Successful Treatment of Alopecia Totalis with Topical Calcipotriol: Serial Case Report and Review of the Literature

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**ABSTRACT**

**Background:** Alopecia totalis (AT) often responds poorly to standard therapies. This disease is chronic and relapsing, so effective cure treatment has been established. Calcipotriol is a vitamin D analog and acts as a potent immunomodulatory agent that can be used in the treatment of alopecia areata (AA) with promising results. The active form of vitamin D mediates its action by binding to specific vitamin D receptors (VDR) located in the nuclei of target cells. Expression of VDR in keratinocytes is necessary for maintenance of the normal hair cycle.

**Objective:** Our study aims to show the effectiveness of topical calcipotriol in the treatment of Alopecia Totalis patient.

**Methods:** Three patients diagnosed with AT, duration of disease 6 – 12 months, refractory to other treatments were selected and were started on topical calcipotriol and were followed up every 4 weeks for 12 weeks. The efficacy was measured by hair regrowth using photographic assessment, Severity of Alopecia Tool score (SALT), Hair Pull Test and physical examination. Patients will be followed up for 6 months after stopping treatment for assessing disease relapse.

**Results:** The patients showed excellent response with complete regrowth of scalp hair after a single 12-week treatment course of topical calcipotriol and no hair loss relapse was observed over the next 6 months.

**Conclusion:** In our patients, a novel treatment option topical calcipotriol was successfully used in the management of AT, in the absence of significant adverse side effects. We recommend that further controlled studies be required to establish safety, confirm efficacy, and disease remission protocol. To our knowledge, this is the first published case series of successful treatment for AT with single topical calcipotriol although the sample size was small.

**Keyword:** Alopecia Areata, Alopecia Totalis, Topical Calcipotriol, Vitamin D receptor

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**INTRODUCTION**

Alopecia areata (AA) is a chronic and relapsing hair loss specific autoimmune disease that leads to non scarring hair loss.1,3 The deterioration in the quality of life caused by the disease and the temporal and financial burden of treatment are the major issues among patients with AA.2 The preferred treatments for AA include therapeutic agents, such as topical or intralesional corticosteroids, and contact immunotherapy.1,3 Other treatments, including systemic corticosteroids, anthralin, excimer laser, and novel therapeutics, such as Janus kinase inhibitors, have also been used. Despite the numerous treatment options, the overall prognosis of AA is not favorable, involving relapse and recalcitrant progression. Specifically, patients with severe subtypes, such as alopecia totalis (AT) and alopecia universalis (AU), which involve complete scalp hair loss, have a lower likelihood of hair regrowth than those with patchy alopecia (PA).3 Management of AT and AU can be challenging, and although multiple treatment modalities have been explored, no therapy is currently FDA-approved. Although certain treatments showed significant hair regrowth, no treatment was completely effective. A novel therapeutic option with the use of topical vitamin D analog (calcipotriol) in treatment of AA is emerging. The effectiveness of calcipotriol in the treatment of AA is controversial, but its limited adverse effects need to be considered.4,6,10 Vitamin D (Vit.D) plays an important role in calcium homeostasis, immune regulation, and cell growth and differentiation.6,10 The active form of Vit.D mediates its action by binding to specific Vit.D receptors (VDR) located in the nuclei of target cells.10 The mechanism by which the topical calcipotriol induces hair growth in AA lesions is by regulating the differentiation of B cells, T cells, dendritic cells, and the expression of Toll-like receptors.5,11-13

**MATERIAL AND METHODS**

Three cases, treated topical calcipotriol cream 50 µg/g twice daily for 12 weeks and followed up regularly at 4 weeks intervals. After the end of the 12 weeks, all patient were followed up for 6 months. The efficacy was measured by SALT, hair regrowth using photographic assessment, Hair Pull Test and physical examination. All patients without associated skin diseases like atopic dermatitis, psoriasis, autoimmune diseases (lupus erythematosus, rheumatoid arthritis, scleroderma, and thyroid disorder), patients taking oral corticosteroids in previous 2 weeks, patients applying topical corticosteroid or patients who have received regular Vit.D supplementation in previous 6 months.

