Al-Kindy College Medical Journal (KCMJ)

Review Article

Various types of Alopecia and the options of the treatment

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https://doi.org/10.47723/kcmj.v16i2.253

Article history:
Received 2 November 2020
Accepted 27 December 2020

Keywords:
Alopecia, Type of alopecia , Classification of alopecia, Management of alopecia.

Abstract

Alopecia (Baldness) is very usual trouble in current time. It is accompanied by an intensive weakening of the scalp's hair and follows a specific pattern. Hereditary predisposition plays a very important role in alopecia despite not completely understood. Alopecia can be typed to various categories according to etiology, may be due to hereditary factors, autoimmune disease, and drugs or chemicals. There are many options of strategies of treatment according to the type and causes of alopecia. Chemical or synthetic medications apply for the management of hair loss are accompanied by a wide range of undesirable effects. Naturally occurring drugs also play important role in alopecia management with minimal side effects.

Introduction

Hair is one of the important body parts derived from skin ectoderm, is a protective part of the body, and is considered an accessory structure of the pelt along with sebaceous glands, sweat glands, and nails. During embryological development, they originate from the epidermis and are known as epidermal derivatives (1). Having complete non-falling hair represents the sign of beauty and youthfulness for both males and females, for this reason, alopecia can have a considerable bad influence on self-confidence (2,3). Alopecia is a disorder where an uneven, merging, unsettled way of hair fall occurs from different body regions, commonly the scalp is affected (4). In 1–2% of cases, the disorder may expand to the whole hair or epidermis as in case of losing all body hair including eyebrow and eyelashes. Prevalence of hair fall is usually 0.1–0.2% with a life span tendency of male and female evenly (5). The cause of alopecia is not completely identified, there are different causes documented in the last period and one of the significant causes is accompanied by autoimmune diseases. Elevated frequency of feelings conversion, psychological disorders states is commonly noticed in people with alopecia (6,7).

There are three cycles of hair follicle growth which are i) a delay growing phase (anagen), ii) a short transitional phase (catagen), iii), and a brief resting phase (telogen). At end of the cycle, the hair falls out (exogen) before growing into a new hair (8-10). Hair loss in non–horrible baldness is only a condition of the cycle of hair follicle growth (11,12). Alopecia is commonly provoked by an autoimmune disorder on the root of the hair. This causes damage to the hair bulb and leads to anagen arrest which leads to atypical damage of anagen hairs, which is also called anagen effluvium (13). A resemble state usually noticed in ladies is known as telogen effluvium'. In this disorder, hairs experience an unexpected transformation from anagen to telogen phase. Upon examination, it is noticed as regional sloughing of hair in the telogen stage and can be distinguished by shape as characterized as a hair without color root(14). Traditionally, alopecia is an autoimmune disease with varied hereditary contributions (15).In psychiatric states, stressful condition worsening the condition of alopecia as supposed by various research in which intense shock succeed the hair loss. However, few researchers disagree with these trues and suppose no association between emotional stress and the occurrence of alopecia (16).

A possible interpretation of the mechanisms worsened by psychological trauma could be accompanied by the secretion of specific messengers, which antagonize the defense mechanism of the body. Calcitonin gene-related peptide (CGRP) (a 37–amino acid neuropeptide) secreted by sensory neurons, has a powerful effect on blood vessels (vasodilatation), causing increment in tissue temperature. Isoflavone and estrogen enhances CGRP releasing in sensory neurons by enhancing its transcription supposed that treatment with isoflavone may lead to enhance Insulin growth factor (IGF–I) release, thereby triggering hair development(17,18). There are different causes for alopecia such as genetic tendencies(19), environmental circumstances, exposure to toxicants and various chemicals, medications as illustrated in table (1)(20), nutritional deficiency, oxidative stress, or long-term illness, and others (21).

Table 1. Drugs causing hair loss [20].

