



Effects of Ancient Unani Methods of Microinjuries on Hair Regeneration: A Review

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ABSTRACT

Hair loss is a common cosmetic problem and is usually associated with many psychological disorders, distress, and depression. It can be temporary, such as telogen effluvium, or long-lasting, such as Androgenetic alopecia (AGA). AGA is one of the most common types of hair loss that affects equal numbers of men and women and is clinically characterized by progressive baldness⁵. It affects approximately 30% of white males by the age of 30 and 50% by the age of 50 years. In India, the prevalence of AGA in males aged 30-50 is 58%.

In the Unani system of medicine, it is described under the heading of Intithsar-e-Sha'r. Nutritional deficiencies, poor production of bukharat-e-dukhanīyya (a material required for the synthesis of hair matrix), tkhalkul-jild (skin laxity), Imtela (accumulation of morbid matter beneath the skin), and Indmaal after Quruh (fibrosis) are the common causes for hair loss described in Unani system of medicine.

Despite the introduction of newer drugs and procedures, such as PRP and laser therapy, it remains an outstanding health problem. Although it has no negative impact on general health, psychological impacts make baldness a major concern for adult males and females. That is why hair growth and regeneration have attracted much attention. This article presents some cost-effective and safer Unani classical methods for hair regeneration and how recent scientific studies validate the role of these methods to regrow hair. These methods may provide a basic idea to researchers to find an effective solution to this complex problem.

Keywords: Androgenic alopecia, Hair cycle, Hair follicle, Hair loss, Regrow hair, Unani medicine

INTRODUCTION

Hair loss is one of the common cosmetic problems⁽¹⁾ and is usually associated with many psychological disturbances like low self-esteem, stress and depression⁽²⁾. Hair loss that is supposed to be induced by androgens is known as androgenetic alopecia (AGA) ⁽²⁾⁽³⁾. Among all types of hair loss, it is the most common type of hair loss ⁽¹⁾⁽²⁾ that affects equal numbers of men and women and is clinically characterized by progressive baldness⁽¹⁾. It affects approximately 30% of white males over 30 years of age and 50% of individuals over 50 years of age ⁽⁴⁾. In India, the prevalence of AGA in males aged 30-50 is 58%⁸⁽³⁾. One-third of the individuals having a strong family history of AGA can expect to be affected by it ⁽¹⁾.

AGA is a multifactorial disorder ⁽⁵⁾; miniaturization of hair follicles caused by the effects of androgen hormones is the main factor. It represents a progressive reduction in the diameter and length of the hair shaft shortened anagen phase ⁽¹⁾. These miniaturized hairs are characteristic of AGA ⁽²⁾. Thinning of the hair shafts usually begins between 12 to 40 years of age and 50% of the population experience some degree of thinning before 50 years ⁽¹⁾. The pattern of hair loss is quite variable ⁽⁵⁾.

In classical literature of Unani medicine; Sula, Inteshar-e-Shaar, Daaul saalab, and Daaul haiyyah are commonly described disorders related to hair loss. The term Inteshaar e-Shaar, Daaul saalab, Sula is used for diffuse non-scarring alopecia, alopecia areata, and AGA respectively. The causes and treatment described for Inteshaar e-shaar are the same as those described for Sula ⁽⁶⁾. Nuks-e-taghiya (Nutritional deficiencies), Takhakul-e-Jild (Laxity of scalp), Yaboosat-e-jild (Dry temperament of scalp), Imtela-e-balgham (Accumulation of Phlegm), and accumulation of morbid material under the skin are the commonly described causes ⁽⁶⁾ ⁽⁷⁾. In all cases the main pathological factor behind the hair loss is poor production of Bukharat-e-dukhanīyah (matter responsible for hair production i.e., hair matrix) ⁽⁸⁾. When some morbid material is accumulated beneath the skin production of this matter diminishes

resulting in restriction of hair growth and ultimately hair loss (7) (9). In case of Takhakhul-e-Jild, bukhraat-e-dukhaniya (hair matrix) could not get accumulated in the hair follicle, resulting in poor health and stability of the hair shaft in the hair follicle (10) (6).

