sup>

**Basic and specific androgenic alopecia categorization:** figure (3) [8].

The anterior hairline's form, the density of the hair on the frontal and vertex regions, and the pattern of baldness are the basis for this categorization. The anterior hairline's form serves as the basic type, while the density of the hair on the frontal and vertex regions serves as the specific type. two specific kinds (F and V), four basic types (L, M, C, and U) were existed, and each of them is further classified into three or four subtypes depending on the severity [8].

**A) Basic types of androgenetic alopecia**

These styles depict how the front hairline looks.

- **Type L:** The anterior boundary in the frontotemporal area shows no signs of recession and seems as a straight line, indicating that there has been no loss of hair.
- **Type M:** The hairline resembling the letter M and shows recession in the fronto-temporal hairline, which is more pronounced in the mid-anterior hairline.
- **Type C:** The fronto-temporal hairline shows less recessions than the mid-anterior hairline. In the form of

a half-circle that resembles the letter C, the whole front hairline recedes posteriorly.

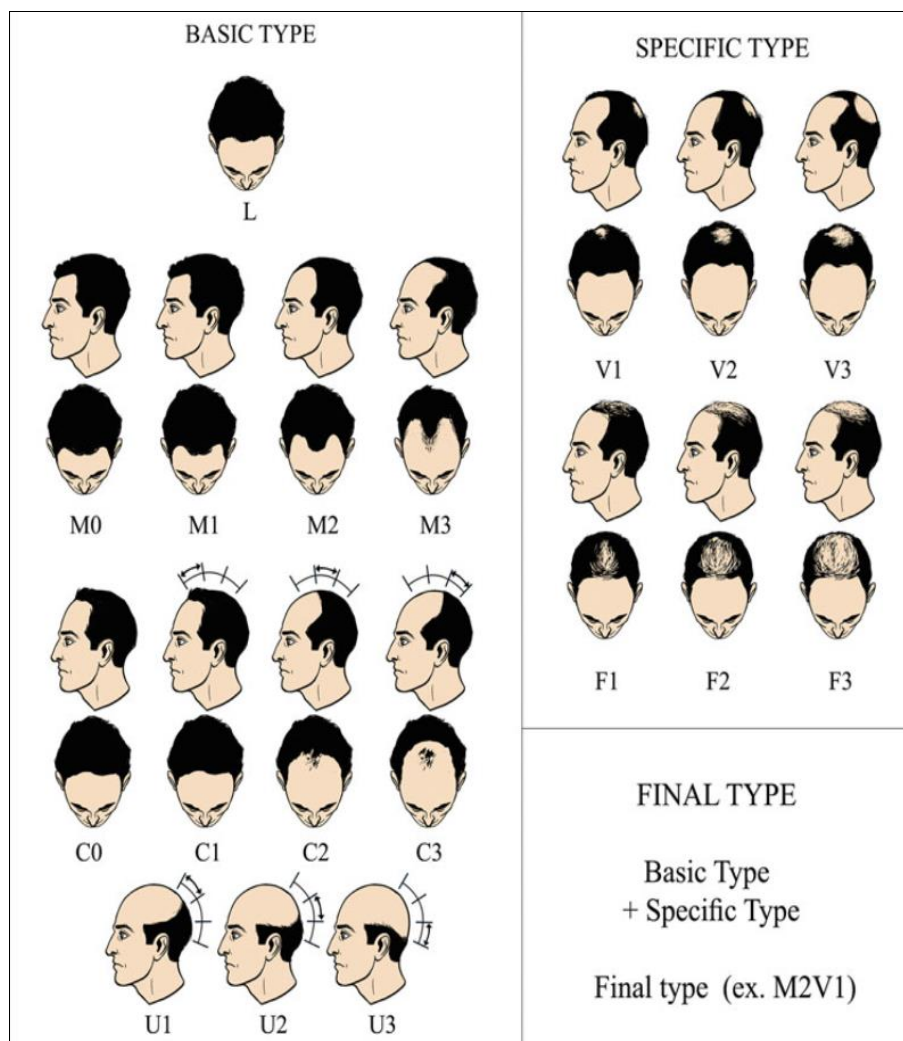
- **Type U:** A horseshoe-shaped pattern that resembled the letter U is formed when the anterior hairline subsides posteriorly beyond the vertex. It is the sort of hair loss that becomes particularly severe. Based on the degree of baldness, it is further split into three subcategories.