Number	Category of drugs	Drugs causing hair loss
1	Chloesterol lowering drugs	Clofibrate and gemfiprozil
2	Parkinson medications	levodopa
3	Ulcer drugs	Cimetidine, ranitidine, famotidine
4	Anticoagulants	Coumarine and heparin
5	Agents for gout	Allopurinol
6	Antiarithritis	Penicillamine, indomethacin, naproxen, sulindac
7	Drugs derived from vitamin A	Isotretinoin, etretinate
8	Anticonvulsant for epilepsy	trimethadione
9	Antidepressants	Tricyclics, amphetamines
10	Beta blocker drugs	Atenolol, Nadolol, timolol, propranolol, metoprolol
11	Antithyroid agents	Carbimazole, iodine, thiouracil, thiocyanate
12	others	Male hormone (anabolic hormones), antineoplastics

1.Types of alopecia

1.1. Androgenic alopecia (AGA)

Is the famous cause of baldness in male and female, which is a hereditary determined, aging symptom, intensifying hair loss condition with sex-specific contestation in prevalence and intensity (3,22, 23,24).

In the male, AGA commonly starts beginning above both temples. Over time, the hairline recedes to form a characteristic "M" shape. Hair also thins at the crown (near the top of the head). As the condition progress, the hair loss areas may become greater until the upper region of the head is entirely bald with only a border of hair staying at the end of the head and the temples (25,26).

The AGA commonly developed less progressively in female than in male and is associated with a slow, spread the weakening of the hair on the upper head with preservation of the hairline along the forehead(27). Two drugs have been approved in the past by the medical organizations: Oral finasteride (for male) and topical minoxidil (for male and female)(2), due to poor efficacy of these therapeutic agents and adverse effects which can decrease the patient adherence and lead to discontinuing of the treatment (e.g., occasionally gynecomastia with finasteride(28), and frequently hirsutism in the case of minoxidil(29)).

Fig 1 shows the male pattern of alopecia androgenitica(30).

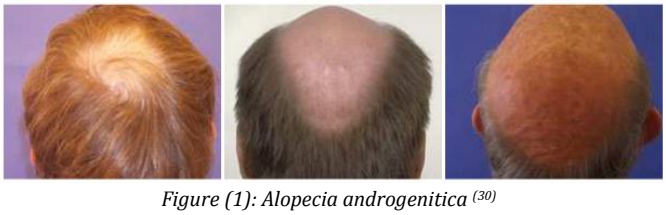

Figure (1): Alopecia androgenitica [30]

Microscopical examination of the dermis showed 20% heterogeneity in the diameter of the hair (Figure 2) [31]

Figure (2) : Androgenetic alopecia: hair diameter heterogeneity (31)

2.2. Alopecia areata

Alopecia areata is a noncicatricial fall of hair in all body region, along with a multiple causes as autoimmune disease and unrecognized cause (32). Causes and pathogenesis of alopecia areata being not totally comprehended are accepted to be multifactorial in ancestry (33,34).

This disorder strikes up to 2% of men and women and exhibits with an expanded field of symptoms diversity (35). People with alopecia areata may suffer from an abrupt and progressive hair loss. Objectively, well defined, smooth, hairless, without scars patches that distend in a diffusive design can be noticed. Advance cases including the whole head hair or all body hair. Alopecia areata can be accompanied by autoimmune pathogenesis, involving thyroid disease, celiac disease, vitiligo, and atopy (36). The oldest attack of alopecia areata may mostly cure instinctively spontaneously with no any drug treatment (36,37). The severity of the first attack of is of significant out coming agent. Additionally, response to topical medication may be accompanied by an excellent outcome. Trichoscopy, or dermoscopy and video dermoscopy of the scalp, may confide promote of especial type of hair fall. As a case, in the case of alopecia areata, a specific “yellow dot” scenario is mostly noticed, further, microexclamation hairs and black cadaverized hairs or “black dots” (Figure 3) (38,39).