PATHOGENESIS

Normal hair has three phases in its life cycle, the anagen phase is a growth phase which can last from two to three years. This is followed by the catagen phase, a brief stage of transition that lasts one to two weeks and then telogen, a resting phase of five to six weeks. After going to the resting phase, a new anagen phase begins and newly growing hair pushes the hair upward, resulting in shed of resting hair.

Understanding of the hair cycle is important to diagnose and treat the patients as majority of patients with different disorders of hair have different alteration of hair follicle cycling. Hair loss in the anagen phase is caused by disorders that alter mitotic activity in anagen phase, such as alopecia areata and certain drugs (11). On the other hand, telogen hair loss occurs due to injuries that can cause premature telogenization of the follicle (11). Gradual decrease in the anagen phase and increase in the telogen phase occurs in AGA. As the duration of the anagen phase determines the hair length, the maximum length of the new anagen hair becomes shorter than that of its predecessor, leading to miniaturization and eventually to a bald appearance.

This progressive miniaturization of the hair follicle, a characteristic feature of AGA, results from changes in dermal papilla and growth factors secretions. Due to progressive deamination of the dermal papilla and decreased secretion of growth factors, the anagen phase becomes shorter, leading to the transformation of terminal hair into villus hair. Etiological factors can give an overview of this concept evolution.

Causes of AGA

AGA is a complex multifactorial disease (12). The following factors contribute to AGA.

Genetic factors

AGA is autosomal dominant, Polygenic, and inherited disease(5). Positive family history of AGA plays an important role in the onset of disease. However, mechanism of genetic predisposition in the initiation and progression of AGA remains unclear(12) (11) (5).

Hormones

In pathogenesis the effect of androgen hormones and enzyme 5- α -reductase is well established. 5- α -reductase converts testosterone to the more potent dihydrotestosterone (DHT) hence increases effects of androgen on hair follicles causing miniaturization of hair follicles (11).

Environmental and dietary factors

Oxidative stress caused by various metabolic and environmental factors inhibits hair matrix synthesis by negatively influencing dermal papilla cells (13). Recently, in a study cold temperature was found to have an impact on Hair follicle stem cells (HFSCs) through a neuroendocrine mechanism, specifically norepinephrine from the sympathetic nerves promotes activation thus hair regeneration (14). The activity of HFSCs is also reduced by dietary fat through an oxidative mechanism. Dietary fat affects the hedgehog signaling pathway, which may link obesity with alopecia (15).

Loss of contact between arrector pili muscle (APM) and bulge

In studies of APM health, its degradation, and its contact with the hair follicle bulge, it is found that APM remains connected to the bulge in telogen effluvium (TE) and alopecia areata (AA) but not in AGA (16). This finding suggests that poor contact of APM with bulge of hair follicle has a relation with AGA. A good attachment between APM and bulge is essential to prevent miniaturization of hair follicle (5).

Pathogenesis of hair loss described in Unani Classical literature

In classical literature of Unani medicine Sula, Inteshar-e -Shaar, Daaul saalab, and Daaul haiyyah are commonly described disorders related to hair loss. In all cases the main pathological factor behind the hair loss is poor production of bukhraat-e-dukhaniya (hair matrix) (9). When some morbid material is accumulated beneath the skin production of this matter i.e. bukhraat-e-dukhaniya diminishes resulting in restriction of hair growth and ultimately hair loss (9). Similar pathological event occurs in case of Takhakhul-e-Jild, bukhraat-e-dukhaniya (hair matrix) could not accumulate in the hair follicle resulting poor health and stability of the hair shaft in the hair follicle (9). Thakhalkul-e-jild is predominantly caused by decreased regeneration of cellular component of skin that may leads to poor health and attachment of APM to the bulge. It has been observed in many studies that a good attachment of APM to the bulge plays a key role in maintaining hair cycle (16). Enforcement of hair in hair follicle is directly related to the contractability of erector pili muscles (17). It is also needed to revert miniaturization of hair follicle (1) (5).

