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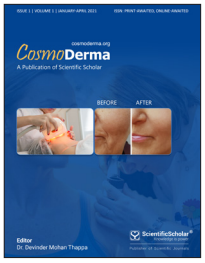

Perspective

Role of oral minoxidil in the treatment of androgenetic alopecia

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ABSTRACT

Patterned hair loss is the most common cause of alopecia, typically presenting with progressive thinning, miniaturization, and loss of hair at classical topography depending on the sex of the patient. In the 1970s, Minoxidil was used to treat severe refractory hypertension due to its vasodilator properties. It became popular after its coincidental finding on the promotion of hair growth and stimulation of new hair production. In 1988, the Food and Drug Administration approved topical minoxidil (TM) 2% for the treatment of male androgenetic alopecia and in 1992, for female pattern hair loss. It is also used as an off-label treatment for other hair loss conditions such as telogen effluvium and alopecia areata. However, there are frequent reports of TM-induced contact dermatitis and its reversible effect, which has reduced compliance in the patients and resulted in a poor outcome. Hence, they have studied using low-dose oral minoxidil (LDOM), which showed good efficacy and safety profile in the treatment of patterned hair loss along with avoidance of high-risk adverse cardiac effects that resulted due to doses used for hypertension. The added advantages of LDOM over topical formulation are good compliance, cost savings, effective in people with low hair follicle sulfotransferase activity, and the possibility of cotherapy with other topical or oral medications.

Keywords: Minoxidil, Androgenetic alopecia, Patterned hair loss

PERSPECTIVE

Androgenetic alopecia (AGA) is characterized by progressive thinning and miniaturization of the hair follicle with a pattern distribution in predisposed men and women causing a strong psychological impact of low self-esteem and distress. Management depends on various factors such as grading of AGA, efficacy, cost, and risks. Food and Drug Administration approved treatment options for AGA are topical minoxidil (TM) and oral finasteride. However, their use is limited by their side effects notably contact dermatitis, need for long-term use, reversible efficacy, non-compliance with TM, sexual adverse effects, post-finasteride depression syndrome in men, and teratogenicity in female patients with oral finasteride. To overcome this, studies are going on oral minoxidil and its dosage for better efficacy with lesser side effects.

MINOXIDIL

During 1970s, a dose of 10–40 mg/day was used to treat severe refractory hypertension due to its vasodilator properties. At that time, they observed an unforeseen effect, i.e., hypertrichosis in approximately 80% of patients. Even though oral minoxidil (OM) has hair-growing properties

when used as antihypertensive at such high doses, there is always a risk of developing a pericardial effusion that may progress to cardiac tamponade and angina pectoris, which led to the development of TM in 1986. Since then, the TM is being used for AGA in both men and women of all ages and also found effective for other alopecia as well.

Recently, there have been multiple studies exploring the use of low-dose oral minoxidil (LDOM) for treating many forms of alopecia, with the goal of gaining hair while keeping adverse reactions at bay. Less than 5 mg daily is considered as LDOM in adults.

PHARMACOLOGY

As a pro-drug, after entering the body, it gets converted to its active metabolite form "minoxidil sulfate" by sulfotransferase, which is responsible for all actions of minoxidil on hair follicles. Estimation of sulfotransferase enzyme activity in plucked hair follicles is a valuable tool in predicting TM response, as it is variable in different individuals, which is not necessary for oral minoxidil. It is activated by sulfotransferase present in the liver and platelets.[1,2]

Minoxidil acts as a vasodilator by opening potassium channels localized on the smooth muscular cells of the peripheral artery. By upregulating vascular endothelial growth factor, it increases cutaneous blood flow thereby more oxygen and growth factor delivery to the hair follicle.

Minoxidil induces the β-catenin signaling pathway. This shortens the telogen phase and prolongs the anagen phase with progressive growth in hair diameter and length. Minoxidil also decreases catagen by inhibiting transforming growth factor β-induced apoptosis of hair matrix cells apoptosis.

It also has anti-fibrotic activity by inhibiting the enzyme lysyl-hydroxylase in human skin fibroblast leading to the synthesis of a collagen deficient in hydroxylysine making it more susceptible to degradation by collagenase. By this, its use in scarring alopecia can be justified.

Minoxidil given orally is almost completely absorbed (⩾90%). Peak plasma levels are reached within 1 h and fall rapidly afterward. The 90% of the administered drug excreted unchanged in urine and as a metabolite (glucuronide conjugate) within four days. It does not cross the blood–brain barrier.