Figure (3) : Alopecia areata (38,39)

2.3. Cicatricial alopecia

Cicatricial alopecia involves a collection of disorders distinct by inflammation and subsequent hair follicle damage, causing an irretrievable loss of hair (40).

2.4. Telogen effluvium

Telogen effluvium is the damage of telogen hair due to unusual hair cycling (41). Progressively regularly falling of approximately 100–200 telogen hairs is frequently noticed (42).

2.5. Alopecia universalis

Alopecia Universalis (AU) is a category of hair loss distinguished by the hair fall that occurs from all body parts. AU is commonly noticed in people with thyroid dysfunction and vitiligo. In this type of alopecia, the patient doesn’t suffer from any symptoms except burning and itching. It is accompanied by other disorders as in the case of atopic dermatitis and nail changes (such as pitting) (43).

2.6. Syphilitic alopecia

Treponema pallidum caused Syphilis disease. Patients with syphilitic alopecia complained of abrupt and partial hair fall (44).

2.7. Trichotillomania

Trichotillomania is a disorder characterized by pulling off one’s own hair for enjoyment, or comfort. Hair loss in this disorder is characterized by regional or complete alopecia of the scalp. (45,46).

2.8. Chronic cutaneous lupus erythematous

Cutaneous lupus erythematosus, an autoimmune disease characterized by inflammation of the skin with persistent hair loss. Predisposing causes included in chronic cutaneous lupus erythematous are hereditary contribution, sunlight liability, pollution such as cigarette smoke, and hormones. (47)**3. Uncommon types of Alopecia**

3.1. Alopecia triggered by a chemotherapy

Chemotherapy deranges the propagation of matrix keratinocytes in the anagen bulb, which responsible for the production of the hair shaft during proliferation. Baldness is one of the very important exhausting and emotional trouble with chemotherapy. After cessation of management course with chemotherapeutic agents, hairs regrow again eventually. (48,49).

3.2. Stress induced alopecia (SIA)

Stressful conditions either emotional or behavioral can be considered as risk or trigger factors for hair loss. Thus, healthy diet, daily work out and decreasing in stress level is the most successful approach of management for SIA. Nerve growth factor (NGF) is the chief and core agent in perifollicular neurons. Neurogenic inflammation of nerve cells occurs when the body enters with stressful state and this counteracts the effect of NGF, which is in charge of the development of hair follicles. There were supposed that sensory nerves and immune cells in the hair cells trigger the production of NGF in stress circumstance, which eventually triggers mast cell and resulting in white blood cells responsible for engulfing the foreign bodies to migrate neighboring the hair follicle. As a resultant, apoptosis of hair follicles and hair follicle stem cells is exaggerated in suffering animals in research done on this topic, which causes hair loss (50,51).

4.Medical treatments for alopecia

Medical treatments approved by the US Food and Drug Administration (FDA) for alopecia include:

4.1. Topical minoxidil

Topical minoxidil 2% for women and topical minoxidil 5% (52). Many studies favored the use of minoxidil 5% for females, but this is not documented by the FDA (53). Its mechanism of action is promoting growth and differentiation of the dermal papilla. In alopecia management when minoxidil is applied, it causes telogen hair premature cessation and delaying the anagen phase which causes hair growth.

Minoxidil has demonstrated respectable outcomes in the treatment of hair loss. It remains in oldest medication in the management of AGA, still, it stays the sole agent and drug intervention in alopecia which confirms effectiveness when used topically and is the only drug documented for baldness in a lady's hair fall (54).

4.2. Oral type II 5-α-reductase inhibitor

Finasteride (1 mg/day) is used for treating alopecia in men (52,53). The oral type I and II 5-α-reductase inhibitor, dutasteride, is also effective at the dosage of 0.5 mg/day but is not approved for this indication (55).

