THERAPEUTIC UPDATE


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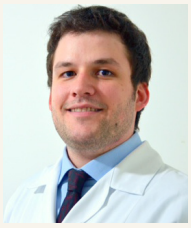
Update on Male Pattern Hair Loss



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Male pattern hair loss (MPHL) is the most common cause of alopecia in men. It affects approximately 30% of Caucasian men by the age of 30 and its prevalence increases with age. The influence of male hormones has been well studied and is the main target of the some of the most effective treatments. The main alteration in MPHL occurs in the hair growth cycle where the anagen phase becomes shorter resulting in shorter and thinner hairs. This process is called miniaturization. Generally, hair loss starts with a receding hairline and rarefaction at the vertex and progresses until the top of the scalp is completely bald. The sides of the scalp and the lower occipital areas are preserved even in longstanding MPHL. Other diseases such as diffuse alopecia areata and telogen effluvium must be excluded. To date, the first-line treatment still is topical minoxidil combined with oral finasteride. Surgery and other treatments will also be discussed.

Minoxidil

The literature shows that minoxidil acts by shortening telogen phase and increasing hair diameter especially in miniaturized hairs. The mechanism of action is not established yet but the hypothesis involves increasing level/activity of vascular endothelial growth factor (VEGF). New insights into its mechanism are the stimulation of production of PGE2 and minoxidil influences on androgen receptor.[1]

Topical minoxidil 5% solution has been proved to work better than minoxidil 2% in men.[2] Minoxidil 5% foam once daily is as effective as minoxidil 2% solution twice daily in women.[3] Approximately 40% of male patients experience hair regrowth with 5% minoxidil and therapeutic response should be seen within 3-6 months. A new method to detect patient responsiveness to the treatment has been suggested using sulfotransferase activity in plucked hair.[4]

Minoxidil is a topical treatment that should be applied on dry scalp twice daily. It is a lifelong treatment and hair shedding can occur in the first 1-3 months. The most common side effects are irritant dermatitis, contact dermatitis, and hypertrichosis on the face. The latter side effect is not of much consequence is adult males. Topical minoxidil is available in solution as the 2% and 5% and as a 5% foam.

5-alpha-reductase Inhibitors (5ARI)

This group of medications inhibit the 5-alpha-reductase enzyme type I, II, and/or III resulting in decreased conversion of testosterone to dihydrotestosterone (DHT).

Finasteride mainly inhibits type II/III enzyme. The approved dose to MPHL is 1mg daily. Two thirds of the patients are expected to improve their condition and one third to stabilized hair loss. Patients are asked to be on finasteride for one year until deciding to discontinue if there is no improvement. Improvement is not only due to hair regrowth but also to changes in hair growth rate (length) and thickness.[5]

Dutasteride inhibits types I/II of 5-alfa-reductase enzyme. It is three times more potent than finasteride. Dustasteride 0.5mg is prescribed off-label for MPHL. Olsen et al found that 2.5mg of dutasteride was superior to 0.5mg in promoting hair growth. Also 2.5mg was more efficient in suppressing scalp DHT compared to 0.5mg dutasteride and 5mg finasteride (79% x 51% x 41%). As a result, 2.5mg dutasteride was associated with higher prevalence of sexual complaints (decreased libido).[6] Jeung et al treated non-responders to 1mg finasteride with 0.5mg dutasteride. Following 6 months of dutasteride, 75% of the patients showed improvement on global photographic assessment and phototrichogram. How-

ever, the author raises that the selected patients could have been called slower responders to finasteride vs non-responders since they had improvement in a prior phototrichogram after 6 months of finasteride.[7]

Nowadays, the main concern of men regarding 5ARI is the sexual side effects. In a long-term (5-year) multinational study with 1mg finasteride, 4.4% reported sexual dysfunction in the first year. These side effects resolved after discontinuation of medication in all patients and in most men that stayed on treatment.[8] Gupta et al, on the other hand, didn't find any significant difference among finasteride, dutasteride, and placebo regarding sexual disturbance.[9] In summary, close follow up and further evaluation of these patients are needed to clarify the relation between 5ARI and sexual side effects.

Other important side effects that have been mentioned in some studies but not confirmed in controlled trials are depression, gynecomastia, and breast cancer.

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Surgery

Hair transplant (HT) is the only treatment that can substantially increase the number of hairs. Basically, hairs from the back of the scalp are removed and transplanted to the recipient site. Two techniques have been proposed: follicular unit transplantation (FUT) and follicular unit extraction (FUE).