Ancient Unani scholars not only described scalp laxity, but also provided solution to revert this condition. They advocated various herbs for strengthening and tightening of the scalp (9). By working on tightening and strengthening of the scalp, they unknowingly worked on the cellular regeneration, APM health and its contractibility and healthy attachment with the bulge. Apart from herbomineral formulations, some easy, safe and cost-effective methods of mechanical stimulation and wounding for the management of hair loss are written in classical Unani literature and after several centuries are still in practice in Indian subcontinent. Here we are enlightening that how these procedures of Unani medicine have a co-relation with some evidence-based regeneration theories.

How recent regeneration theories validates classical procedures

As baldness has psychological impacts on society, increasing demand to look good and psychological well-being, the management of hair loss and hair regrowth is in increasing demand and has very promising market prospects (2), due to lesser side effects, and the belief in alternative medicine to provide a better solution, this demand is inclined towards alternative methods of treatment.

The hair follicles regeneration and maintenance of hair cycle

Hair follicle is dynamic mini organ originating from the ectoderm (2). It undergoes periods of regeneration and rapid growth to apoptosis-driven regression, and then, the HF returns to regeneration. The interaction between epithelial hair follicle stem cells (eHFSC) and dermal papilla cells (DPCs) plays a significant role in hair cycle regulation (2) (4). The maintenance of hair cycles is a key factor in stability and longevity of hair follicles, on the other hand loss of hair follicle functions most of the times accompanied by the discontinuation of hair cycling (2).

Thus, good functions of hair follicles and maintenance of hair cycle are paramount to keep it regenerating (2) (11). Ancient Unani scholars unknowingly worked on the hair follicles regeneration and maintenance of hair cycle by working on hair health and baldness prevention. That they not only described the causes of hair thinning and falling but also suggest various medicine and treatment procedures to revert these conditions. Prevention of thinning and falling of hair also described frequently. The description of reversible (e.g. Inteshaar e-Shaar) and irreversible hair loss (e.g. Sula) in the classical Unani literature also suggests that they were familiar with the regeneration of hair. Some evidence-based theories regarding maintenance of hair health, hair cycle, and hair regeneration published recently and their correlation with the method of treatment mentioned in the classical literature of Unani medicine are mentioned below;

Skin tightness and regeneration leads to hair growth

Skin's physical properties like nonlinearity and viscoelasticity are determined by dermal extracellular matrix, consisting of collagen and elastic fibers. Infiltration of fat into the dermal layer leads to its physiochemical impairment. Fat infiltration decreases the skin's elasticity and induces sagging (18). This fat infiltration is also associated with APM degeneration, follicle miniaturization and hair loss (15). This view of skin tightness, laxity and their association with the hair follicle cycling and regeneration was also described in classical Unani literature.

Hair follicle is the only structure in mammals that repeatedly transits from a growth phase to a resting phase and regeneration. This regeneration of hair relies on the activation of stem cells. Multipotent stem cells reside in the bulge of hair follicle. Although stem cells have been found on various sites along hair follicle, the bulge is an essential reservoir of hair follicle stem cells (5).

Each APM in scalp is attached at one end to the hair follicle and to the inner surface of the basal layer of the epidermis at other end. Its contraction can be stimulated directly by mechanical, electrical, thermal, or pharmacological stimuli or indirectly via an axon reflex (16). Enforcement of hair in hair follicle is directly related to the contractability of erector pili muscles. During piloerection, caused by contraction of erector pili muscle, greater force is required for epilation. During contraction Arrector pili muscles applies force to the hair shaft in opposite direction of epilation hence stimulation of piloerection in the scalp greatly increases the threshold of force required to pluck hair (16). In a study conducted on epilation force and shedding of hair during cosmetic procedures, it is found that contraction of the arrector pili muscle via topically applied phenylephrine, a selective $\alpha 1$ adrenergic receptors ($\alpha 1$ -AR) agonist, increased the force of epilation. In 80% of subjects reduced shedding on days using phenylephrine compared to days using a placebo solution was observed. The average reduction in hair loss was approximately 42% (17).