4.3. Hair transplantation

Hair transplantation is a choice for both sex people aged 30 and older with progressive baldness. The extent and category of baldness by reason might be weighed because the ideal choice for hair transplantation is those with frontal and mid frontal hair loss (66). Follicular unit hair transplantation is the best choice because it maintains the natural feature of the hair units and shows the best outcome (56). The damaging of progenitor cells, with preservation of the stem cells, in fact in haired vs non-haired scalp areas in people suffered from androgenetic alopecia. These results documented by Garza et al agree with the assumption that a deformity in the transformation of hair follicle stem cells to progenitor cells has a significant impact on the pathogenesis of androgenetic alopecia (57).

4.4. Glucocorticoids

They take refuge by using systemic corticosteroids in case of progressive alopecia. It has a wide range of side effects that involve hyperglycemia, osteoporosis, cataracts, immunosuppression, weight gain, and Cushing syndrome. Glucocorticoids are familiar because it has anti-inflammatory effects (58).

4.5. Intra lesional corticosteroids

Intralesional corticosteroids are the oldest choice treatment for circumscribed alopecia areata. (59)

4.6. Anthralin

Anthralin mechanism of action is due to immunosuppressive and anti-inflammatory activities related to antioxidant proprieties which are represented by free radicals' destructive effect and it is a very good choice for the management of children (60).

4.7. Topical immune–modulators

Topical immunotherapy depends on stimulating allergic contact dermatitis (ACD) by impressive using contact allergens to the involved skin. (61,62).

4.8. Phototherapy

8–methoxypsoralen with UVA radiation (PUVA) is the strategy used in the treatment of alopecia Universalis. Inadequate information in addition to the risk of cutaneous malignancies with PUVA limits its application (63).

4.9. Cyclosporine–A (CSA)

Cyclosporine A is a familiar antimetabolite agent managed by a patient undergoing organs transplantation, it inhibits T–cell activation. (64).

5. Another options of management that may be successful in AGA

5.1 Low–level laser/light therapy (LLLT)

The LLLT laser comb is official by the FDA as an option for the management of alopecia in both sexes. LLLT triggers anagen re-entry in telogen hair follicles, an elongate period of anagen stage, and enhancing proliferation degree in an active anagen hair follicles and to handle untimely catagen improvement. It acts by enhancement of energy production, scavenging of free radicals, and other reactive oxygen and nitrogen species. (65)

5.2. Prostaglandin–based therapies

Medications based on prostaglandin signaling and production have been evaluated for the management of baldness. The prostaglandin analog latanoprost and bimatoprost are usually identified to promote hair gain (66).

5.3 Nitric oxide and vitamin D3

It was found that using Nitric oxide (NO) gel triggers the regrowth of hair and enhancing regeneration in laboratory animals. The vitamin D receptor (VDR) is expressed in hair follicle keratinocytes during the last anagen and catagen stage. Using vitamin D can help in the regrowth of new hair and stop further hair fall. (67,68).

5.4. Herbal drugs used in the treatment of alopecia

There is favorability for herbal medications in all words because of their broad therapeutic properties, low incidence of adverse effects, a high and wide margin of safety, and less cost (Ghaudhary et al., 2010) (69,70).

The use of chemical medicines is accompanied by different adverse effects so can't be used for the treatment of alopecia safely. Therefore, naturally occurring medicines have appeared as another option to avoid the adverse effects of drugs associated with chemical drugs (71).

The biological products manage alopecia are commonly DHT antagonists and 5–α–Reductase inhibitors, they act by the support the hair follicle with essential compound necessary for growth and proliferation and improve the microcirculation to the scalp. Iron, copper, chromium, zinc, and magnesium are essential to preserving well scalp

and natural products supplied these essential compounds necessary for proliferation and regrowth of the hair. Vitamins like B complex (thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, folic acid, and the cobalamins) biotin, and retinoic acid are essential for maintaining of healthy hair, as it maintains lubricated hair root (72).