**B) Specific types of androgenetic alopecia**

These varieties show the extent of hair thinning.

- **Type F:** No matter what of the anterior hairline, refers to a general loss in hair density throughout the whole top of the scalp. It is often more pronounced over the frontal part of the scalp.
- **Type V:** Hair is more pronounced at the vertex than in the frontal region, and it is noticeably sparser surrounding the vertex.

Combining the specific and basic categories results in the final type. For instance, final type C1V1 is indicated by basic type (C1) plus particular type (V1) [8].



**Fig 3:** Basic and specific classification of androgenetic alopecia. [8]

**Treatment of androgenetic alopecia**

**A) Systemic therapy**

**1. 5α-reductase inhibitors**

They are FDA approved treatment for androgenetic alopecia in men but not approved for women. They inhibit 5α-reductase type II enzyme that leads testosterone to be

converted into dihydrotestosterone which is the main cause of androgenetic alopecia.

They present as two pharmaceutical preparations as finasteride and dutasteride [9].

This drugs are well tolerated for both men and women, but may show some side effects as headache, gastrointestinal

upset and menstrual irregularities. little likelihood of gynecomastia, impotence, and libido loss may occur in men treated with finasteride or dutasteride [10, 11].

Dutasteride, that's available in soft capsule form and is taken orally in dosages  $\geq 0.5$  mg per day, reduces mean dosages of dihydrotestosterone more effectively than oral finasteride at 5 mg per day [12].

## 2. Spironolactone

It is a potassium-sparing diuretic with anti-androgenic effect. Female pattern hair losses were being treated using it at a dosage of 50–200 mg daily. There may be an increase in urination incidence, tenderness of breast, Hyperkalemia, and hypotension [13].

## 3. Hormonal contraception

Treatment for female pattern' hair losses is possible with it. Both of estrogens and progestins have anti-androgen effect [14]. The safety of the hormonal contraception is that they are tolerated but with some side effects may be present as vaginal bleeding, breast tenderness, headache, nausea, hypertension, mood changes and increased risk for cancer [15].

## B) Topical therapy

### 1. Topical minoxidil

It was initially authorized in 1998 for male-pattern' loss of hair and later in 2001 for females as a 2% and 5% minoxidil solutions. FDA also authorized the 5% foam minoxidil in 2006, but exclusively for males. Topical solution recommended as 1mL twice per day [16].

### 2. Nanoxidil

It has been developed to maximize the stimulation of hair growth and with minimum side effects compared to minoxidil. The nanoxidil 5% form has lower molecular weight providing better results [17].

### 3. Finasteride

It can be used locally on the scalp as 1% gel twice daily giving better results by inhibition of 5 $\alpha$ - reductase type II enzyme locally in the scalp That leads testosterone to be converted into dihydrotestosterone that represents the main cause of androgenetic alopecia [4, 18]. So it is a safe method with less side effects as menstrual irregularities in females and gynecomastia and erectile dysfunction in male but less than the oral form [10, 11].

### 4. Spironolactone

Topically applied Spironolactone spray or gel with maximum efficacy and safe modality with less side effects as hyperkalemia hypotension as present with the oral form [19].

## C) Invasive therapy

### 1. Scalp micro-needling

It is suggested that micro-needling sessions may increase the hair count via activation of platelets, platelets-derived growth factor release, and wound healing [20].

