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Research Article

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Current Advances in the Treatment of Androgenic Hair Loss

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Abstract

Male androgenic alopecia (MAA), the most common cause of progressive hair loss in men, affects up to 50% of men by age 50. Characterized by the miniaturization and loss of hair follicles, MAA results from a combination of genetic and hormonal factors. Conventional treatments, including topical minoxidil and oral finasteride, have demonstrated effectiveness in slowing hair loss but are associated with side effects, such as scalp irritation and sexual dysfunction. This review highlights emerging treatments for MAA, including oral agents like dutasteride, which has shown superior hair regrowth compared to finasteride but with similar side effects. Oral minoxidil has also demonstrated efficacy in promoting hair growth, though large-scale trials are needed to confirm its safety. Topical treatments, including finasteride sprays, clascoterone, and cetirizine, offer alternative options with fewer systemic effects. Additionally, low-level laser therapy (LLLT), platelet-rich plasma (PRP), microneedling, and hair transplants are explored as non-pharmacological interventions. Novel therapies, such as KX-826, a topical androgen receptor antagonist, and monoclonal antibodies like HM-115, show promise in ongoing clinical trials. However, further research is needed to confirm the safety and efficacy of these emerging treatments in managing MAA.

Keywords: Androgenic Hair loss, Alopecia, Platelet Rich Plasma PRP, Hair Transplant

1. Introduction

Male androgenic alopecia (MAA) is the most common progressive hair loss condition affecting men, up to 50% of men by the age of 50 [1]. It usually starts between adolescence and the age of 30 years. The condition is caused by a combination of genetic and hormonal factors and is characterized by progressive miniaturization and loss of hair follicles on the scalp. The two conventional treatments for MAA are topical minoxidil and oral finasteride [2]. Minoxidil is a vasodilator that increases blood flow to the hair follicles, while finasteride is a 5-alpha reductase inhibitor that blocks the conversion of testosterone to dihydrotestosterone (DHT), a hormone that is thought to play a role in hair loss. Both minoxidil and finasteride have been shown to be effective in slowing hair loss and promoting hair growth in men with MAA. However, they are not without side effects. Minoxidil can cause scalp irritation and hair growth in unwanted areas, while finasteride can cause sexual side effects such as decreased libido and erectile dysfunction.

In recent years, there has been a growing interest in the development of new treatments for MAA. In this review, we will highlight the emerging evidence regarding the newer treatments.

2. Oral Agents

2.1. Oral Dutasteride

Dutasteride is an anti-androgen medication that belongs to the same family of medication to finasteride. It is licenced in the management of benign prostate hypertrophy (BPH), however like finasteride, it works by blocking the production of dihydrotestosterone (DHT), which is responsible for male pattern baldness, by blocking the enzyme 5-α-reductase I and II [3]. A study by Vano- Galvan et al, reviewed the effectiveness of low-dose oral dutasteride for 12 months [4]. Over 90% percent of the subgroup on the low-dose (0.5mg per week) showed significant hair improvement. However, several reversible adverse effects were reported including decreased libido, erectile dysfunction, and gynecomastia.

Another prospective study by Tsunemi et al, showed significant hair regrowth at 52 weeks on daily oral 0.5mg Dutasteride with

similar reversible adverse effects [5]. A randomized controlled trial by Gubelin et al, compared dutasteride 0.5mg/day to finasteride showing better hair regrowth with the dutasteride subgroup, and no significant difference in side effects [6]. A key meta-analysis by Gupta et al, suggests a superior effectiveness for the use of dutasteride than oral finasteride with no real difference in the side effects profile [7].

2.2. Oral Minoxidil

An antihypertensive medication, minoxidil hyperpolarizes cell membranes by opening potassium channels which in effect vasodilates vascular smooth muscles. Crucially, minoxidil appears to lengthen the anagen phase of the hair cycle via unknown mechanisms. Topical use of minoxidil remains the standard recommendation in the management for MAA. Jimenez-Cauhe et al, retrospectively reviewed male patients with MAA who had oral minoxidil 2.5 or 5mg daily for a minimum of 6 months [8]. They reported clinical improvement in over 90% of their sample group, with minimal adverse effects reported including limb oedema and hypertrichosis. Similarly, a prospective study by Panchaprateep and Lueangarun, reviewed the effects of low-dose minoxidil on 30 patients with MAA, concluding clinically increased hair growth with 5mg daily dose. They do however caution its use in patient with severe hypertension [9].

