Chapter 63

Minoxidil: main differences between topical and oral use

https://doi.org/10.56238/colleinternhealthscienv1-063

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1 INTRODUCTION

Minoxidil was, in the seventies, introduced as an oral medication that was initially used for the treatment of hypertension, in view of its vasodilator potential - activation of the potassium channels located in the smooth muscles of the peripheral arteries, allowing the efflux of potassium so that hyperpolarization of the cell membrane and relaxation of the smooth muscles occur. However, a side effect observed by patients using this drug was hair and body hair growth. Soon, in the eighties, it was launched in the market under a new presentation: the topical version - in concentrations of 2% and, later, 5% -, aiming to be an alternative for hair loss disorders and to promote hair growth. Currently, it is the most widely used drug for the purposes described above. Thus, this work has as main objective to analyze differences, especially regarding adverse reactions, between topical and oral use - which has also been implemented, but in lower doses than the treatment for hypertension - of minoxidil, and the efficacy of the two routes of administration.

2 DEVELOPMENT

A literature review was conducted from journals indexed in the PubMed platform, using the descriptors "minoxidil," "oral minoxidil," and "topical minoxidil. Four articles published in the last ten years were selected. For several decades, minoxidil has been the main treatment, approved by the "Food and Drug Administration", for androgenetic alopecia - non-scarring, genetically determined alopecia in which terminal hairs turn into miniaturized hairs - in men and women, and also used as *off-label treatment*

for other hair loss conditions, such as chemotherapy-induced alopecia - hair loss as a side effect of chemotherapy treatment -, alopecia areata - an autoimmune disease of the hair follicles, which ranges from irregular, non-scarring alopecia to complete hair loss on the scalp and body -, chronic telogen effluvium - common non-scarring alopecia characterized by excessive hair loss triggered by stressful events such as pregnancy, serious illness, and surgery -, hereditary hypotrichosis - an autosomal dominant disease characterized by non-syndromic alopecia caused by mutations that course with gradual and diffuse hair loss of the scalp. In addition, it is also used to improve body hair growth in other areas, including eyebrows and beards. The positive effect of minoxidil on hair growth is primarily due to its metabolite, minoxidil sulfate, and the enzyme responsible for its conversion, sulfotransferase, which is located in the hair follicles. This enzyme varies between individuals, and patients with higher enzyme activity tend to respond better to treatment with minoxidil. Despite its global acceptance for over 40 years, the exact mechanism of action of this drug for hair disorders is still unknown and remains to be elucidated, but it is known that minoxidil causes a shortening of the telogen phase - where hair is released and falls out of the hair follicle - and prolongation of the anagen phase - which activates hair growth. It is important to note that even though there are very limited data on teratogenicity and even though no serious adverse outcomes have been reported, minoxidil should, as a safety measure, be avoided during pregnancy and lactation (4). Although topical minoxidil is an effective option for hair loss, many patients are poorly adherent to treatment due to the need to regularly apply the medication once or even twice daily, often leaving the hair with an undesirable texture (2). In addition, some adverse reactions have been reported with its use, and over time, some patients may develop irritant and allergic contact dermatitis, seborrheic dermatitis, itching, scaling of the hair scalp, and hypertrichosis in areas of the face if improperly spread over it. Thus, the most common reactions to the topical formulation, fortunately, are related to dermatological complaints limited to the scalp and, more rarely, to the patient's face. Unfortunately, patients allergic to topical minoxidil are not long-term candidates for its use (3). Thus, after some time, low-dose oral minoxidil - different from that used for hypertension - has become an equally effective alternative for a variety of hair loss disorders in patients who have difficulty fitting with topical minoxidil preparations (1). However, with the oral route of administration there are also adverse effects, which are systemic, such as sodium and water retention, headache, palpitations, pulmonary hypertension, and hypertrichosis that can affect the face and other body sites (4). Importantly, both formulations-in studies comparing the efficacy of 1 mg per day of oral minoxidil with the 5% topical solution for daily use-have been shown to be effective and with effects that are generally well tolerated or managed (1).

3 FINAL CONSIDERATIONS

We conclude that the choice of route of administration for minoxidil should be made after a doctor-patient consensus, since we are talking about effective treatments for conditions that involve both aesthetic, psychological, and even health repercussions, but that are not free of adverse reactions. The best course of action must be evaluated to ensure safety and successful results.

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