### 2. Intradermal injection

This is an effective method for treatment by creating tiny channels providing more penetration of therapy and release of platelets-derived growth factors and epidermal growth

factor at the injection site. In the process of healing a wound, it stimulates stem cells. Thus, it is a procedure that is secure and has little adverse effects as pain and ecchymosis at site of injection [21]. It can be done with different modalities:

### 1. Platelet-Rich Plasma

Platelets-rich plasma is a concentrated autologous activated platelets which helps to release growth factors and cytokines leading to prolongation of the hair cycle's anagen phase, help stem cell differentiation and enrich the perifollicular blood supply through platelets-derived growth factors and vascular-endothelial growth factors [22].

### 2. Minoxidil

It shows good result compared to the topical form. The safety of intradermal injections was demonstrated by absence of side effects as change in the blood pressure owing to its hypotensive outcomes but some adverse impacts as mild pain and burning sensation at site of injection may be present [23]. In Uzel et.al study the intradermal injections with 0.5% minoxidil showed good efficacy in the managing of androgenic alopecia with minimal side effects [24].

### 3. Dutasteride

Treatment with intradermal injection of dutasteride in the scalp may be a useful modality for individuals with androgenic alopecia by inhibition of 5 $\alpha$ - reductase type II enzyme locally in the scalp That leads testosterone to be converted into dihydrotestosterone, that represents the main cause of androgenetic alopecia [4, 25]. So it is a safe method with minimal side effects as menstrual irregularities in females and gynecomastia and erectile dysfunction in male but less than the oral form [10, 11].

### 4. Mesotherapy

The mesoderm, or the skin' middle layer, is injected with tiny amounts of traditional medications and/or vitamins to achieve this. The mechanism of action of mesotherapy is by increases the expression of keratin-associated protein responsible for keratinizing the cortex of the hair, there are several cofactors for carboxylase enzymes present in the hair follicle's numerous metabolic pathways, protein synthesis and increasing blood supply to the hair follicles and in the production of keratin promoting healthy growth of hair [26].

It is a secure method with little adverse effects as pain or infection at site of injection so the mesotherapy can be used as adjuvant therapy in treatment of androgenetic alopecia [27].

### 3. Stem Cells

A bio-engineered follicular germs implanted intracutaneously as part of stem cell therapy proved successful in creating a functioning hair follicle. There is an increase in hair density in about 6 months [28].

Autologous stem-cells could be retrieved from patient bone marrow, blood hair follicle or adipose tissue [29].

### 4. Botulinum toxin

The mechanism of action is a relaxing of the scalp' muscles that results in greater oxygenation of the tissues, a reduction in muscular tension on the blood vessels, an

increase in the turnover of testosterone to estradiol, and the removal of dihydrotestosterone <sup>[30]</sup>.

### 5. Hair transplantation

In patients with stabilized hair loss. When transplanted into androgen-sensitive regions, the hair follicles located in androgen-insensitive areas preserve their characteristics <sup>[31]</sup>. Complications may occur as infection, pain, hematoma, edema, and the transplanted hair's inability to grow <sup>[32]</sup>.

#### D) Light therapy

There is potential for low-level light therapy to be a successful, secure, and tolerated effectively therapy for androgenetic alopecia but with limited value <sup>[28]</sup>. The helmet-type light therapy is simple device used at home, stimulate the whole scalp, making it suitable for treatment <sup>[33]</sup>.

Yoon *et al.* showed in their study that patients of androgenic alopecia treated with low-level light therapy on one-half of scalp and sham light (placebo device) therapy on the other half, 3 times a week. After assessment substantial enhancement in thickening of hair and hair count in the low level light therapy-managed area as contrasted to the sham light managed area <sup>[34]</sup>.

Also in another study, androgenetic alopecia patients who were treated with cold laser, 2 sessions per week for maximum of 6 weeks, they were followed up monthly after end of treatment sessions for 3 months, showed a statistically significant improvement after treatment <sup>[35]</sup>.

#### E) Camouflage and wigs

Camouflage techniques may be suggested to individuals who are dissatisfied with their medical care or hair transplantation results. Using hair fibres, masking creams, and scalp spray thickeners to blend in and create the appearance of thicker hair. They are easily washed <sup>[36]</sup>.

#### Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not available

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