A review by Randolph and Tosti of 17 studies to assess the use of oral minoxidil as treatment for hair loss [10]. They concluded that larger randomized studies are needed to look at the efficacy and safety of oral minoxidil, however, oral minoxidil is found to be safe and effective as an alternative for patients who struggle with topical formulations. However, a systematic review by Do Nascimentos et al, raised concern that there is absence of high quality randomized controlled trials for the effectiveness and safety of oral minoxidil use for MAA [11].

2.3. Oral Bicalutamide

Bicalutamide, a nonsteroidal androgen receptor inhibitor, is a licensed medication for the treatment of prostate cancer. It has been used off-label for the management of hirsutism and female pattern hair loss. A study by Ismail et al, albeit for female pattern hair loss, showed around 20% reduction in reported hair loss; however, reported adverse effects included hepatic enzyme derangement. There appears to be very limited data on its use on MAA [12].

3. Topical Treatments

3.1. Topical-Antiandrogens

Topical Finasteride in the form of a spray solution has been proposed as a possible treatment for MAA, to avoid the undesired systemic adverse effects associated with toral form. Piraccini et al, conducted a randomized controlled trial for the use of topical finasteride on over 300 patients with MAA. Significant hair regrowth was reported by 24 weeks when compared to placebo [13]. Further, no serious adverse effects were reported. A new direct androgen inhibitor, clascoterone has been suggested as possible treatment for MAA. Cartwright et al ,assessed the efficacy and safety of clascoterone by completing in-vitro, Phase I and Phase II trials. The results from the reported studies suggest that topical clascoterone 5% solution was very well tolerated, had minimal systemic exposure, and yielded significantly more hair growth compared to the topical minoxidil group. These findings pave the way for further Phase III trials [14].

3.2. Topical Cetirizine

Cetirizine, a common and readily available anti histamine medication, helps in the release of prostaglandin-E2 which has a stimulatory effect on hair cycle. Zaky et al ,studied the effects of topical cetirizine 1% on 60 patients with MAA. They reported significantly higher hair regrowth rates in the cetirizine group compared to placebo use [15]. A comparative randomized controlled study for the topical use of cetirizine 1% and minoxidil 5% showed that hair growth was more substantial as a combination therapy than placebo or when used alone [16]. Furthermore, no serious adverse effects were reported with the administration of cetirizine. These studies suggest a safe topical treatment option that may be used in combination therapies for the treatment of MAA.

4. Low-Level Laser Therapy (LLLT)

LLLT is a non-invasive treatment that uses light of wavelengths between 630 and 660 nm, to stimulate hair growth. A randomized double-blinded controlled study reviewed the effects of LLLT over a period of 24 weeks. A sham device was used on the contralateral side of the same patients as placebo. The LLT-treated area showed significantly greater improvement from baseline in hair thickness and count when compared with contralateral side treated by sham-device [17].

4.1. Platelet-Rich Plasma (PRP)

PRP is a blood-derived therapy that is injected into the scalp and is thought to promote hair growth by stimulating the production of new hair follicles [18]. The isolated growth factors from centrifuged venous blood are believed to stimulate the transition from telogen to anagen and increasing blood supply on the hair bulb region. It is typically used as mesotherapy onto balding areas of the scalp. A randomized controlled trial by Singh et al, compared PRP versus PRP plus topical 5% minoxidil for 80 patients with MAA over a period of 5 months. More significant hair regrowth was observed in the patients who had PRP in addition to Minoxidil. No long-term data was produced however [19].

5. Microneedling

Microneedling is a minimally invasive procedure that uses needles to produce micro-injuries to the skin triggering collagen and elastin synthesis. It is achieved by the used a handheld device called a derma roller that has a roller covered with small needles. It is hypothesized that the controlled microinjury of the skin may help stimulate hair regrowth in alopecia. A case study reported the use of 1.5mm derma roller needles for 20-25 minutes per session once weekly for 4 weeks, then fortnightly for another 11 sessions. Participants reported improvement of their hair regrowth, subjectively upon review of their scalps after a period of 24 weeks [20]. Further trials have also reported similarly improved outcomes

for MAA cases when microneedling were coupled with topical minoxidil [21]. However, larger randomized controlled trials are needed to elucidate the safety and efficacy of microneedling as treatment modality for MAA. Furthermore, there is no clear consensus on establishing the most effective derma roller needle length for the best outcome in the management of MAA.

6. Absorbable Threads

The insertion of absorbable threads such as Polydioxanone and poly-L-lactic acid (PLLA) has shown admirable hair regrowth cases of female pattern hair loss, despite no clear understanding of its mechanism of action. A comparative study demonstrated improved hair regrowth (by 27%) in patients with female pattern hair loss who used minoxidil 2% in addition to a session of thread therapy compared to minoxidil 2% alone (5%improvement only) [22].