As we discussed earlier that the main reason behind AGA is miniaturization of hair follicle, to grow new hair and prevent progression of baldness it is necessary to revert the miniaturization of hair follicles. Significant decreases in APM volume and an extensive fat infiltration around the residual APM of hair follicles was demonstrated in AGA patients (15).

A good attachment between the arrector pili muscle and the bulge of the hair follicles is of prime importance to reverse the miniaturization of the hair follicles (1). For this good attachment, arrector pili muscle health and voluminous maintenance of other connective tissues, regulated by regeneration capacity of dermis is required. Since arrector pili muscle plays an important for skin regeneration (19), it may be concluded that skin laxity and its reversal is very much dependent on health of arrector pili muscle.

Apart from relation to the pathogenesis of acne sebaceous gland also seems to be linked to androgenetic alopecia (18) Optimum function of hair follicle, maintenance of hair cycling, and secretion of sebum that help prevent hair and skin from drying out depends upon its cellular component, regeneration of connective tissue and contractibility of arrector pili muscle (20). Cellular dysfunction and irreversible growth arrest are the two most common factors responsible for overall thinning and sagging skin (21). In response to various stress factors like DNA damage, dermal connective tissue cells enter into a state of irreversible growth arrest, which is known as cellular senescence. The temporary cellular senescence signals that physiologically occur during wound healing promote the formation of granulation tissue and skin regeneration (22).

Thermal energy stimulus given by various energy-based devices, such as lasers, high-intensity focused ultrasound (HFU), and radiofrequency (RF) devices to reticular dermis and subcutaneous tissue causes tissue contraction and stimulates neocollagenesis, leading to improvement in skin laxity (21). It is evident that skin tightness and strength depends upon its regenerative capacity.

We discussed earlier that the role of skin laxity (*Takhakhul-e-Jild*) in the pathogenesis of hair loss was described by ancient Unani Scholars. They also recommended the tightening and strengthening the scalp skin for the management of hair loss (9). Therefore, it can be presumed that ancient Unani scholars unknowingly worked on the various components of scalp skin like arrector pili muscle which provide mechanical strength to the skin, to maintain hair follicle cycling.

Pachne, A classical method of mechanical stimulus, can induce hair regeneration

The ancient scholars of Unani medicine advocated the treatment of baldness by mechanical stimulus and wounding the scalp. Pachne are the classical methods for creating micro injuries by using small needles or surgical blades. These pachne create mechanical stimulus and wounding to the scalp. Mechanical stimulations affect cell proliferation, differentiation, and migration, as well as determining tissue homeostasis and repair. These processes are influenced by several factors and interactions that require robust control for safe and effective tissue regeneration (22).

However, more emphasis has been given to chemical methods to achieve functional tissue regeneration, it is indicated by some researchers that cellular proliferation and differentiation can be induced not only by chemical factors but also by mechanical stimulation, which initiates upstream signals to activate downstream chemical signaling (23).

regeneration potential in response to mechanical stimulation can be evaluated effectively by mammalian hair as hair follicles undergo a continuous cycling throughout life (24). In several studies it is found that micro injuries can potentially lead to hair regeneration. Some scientific studies on regeneration of hair in response to mechanical stimulus or microinjuries are given below;