Table 1: Patient Details and Treatment Response of Topical Calcipotriol
### Table 2: Severity of Alopecia Tool Score (SALT) Before and After Treatment

<table>
<thead>
<tr>
<th>SALT</th>
<th>case 1</th>
<th>case 2</th>
<th>case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>100%</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>After treatment</td>
<td>0%</td>
<td>5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

### RESULTS

The clinical profile of patients and dramatic response is summarized in Table 1, and SALT score of disease in Table 2. The efficacy was measured by hair regrowth using photographic assessment in Figure 1.
Alopecia areata (AA) is an autoimmune disease directed at the hair follicle. Although usually limited to patchy hair loss over the scalp (focalis), AA can present as total loss of scalp hair (AT) or as total loss of both scalp and body hair (AU)\textsuperscript{13,15}. Although the exact pathogenesis of AA still unknown up to now, there is a widely accepted hypothesis that AA is related with autoreactivity of cytotoxic T cell. Therefore, intralesion corticosteroid is frequently used for AA to suppression immune response with ongoing disease progression\textsuperscript{1,3,6,8,9}. In our case 3, Oral corticosteroid and topical clobetasol could not be continued due to ongoing disease progression. In case 1 and 2 of this study showed no response with intralesion corticosteroid. The other hypothesis is associated with VDR. The keratinocytes lining the outer layer of the hair follicle possess VDR. This VDR plays important role in hair cycle, especially anagen initiation\textsuperscript{2,3,5,9}.

Although AA associated with reduced VDR expression reported a complete. A clinical remission after topical calcipotriol ointment 50 µg/mL applied once daily for 3 months\textsuperscript{6}, AA patients using topical 0.005% calcipotriol cream twice daily for 12 weeks had greater than 50% hair regrowth in 65% of patients, greater than 75% hair regrowth in 62.5% of patients, and complete regrowth in 27.1%\textsuperscript{7}. Twice daily topical 0.005% calcipotriol in 22 patients with patchy AA resulted in 59.1% of patients demonstrating hair growth within 4.21 ± 2.13 weeks.\textsuperscript{6} Berth et al, reported they failed to support its benefit in AT/AU\textsuperscript{14}. Studies using topical Vit.D in alopecia are inconsistent and limited by small sample size or lack of appropriate controls\textsuperscript{5,6}. Molinelli et al, found evidence to support the efficacy of the topical Vit.D analogue formulation for the treatment of limited AA, with a lower incidence of adverse events compared with the topical clobetasol\textsuperscript{14}.

In our case 3, Oral corticosteroid and topical clobetasol could not be continued due to ongoing disease progression. The most promising therapies with the highest quality data include diphenylcyclopropenone, squaric acid dibutylester, photodynamic therapy, steroids, and cyclosporine in combination with methylprednisolone. High-quality randomized-controlled trials with large sample sizes are lacking. Unified outcome guidelines are encouraged to facilitate the comparison of future studies\textsuperscript{14,15}. Orecchia et al, reported topical use of calcipotriol does not potentiate squaric acid dibutylester effectiveness in the treatment of alopecia areata but suggests that calcipotriol has an inhibiting action on cell multiplication\textsuperscript{16}. Therefore none of the treatments mentioned above has been ratified by the US FDA, indicating that a new and more effective therapeutic intervention aiming at new targets is needed\textsuperscript{10}. Preliminary results suggest a potential therapeutic benefit for topical Vit.D with minor side effects\textsuperscript{13,6,9}. It has been demonstrated that VDR are strongly expressed in the keratinocytes of human and murine hair follicles and that the lack of expression of VDR is associated with reduced hair follicle growth and epidermal differentiation. Studies of the scalps of AA patients have also shown reduced VDR expression in the hair follicles of affected area. Results from recent studies suggest that topical application of topical calcipotriol has a beneficial effect on patchy AA of the scalp\textsuperscript{10,12}. These explain why topical analog of Vit.D can be used to treat AA. In this study, serial case with AT in their scalp wth fully recovered after application of calcipotriol and we have evaluated the efficacy and safety profile of the topical calcipotriol. All our patients showed a response starting at 4 weeks, 8 weeks n 12 weeks, there was no recurrence after 6 months of therapy was stopped.