7. Stem Cell Therapy

Stem cell therapy is a promising new treatment that uses stem cells to regrow hair follicles. The sources of multipotent cells with potential for regeneration are adipose tissue, blood, bone marrow, Wharton's jelly, and hair follicles from unaffected regions. Numerous studies have looked at the effects of stem cell therapies on MAA. A systematic review of 15 studies including 653 patients concluded that stem cell therapies have positive effects on hair regrowth regardless of the origin of the stem cells. A plethora of reported side effects ranging from fatigue, chills, bone pain, scalp irritation to haematomas have been reported across the studies. These findings are promising for the use f stem cells in the treatment for AGA [23]. Comparative analysis of the origin of stem cells may need to be clarified in the future studies to assess best efficacy.

8. Botulinum Toxin

Botulinum toxin has shown promising results in the treatment of MAA in certain reported studies [24]. Several mechanisms of action have been proposed including vasodilatory effect on the scalp to help clear DHT. Alternatively, botulinum toxin has been shown in-vitro studies to suppress agents that stimulate tissue fibrosis. A systematic review unfortunately has cast doubt on the effects of botulinum toxin in the treatment of MAA, with mostly inconclusive results based on the studies included [25]. Large randomized controlled trials are necessary to elucidate the role of botulinum toxin in the management of MAA.

9. Hair Transplant

Involves the harvesting of follicular unit grafts from a long-lasting donor area, usually the occipital and parietal scalp, and redistributing them by implanting into the required recipient area where the hairs have been lost [26,27].

There are essentially two techniques to harvest the grafts: Follicular Unit Excision or Extraction (FUE)Here, the follicular unit grafts are individually extracted using 0.75-1.2 mm punches. The procedure is carried out manually, mechanically, or robotically using various equipment.

The technique results in a large number of very small dot scars in the donor area. These are generally very difficult to detect unless the area is nearly shaven. The number of grafts available per procedure and over the life of the patient relies on the surface area and the follicular unit density [26-28]. FUE is currently the most common graft harvesting method.

10. Strip FUT Transplantation

This technique involves the removal of a hair-bearing strip of scalp from the donor area. Using stereoscopic dissecting microscopes, it is then dissected by surgical staff into the individual follicular units [29]. This technique results in a linear scar across the donor area hidden by the surrounding downward growing hairs. The choice of harvesting technique could be down to the patient preference, but there are also certain indications depending on the patient's hair loss circumstances that could favour one technique over the other.

Once the grafts/hairs have been removed from the donor area by either technique, they are then individually inserted surgically into the recipient area. This is either done by creating recipient sites first then implanting with forceps or implanter pens, or directly implanting the grafts using sharp-edged implanter devices [27].

The aesthetic skill and experience of the surgeon will largely determine the cosmetic outcome in terms of design, naturalness, density, and expected progression of the patient both in terms of age as well the ongoing development of the hormonally and genetically influenced hair loss [30].

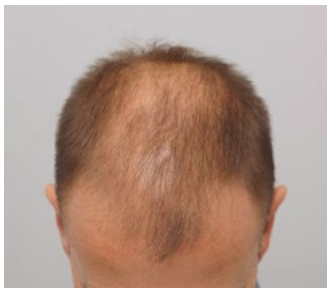

Figure A FUE Male Before

Figure B FUE Male After

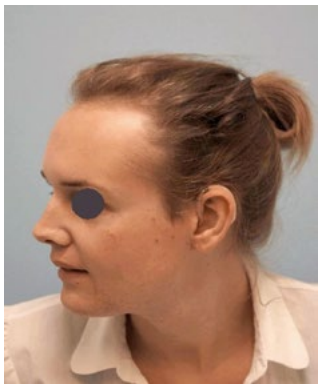

Figure C FUT Male to Female Before

Figure D FUT Male to Female After

11. Novel Therapies

Newer treatments are in clinical pipeline and are showing promising results. A novel androgen receptor antagonist named

KX-826, also named pyrilutamide, is currently undergoing a Phase III randomized double-blinded placebo-controlled trial in the USA and China [31]. It is being tested as a topical solution and tested on male patients with MAA with already promising results based on hair count at Week 24 [32]. Prostaglandin D2 (PGD2) is known to inhibit hair growth and highly expressed on scalps of patients with MAA. PGD2 antagonist, setipiprant has been proposed as a possible novel treatment for MAA. Unfortunately, according to a study showed there does not appear to be any significant difference with placebo and considered inferior to other conventional therapies [33]. Biological therapies may be considered in the treatment of MAA. Currently completed Phase I trial successfully, HM-115, a monoclonal antibody that targets prolactin receptor will now be tested for the management of MAA in Phase II trials.

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