Allergic contact dermatitis to topical minoxidil solution: Etiology and treatment

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After more than a decade of use, topical minoxidil solution has proven to be a safe and effective treatment for androgenetic alopecia. However, some patients present with complaints of pruritus and scaling of the scalp. The most common causes of these symptoms include irritant contact dermatitis, allergic contact dermatitis, or an exacerbation of seborrheic dermatitis. Patients suffering from allergic contact dermatitis may benefit from patch testing to determine the causative allergen. Among the patients we patch tested, propylene glycol was found to be the contactant in a majority of cases, not the minoxidil itself. Many of these patients may be candidates for treatment with alternative formulations using other solvents, such as butylene glycol, polysorbate, or glycerol. Although predictive, patch testing results do not ensure that the compounded preparations will be tolerated. Unfortunately, patients found to be allergic to minoxidil are no longer candidates for topical treatment of their alopecia with any preparations of minoxidil. (J Am Acad Dermatol 2002;46:309-12.)

Topical minoxidil solution is a hypertrichotic agent used to treat androgenetic alopecia (AGA). AGA results from miniaturization of hair follicles in androgen-sensitive areas of the scalp in genetically predisposed persons.[1] Arresting the process of miniaturization remains the goal of medical treatment. Currently topical minoxidil solution (minoxidil, alcohol, propylene glycol, and purified water) and oral finasteride are the only therapies for this condition approved by the Food and Drug Administration.[2] Topical minoxidil solution is approved for this indication in 2% and 5% formulations. Although minoxidil functions as a vasodilator when used systemically for hypertension, its mechanism of action in hair loss involves a direct stimulatory effect on dermal papillae or follicular hair matrix cells.[3]

Topical minoxidil solution has a favorable safety profile and is currently available over the counter. The adverse effects of topical minoxidil solution are predominantly dermatologic and limited to the scalp. The phase III clinical trial listed application site reactions in 5.7% of the patients using the 5% formulation and in 1.9% of the patients using the 2% formulation.[4] These included pruritus, erythema, scaling, and dryness.

The most common causes of these symptoms include irritant contact dermatitis, allergic contact dermatitis, or an exacerbation of seborrheic dermatitis. Differentiation of these conditions is necessary for appropriate intervention because successful treatment of the local adverse reaction is necessary for the patient to continue using topical minoxidil in the treatment of their alopecia. This report focuses on a series of patients whose presentation was most consistent with an allergic contact dermatitis. The goal in these patients was to utilize patch testing to elucidate the specific causative allergen involved. Identifying the specific contactant may allow continuation of the patient's therapy with an alternative topical minoxidil preparation.

SELECTED CASE REPORTS

Case 1. A 67-year-old woman with a history of AGA treated with topical minoxidil solution presented with mild erythema and scaling of the scalp. She was patch tested to a series of allergens and demonstrated a positive reaction to propylene glycol. No reaction to butylene glycol or minoxidil was noted. These results indicated that a propylene glycol–free preparation might have utility. The compounded formulation substituted butylene glycol for propylene glycol. At 10 months, the patient was satisfied with the efficacy and tolerability of the compounded formulation.

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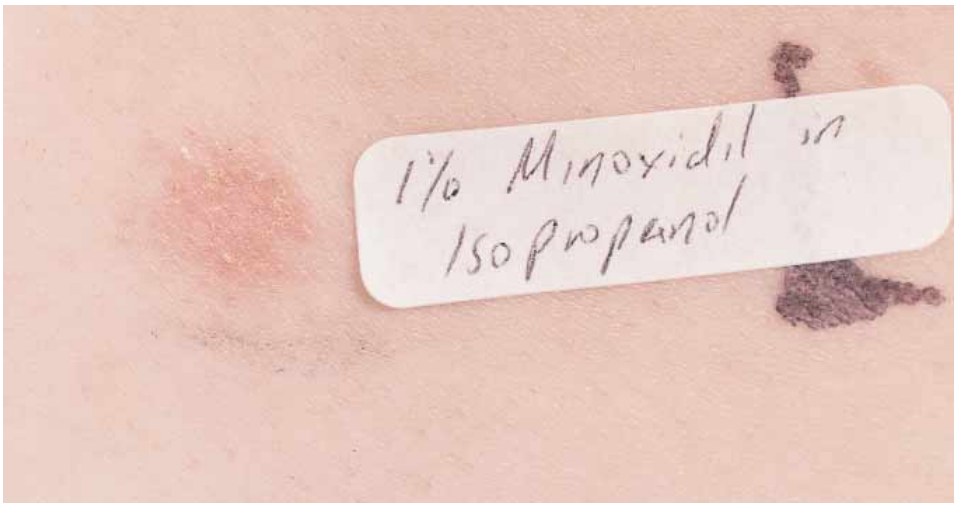

Fig 1. Positive allergic contact reaction to 1% minoxidil in isopropanol demonstrated by patch testing.

Case 2. A 52-year-old woman using topical minoxidil solution to treat her hair loss presented with a complaint of increased scaling and scalp pruritus. Patch testing revealed an allergy to propylene glycol, but no reaction to butylene glycol or minoxidil. Despite these patch testing results, she was unable to tolerate the compounded formulation because of continued scaling and pruritus at the application site.

Case 3. A 63-year-old man treating his AGA with 5% topical minoxidil solution complained of increased pruritus and scaling of the scalp. His presentation was consistent with allergic contact dermatitis, and patch testing was performed. The results demonstrated a positive reaction to minoxidil (Fig 1). As a result, he was no longer a candidate for using topical minoxidil solution to treat his hair loss.