FUT is the traditional HT technique. A strip of hair-bearing scalp is cut out from the occiput. The strip is then dissected. Many holes are made in the recipient site where the grafts are implanted. The advantages of this procedure are the higher number of obtained grafts and less transected follicles. However, it is time-consuming, needs a high-qualified team (surgeon, nurses and technicians), leaves a line scar, and can cause dysesthesia at the donor site.

In FUE, instead of a strip, grafts are removed one by one from the donor site with punches that range size from 0,75mm to 1.2mm depending on follicular unit density. The advantages of FUE are less noticeable scars, no dysesthesia, and shorter downtime. However, there is a higher chance of transecting follicles, fewer grafts are harvested, subdermal cysts may form, and this technique demands a longer learning curve.

New machines have been designed to accelerate and improve the FUE technique. Neograft® is a powered FUE that is composed of a handheld pneumatic press device for harvesting grafts, a micrometer for making holes at the recipient site, and handheld graft implanter. Onda et al had a lower transection rate and less harvest time with this machine.[10] ARTAS® Robotic is an apparatus that can select follicular units and harvest them.[11] This robot will be able to make the holes with its new upgrade.

LLLT (Low Level Laser Therapy)

The first time light was seen as a possible source of hair stimulation was in 1967. Primarily, Metser et al were studying the potential carcinogenic effect of laser in mice and were surprised to discover hair regrowth on shaved areas after exposure to laser.[12]

The most common LLLT devices have wavelengths in the range of 500-1100nm. The mechanism of action is not known but has been proposed that LLLT acts on mitochondria and may alter cell metabolism increasing ATP production, cell proliferation, cytokines, growth factors, and tissue oxygenation. LLLT is believed to result in anagen hair re-entering telogen hair follicules and prolonged duration of anagen phase.[12]

There are a few devices (ie, comb and helmet) that have been used to delivery light in order to promote hair growth. Two RCT studies, Jimenez et al in 2014 and Leavitt et al in 2009, using HairMax LaserComb® (655nm) with different number of beams and regimen treatments demonstrated hair growth improvement in male pattern hair loss.[13,14] Data exclusion in Leavitt study might have compromised its results.[15] Another two RCT studies using helmet devices, Kim et al (630, 650, and 660nm) and Lanzafame et al (655nm), have also shown effectiveness in their treatments.[16,17]

Light treatments are of special interest to non-responders or those who have had side effects from minoxidil or finasteride and are not interested in surgical treatments. Although it seems to be a promising alternative to medications and surgery, uncertainty on LLLT devices remains and questions about efficacy on longer follow-ups, adequate wavelength, best laser modality, treatment regimens, and long-term efficacy need to be answered.

Platelet-Rich Plasma (PRP) and Microneedling

PRP and microneedling are two interesting procedures that are believed to increase growth factors stimulating hair growth. The former would act through releasing growth factors from platelets and the latter from trauma, trigger factors,

and better penetration of a topical drug such as minoxidil. Although these are promising techniques we still need more data proving that they work.

Follicular Cells Implantation (FCI)

FCI is a cell therapy intended to treat hair loss. Two types of follicular cells have been used: dermal papilla and dermal sheath cells (DPC/DSC). These cells possess an inductive property that if they are cultured and implanted into skin allows them to induce formation/rejuvenation of follicles.[18,19]

The procedure consists of: a punch biopsy from the androgen-insensitive area of the scalp (occipital), cells (DPC/DSC) dissection, and replication in a culture medium and injection of replicated cells to bald sites. Finally, the implanted cells would migrate to damaged/dormant follicles and help rejuvenate them or induce keratinocytes to form new follicles.[18,19]

Replicel® has been working with implanting autologous cultured dermal sheath cells (DSC) in pattern hair loss patients in order to regenerate hairs. A phase 1/IIa trial has been carried and has proven that this is a safe procedure. Phase I/IIa trial consisted of a one-time procedure in the beginning of the study and follow-up of 24 months. If there was ≥5% increase in hair density, it was called responder site. Responder-treated sites were more significant than control-treated sites (63% vs 37%). 70% of the responder-treated sites had 11.8% average increase hair density. Phase IIb trial will involve 160 subjects and will be important to optimize treatment regimen (dose and frequency).[20]

Disclosure

Jerry Shapiro is a consultant for Merck, J&J, Applyed Biology, and Pierre Fabre, and is co-founder and stockholder of Replicel Life Sciences. Leopoldo Duailibe Nogueira Santos has no conflicts to declare.

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