BASELINE MONITORING

It includes ECG and chest x-ray. Check urinary catecholamines if the patient has a history of severe headaches, sweating, and high blood pressure.

CONTRAINDICATIONS

Pheochromocytoma, previous hypersensitivity reactions to ingredients, hypotension, cardiac comorbidities, renal failure, pregnancy or breast feeding.

DRUG INTERACTIONS

Salicylate/aspirin inhibits sulfotransferase activity thereby decreasing the activity of OM. Caution to be taken while giving along with other antihypertensive to avoid postural hypotension.

DOSAGE

Male pattern hair loss (MPHL)

Start minoxidil at 1 mg/day for 2–3 months then gradually increase the dose by 0.5 mg every 2–3 months until it reaches a maximum daily dose of 5 mg.

Female pattern hair loss (FPHL)

Start with 0.25–0.5 mg for 2–3 months then gradually increase the dose by 0.5 mg every 2–3 months until it reaches a maximum daily dose of 5 mg.

IN PREGNANCY AND LACTATION

Oral minoxidil is not recommended during pregnancy and lactation as it belongs to category C. Although it is not recognized as a teratogenic agent, there are occasional reports of neonatal hypertrichosis if taken during pregnancy. The drug may be secreted in breast milk and potentially pose a risk to a nursing infant. Besides, there is no definitive safety information available on LDOM use by males whose female partners are pregnant. On the other hand, TM is generally considered to be a safer option.[3,4]

IN PEDIATRIC AGE GROUP

A retrospective review of eight young patients with loose anagen hair syndrome (seven years of median age) found that oral minoxidil ranging from 0.10 to 0.50 mg as a daily dose could be a promising treatment. Hair length increased in all patients, and seven of eight patients experienced improved global hair density.[5] In another study of accidental exposure to oral minoxidil in children, hypertrichosis was seen in 65% of them. The initial zone of appearance was the face, mostly the forehead, and temples. Later on, all patients finally developed hypertrichosis in the facial area, which progressed to a generalized hypertrichosis in follow-up period. About 61.5% (8/13) of the patients showed resolution within six

months while 38.5% (5/13) of the patients had persistent hypertrichosis.[6]

IN POSTMENOPAUSAL WOMEN

The prevalence of FPHL was high in postmenopausal women at 52.2%, and its prevalence increased with age and years since menopause.[7]

COMBINATION WITH OTHER MEDICATIONS

Oral minoxidil can be used in combination with topical serums, drugs such as spironolactone, finasteride, and dutasteride or procedures such as platelet-rich plasma and growth factor therapy. Sinclair combined 25 mg of oral spironolactone with 0.25 mg of OM for the treatment of AGA while 50 mg of spironolactone was used along with 2.5 mg of OM in another study. The reason for the combination treatment was to allay fluid retention that may arise as a result of the use of OM.[8] Oral dutasteride 0.5 mg/day was combined with OM 5 mg/day by a few and found as one of the most effective therapies for MPHL.[9]

Jerjen *et al*., also conducted a study on using sublingual administration of minoxidil, as it bypasses hepatic metabolism for greater bioavailability. At a dosage of 0.45 mg daily, both male and female patients had improvements in terms of Sinclair stage and Sinclair hair shedding score. It also showed that temporary hair shedding is less common with OM compared with TM and is ceased for most of these women within four weeks.

ADVERSE EFFECTS

Dizziness, hypotension, fluid retention, tachycardia (palpitations and chest pains), headaches, periorbital edema (eye puffiness or swelling around the eyes), hypertrichosis (generalized excessive hair growth – with higher doses), insomnia, and urticaria.[2] Patients are advised to take oral minoxidil at bedtime with the increase of fluid intake and getting up slowly from a lying/sitting position to prevent lightheadedness. Sinclair described the use of 50 mg of sodium chloride daily for treatment of patients reporting postural hypotension. Limiting salt intake to <2 g/day, the use of diuretics, furosemide, and spironolactone (in females) is helpful to relieve fluid retention. Coadministration with β-blockers can also be helpful.[10] Keep a record of blood pressure and pulse rate reduce alcohol intake to prevent sudden falls in blood pressure, and reduce caffeine-containing products and tablets for cold to avoid rapid increase in heart rate.

CONCLUSION

Patients who can benefit from LDOM are those with FPHL and MPHL with no cardiac comorbidities, young adults with moderate patterned hair loss, and those with low compliance, local intolerance, or no response to TM. The OM can be used as monotherapy or in combination with other oral or topical medications for AGA.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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