**DISCUSSION**

Alopecia areata (AA) is an autoimmune disease directed at the hair follicle. Although usually limited to patchy hair loss over the scalp (focalis), AA can present as total loss of scalp hair (AT) or as total loss of both scalp and body hair (AU)\textsuperscript{13,15}. A clinical remission after topical calcipotriol ointment 50 µg/mL applied once daily for 3 months\textsuperscript{6}, AA patients using topical 0.005% calcipotriol cream twice daily for 12 weeks had greater than 50% hair regrowth in 65% of patients, greater than 75% hair regrowth in 62.5% of patients, and complete regrowth in 27.1%\textsuperscript{7}. Twice daily topical 0.005% calcipotriol in 22 patients with patchy AA resulted in 59.1% of patients demonstrating hair growth within 4.21 ± 2.13 weeks.\textsuperscript{6} Berth et al, reported they failed to support its benefit in AT/AU\textsuperscript{14}. Studies using topical Vit.D in alopecia are inconsistent and limited by small sample size or lack of appropriate controls\textsuperscript{5,6}. Molinelli et al, found evidence to support the efficacy of the topical Vit.D analogue formulation for the treatment of limited AA, with a lower incidence of adverse events compared with the topical clobetasol\textsuperscript{14}.

In conclusion, although there are astounding therapeutic effects described in this report, further investigation about the role of the topical analog Vit.D in AT through large and well-designed clinical trials is needed to support the clinical application of single topical calcipotriol as a treatment option for this refractory disease.

**CONCLUSION**

In conclusion, although there are astounding therapeutic effects described in this report, further investigation about the role of the topical analog Vit.D in AT through large and well-designed clinical trials is needed to support the clinical application of single topical calcipotriol as a treatment option for this refractory disease.
Table 3: Summary of Clinical Investigations on Single Topical Calcipotriol in Treatments for Alopecia

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Number</th>
<th>Intervention</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orecchia et al, 1995</td>
<td>28 AA</td>
<td>sensitized with a 2% SADBE solution and a 0.001% SADBE solution was applied to the whole scalp. An ointment containing 50 μg/g calcipotriol was applied to the left side of the scalp</td>
<td>Double Blind</td>
<td>Topical use of calcipotriol does not potentiate squaric acid dibutylester effectiveness in the treatment of alopecia areata but suggests that calcipotriol has an inhibiting action on cell multiplication</td>
</tr>
<tr>
<td>Berth et al. 2009</td>
<td>20 AT/AU</td>
<td>calcipotriol ointment 50 μg/g applied b.i.d. for 6 months</td>
<td>Double-blind</td>
<td>No response</td>
</tr>
<tr>
<td>Kim et al. 2012</td>
<td>1 Patchy AA</td>
<td>calcipotriol topical solution 50 μg/mL applied daily for 3 months</td>
<td>Case report</td>
<td>Complete hair regrowth at 3 months No relapse at 9 months</td>
</tr>
<tr>
<td>Suswardana et al. 2014</td>
<td>1 Patchy AA</td>
<td>topical calcipotriol Cream 50 μg/g b.i.d. for 16 weeks</td>
<td>Case report</td>
<td>Complete hair regrowth at 3 months No relapse at 8 months</td>
</tr>
<tr>
<td>Cerman et al. 2015</td>
<td>48 AA</td>
<td>topical calcipotriol 0.005% b.i.d. for 12 weeks</td>
<td>Cohort study</td>
<td>Significantly lower SALT score at 12 weeks compared to baseline Hair regrowth greater than &gt;50% seen in 75% of patients, hair regrowth of &gt;75% seen in 62.5%, and complete regrowth in 27.1%</td>
</tr>
<tr>
<td>Narang et al. 2017</td>
<td>22 AA</td>
<td>topical calcipotriol 0.005% b.i.d. for 12 weeks</td>
<td>Cohort study</td>
<td>59.1% of patients had hair regrowth, with onset at 4.21 ± 2.13 weeks 9 patients with 0% change, 4 patients with 25% change, 3 patients with 25–50% change, 6 patients with &gt;50% change</td>
</tr>
</tbody>
</table>

DEARATION OF PATIENT CONSENT
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

REFERENCES
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