Patterned hair plucking studies

In a trial on hair regeneration, effects of mechanical stimulus by patterned hair plucking on hair regeneration was studied. In this study it was found that patterned hair plucking leads to hair regeneration upto five times more hair than plucked (25). It is supposed to be caused by a coordinated response to skin injury that is collective decision-making (15) (26) (27). In few studies it is found that plucking of hair produces a micro-injury that can stimulate hair regeneration. The decision of hair follicle stem cells to remain latent or functional depends on the inputs coming from neighboring follicles. In a study on micro injuries and hair regeneration it is found that plucking of 200 hair with a proper topological distribution can regenerate upto 1200 hair (25). On the other hand plucking fewer than 50 hair did not induce hair regeneration (25). In a study on mice time required for hair to regrow was compared. When 200 hairs were plucked, the time required for hairs to re-grow became shorter than plucking 50 hair (28). These finds suggest that regeneration response depends upon the extent of mechanical stimulus that reaches to a sufficient threshold.

In several studies it is suggested that micro injuries induce a cascade of inflammatory, cellular, and molecular events (1) (24) (25) (26). Hair plucking leads to hair keratinocytes apoptosis this apoptosis initiates inflammatory changes and overexpression of several inflammatory cytokines locally.

Waxing studies

Other than patterned hair plucking removal of hair by wax strip also leads to microinjuries to that particular region of skin. Wounding leads to follicle differentiation, produce a hair shaft and progress through all stages of the hair follicle cycle (26). Pro-inflammatory cytokines like chemokine (C-C motif) ligand 2 (CCL2), and interleukin 1, beta (IL-1 β) upregulated soon after plucking. CCL2 is primarily produced by HF keratinocytes and accumulates predominantly in plucked HF. CCL2 communicate signaling molecule information, that is required for hair regeneration, from plucked to unplucked hair²⁹ (24). The increase in tumor necrosis factors and platelet-derived growth factors also contribute to hair regeneration after waxing (24) (29).

Mechanical stretch study

In a study on mice, effects of mechanical stretch on hair follicles was evaluated. To generate a programmable stretch, a specially designed skin-stretching device was by fixing it on back skin of eight-week-old mice. Two specific variables, strain and stretch duration, were used. In the first phase of trial, skin was stretched for 7 days with different strains (0 to 40%). On application of strain greater than or equal to 33%, hair regeneration was induced within the whole stretching area. On the other hand, hair remained in resting phase when the applied strain was less than 20%.

In the next phase of trial stretch duration was variable with the same 33% initial strain that was applied in first phase. Three different responses were observed for three different durations i.e. 5, 7, and 10 days. On the application of strain for 5 days, no hair regeneration observed. When it was increased to 7 days, anagen initiation and hair growth were even in the whole stretching area. However, when the stretch duration further increased to 10 days, hair growth occurred only in peripheral region of stretching. Stretching with 33% strain for 7-days was determined to be the optimal condition for hair regeneration induction (24).

Outcome of these aforementioned experiments suggest that mechanical stimulus and micro injuries can play a potential role in the management of hair loss. Few methods of microinjuries like pachne and needling are described by ancient Unani scholars for the management of baldness. For centuries, these cost-effective methods have been used and trusted for their safety and effectiveness.

Conclusion

Regulation of hair growth and regeneration is a very complex issue, which includes genetic factors, neuroendocrine factors, environmental factors, and nutrition. It involves crosstalk among the several components of skin including the adipose tissue, arrector pili muscle, bulge, immune cells, and blood vessels. Regeneration theories, especially related to microinjuries followed by inflammatory cascades and cellular events, look promising. Platelet-derived growth factor A increased after microinjuries plays an important role in hair cycle regulation and regeneration.

Various methods for micro injuries, such as needling and pachne, were described in the classical Unani literature several centuries ago. Science these methods have been used for centuries, they are safe and effective. Despite newer techniques like PRP and laser therapy, it is no wonder why classical methods of microinjuries and wounding are still in use today. With a proven track record spanning several centuries, along with the Animo-Herbo-Mineral pharmaceutical preparations of Unani medicine, these methods may provide an effective solution to this complex problem; however, evidence-based clinical and biochemical studies are required to prove efficacy.

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Conflict of Interest

None

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