6. Complementary and Alternative Options for treatment of alopecia

6.1. Natural Products

6.1.1. Caffeine: Methylxanthine is an alkaloid it acts by triggering hair regrowth by inhibition of phosphodiesterase enzyme, antagonizing testosterone which triggers factors for alopecia, and enhancing keratinocyte proliferation (73).

6.1.2. Amino Acids: Many amino acids have been studied for alopecia management. Most commonly, cysteine and lysine have been tested in humans. (74).

6.1.3. Curcumin: Turmeric herb contains curcumin as an active ingredient that has an anti-inflammatory effect. cyclooxygenase-2, lipoxygenase, and inducible nitric oxide synthetase enzymes down-regulated by curcumin and can inhibits nuclear factor-kB signaling, so the net result is an ant-inflammatory effect by inhibition proinflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1. Curcumin also has antioxidant, antimicrobial, antineoplastic, and antiandrogenic activities (75).

6.1.4. Garlic Gel: This plant contains organosulfur compounds, which have antimicrobial, immunomodulatory, and anti-inflammatory prosperities (76).

6.1.5. Melatonin (N acetyl 5 methoxy tryptamine): The pineal gland secretes melatonin which is a neurohormone that regulates the circadian rhythm of mammals (77). Melatonin is also an antioxidant substance produced in hair follicles, its mechanism of action can be summarized by its ability to scavenging free radicals and other reactive species (78, 79).

6.1.6. Onion Juice: Despite the mode of action of topical onion juice in promoting hair regrowth is unclear, it is thought that sulfur and phenolic compounds cause an irritant contact dermatitis, stimulating hair regrowth through antigenic competition (80).

6.1.7. Procyanidin: Procyanidins are a type of flavonoid produce commonly in herbs, including apples, barley, cocoa, cinnamon, grapes, and tea, have antioxidant, anti-inflammatory, and antifungal properties (81). Procyanidins also promote anagen phase in murine hair models (82). Topical 1% procyanidin B2, derived from apple juice, causing a considerable enhancement in total and terminal hair counts at 4 months and 6 months in 29 patients with AGA compared to placebo (83, 84).

6.1.8. Pumpkin Seed Oil: Pumpkin seed oil (PSO) produce phytosterols which act as5α-reductase inhibiter thus inhibit the formation of active dihydrotestosterone (DHT) from testosterone (85)

6.1.9.Ginkgo Biloba: Botanical name: Ginkgo biloba L. Family: Ginkgoaceae Genus: Ginkgo Plant part: Leaves Chemical constituents: Ginkgolides A, B, C, J, M, bioflavin, sitosterol, lactones, and anthocyanins. The drug is extracted in coconut oil and is massaged for at least 2 minutes.it acts improvement of cerebral microcirculation and increases oxygen supply to the scalp (86). Flavanoides components of the Ginko tree are useful to stimulate the hair growth and treatment of alopecia and baldness triggering the effect of hair regrowth and inhibit platelet aggregation, thrombin activity, and fibrinolysis, lowering of triglycerides these result used as a tonic. Much of the literature has indicated many benefits of Ginkgo; however, most of which were limited only to its antioxidant and anti-inflammatory effects (87–89,90). The individual flavones derived from Ginkgo also stimulated human skin fibroblasts and enhanced collagen and extracellular fibronectin production(91).

Conclusion

Alopecia, a dermatological disorder, it can affect both sex and take big attention for a long time. The etiology of alopecia may be due to specific drugs, chemotherapeutic agent, stressful condition, or may have a genetic predisposition, in this review there is a survey for types of alopecia and their etiology, and for each type, there are various approaches and strategies for treatment, ranging from chemical drugs, herbal preparations that contain a very wide range of chemicals can treat alopecia either by supporting nutritional supplements or by causing as DHT and 5-α-Reductase blocking. The natural compound can support the scalp with protein, nutrition, antioxidants with minimal side effects. Besides, there are new approaches like mesotherapy, laser, and hair transplantation

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