DISCUSSION

Topical minoxidil solution is an effective treatment for regrowth of hair in some patients and stabilizes hair loss and miniaturization in a majority of them.[5] Long-term application is required for continued benefit. As with long-term exposure to any medicament, over time some patients may develop contact dermatitis to a specific ingredient in the preparation. Although the safety profile of topical minoxidil solution is favorable, the most common complaint among users is scalp pruritus and scaling. In addition to irritant and allergic contact dermatitis, these symptoms may be due to an exacerbation of seborrheic dermatitis. While clinically similar, these entities must be differentiated for optimal treatment outcome and, more importantly, to allow the patient to continue treating his or her hair loss.

Patients with a diagnosis of either irritant contact dermatitis or seborrheic dermatitis can be effectively treated with anti-inflammatory agents including tar shampoo or topical corticosteroids while continuing their use of topical minoxidil solution. The subset of patients diagnosed as having suspected allergic contact dermatitis should be patch tested to determine whether the allergen is the active ingredient minoxidil or the solvent propylene glycol.

Eight additional patients were patch tested in the same manner as the patients described in the case reports. In total, there were 7 women and 4 men in the group, with an average age of 46.7 years. Nine of 11 patients (81.8%) showed a positive allergic reaction to propylene glycol by patch testing. Two of the 9 were negative (ie, not sensitive) at a lower concentration and positive (ie, sensitive) at a higher concentration of propylene glycol. One of 11 patients (9.1%) was reactive to butylene glycol, and 4 of 11 patients (36.4%) reacted to the active ingredient minoxidil (Table I).

Among the patients we patch tested, propylene glycol was found to be the agent most frequently responsible for allergic contact dermatitis to minoxidil solution. Two patients in our series demonstrated a threshold sensitivity because they only reacted to a higher concentration of propylene glycol. This concept is evident in previous patch test studies,[6-9] in which increasing concentrations of propylene glycol are less well tolerated. Paradigms for elicitation thresholds for allergic and irritant contact dermatitis have been described.[8-11] Thus there is utility in using the lowest possible solvent concentration in preparations for patients with a history of allergic or irritant contact dermatitis to glycols.

Table I. Patch test results for 11 patients suspected of having an allergic contact reaction to topical minoxidil solution

Patient No.	Age (y)/Sex	Propylene glycol	Butylene glycol	Minoxidil
1*	67/F	Positive	Negative	Negative
2*	52/F	Positive	Negative	Negative
3	63/M	Negative	Negative	Positive
4*	28/F	Positive†	Negative	Negative
5*	27/M	Positive	Negative	Negative
6*	44/F	Positive‡	Negative	Negative
7*	21/M	Positive	Negative	Negative
8*	45/F	Positive	Negative	Negative
9*	59/M	Positive	Negative	Positive
10	39/F	Positive	Positive	Positive
11	69/F	Negative	Negative	Positive

*Started on compounded preparation.
†Positive at 50%, negative at 20% concentration.
‡Positive at 50%, negative at 10% concentration.

Data from the phase III clinical trial for 2% and 5% topical minoxidil solution support the concept of threshold sensitivity. The 5% minoxidil formulation, which contains more propylene glycol (50%) than the 2% minoxidil formulation (30%), was associated with a higher number of cases of itching, erythema, and dryness. This difference is not due to the minoxidil concentration because the patients using the vehicle with 50% propylene glycol reported a similar incidence of adverse events to the patients using the 5% minoxidil formulation.

Previous reports have suggested that the active ingredient, minoxidil, was the more common allergen.[12-18] However, it should be noted that the series of allergens utilized in these studies were not consistent and the patient numbers were small. Our patch test study was specifically designed to determine whether each individual patient was allergic to minoxidil or propylene glycol.

Patients found to be allergic to propylene glycol were candidates for compounded preparations of topical minoxidil formulated without propylene glycol. For these patients, we chose butylene glycol when possible as a substitute. Chemical similarity between butylene glycol and propylene glycol gives a high degree of confidence with regard to its potential for transcutaneous delivery of minoxidil. Despite this chemical similarity, an immunologic distinction between the two solvents has been confirmed by previous patch test studies.[19] However, in actual clinical use, some patients whose patch tests were negative to butylene glycol subsequently proved to be intolerant to the compounded preparation. This may be due to the inflamed state of their scalp, leaving it more susceptible to further irritation. If, in fact, patients are found to be clinically intolerant to butylene glycol, glycerin and polysorbate are possible alternative solvents.[20,21] Given the concept of threshold elicitation demonstrated in our series, as well as in previous studies, there is utility in using the lowest solvent concentration required to solubilize the minoxidil.

No clinical studies have been performed comparing the efficacy of topical minoxidil prepared with alternative solvents. However, these preparations provide a method for delivering minoxidil to the scalps of propylene glycol–sensitive patients.

Because topical minoxidil solution is the only Food and Drug Administration–approved topical treatment for AGA, the treatment options for hair loss in these patients are very limited. Patients suspected of suffering from allergic contact dermatitis should be advised to undergo patch testing to determine the causative allergen. If the patients are found to be sensitive to propylene glycol, then they should be given the option of formulations compounded with alternative solvents. Unfortunately, patients found to be allergic to minoxidil are no longer candidates for the topical treatment of their alopecia with minoxidil; our data suggest that this is not an infrequent scenario. Systemic androgen modulators provide an alternate treatment option for some of these patients.

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