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Effect of Fexofenadine as an Adjunct to DPCP in Non-Atopic Patients with Alopecia Areata: A Randomized Clinical Trial

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Abstract

Introduction: In this study the effect of fexofenadine as an adjunct to diphenylcyclopropenone (DPCP) in non-atopic patients with Alopecia areata (AA) is investigated.

Patients and methods: Prospectively 100 patients with AA having hair loss of more than 25% of the scalp are randomly divided into two groups in group A patients received topical DPCP plus oral fexofenafine, in group B patients received only topical DPCP.

Results: Regrowth in group A was better than group B but this was not statistically significant. Eczematous reaction and pruritus was significantly lower in group A than in group B.

Discussion: Fexofenadine seems to be of no benefit in patients without underlying contributing situation. Therefore, it can be added to conventional regimen in order to enhance the compliance of patients by reducing discomfort of DPCP treatment.

Keywords: Alopecia areata; Diphenylcyclopropenone; Fexofenafine

Introduction

Alopecia Areata (AA) is a relatively common dermatosis characterized by non-scarring hair loss. It may start at any age with an estimated lifetime risk of 1.7% among the general population [1]. A peribulbar activated T-lymphocytic infiltrate is the hallmark of AA [2]. γ-Interferon (IFN-γ) produced by these activated T cells induces the expression of major histocompatibility complex (MHC) class I and II, intercellular adhesion molecule-1 (ICAM-1) and human leukocyte antigen (HLA)-DR on the hair epithelium and dermal papilla in AA [3,4] causing the collapse of MHC class I-dependent immune privilege of the hair follicles [5]. Treatment modalities include topical, intralesional and systemic corticosteroids, topical irritants and PUVA [6-8]. At present, topical immunotherapy with DPCP is considered the most effective treatment of AA with success rates ranging from 4% to 85% [9,10].

Other than CD4+ Lymphocytes, degranulating mast cells are observed adjacent to affected hair follicles in AA [11] and histamine reportedly enhances the IFN-γ-induced expression of ICAM-1 and MHC class I on keratinocytes [12].

Fexofenadine, an H1 receptor antagonist decreases the production of IFN-γ from T lymphocytes [13], as well as the expression of ICAM-1 on epithelial cells, supporting its efficacy for AA [14]. From these findings, antihistamines are expected to be effective for AA treatment. Indeed, the efficacy of antihistamines for AA has been reported [15-19].

Recently, it has been reported that fexofenadine rapidly suppresses itch due to DPCP immunotherapy for AA, indicating that fexofenadine is an adequate concomitant drug [20]. Also it is found that fexofenadine is effective for AA of atopic background [19,21]. In this study which is a prospective randomized clinical trial we investigate the effect of fexofenadine as an adjunct to DPCP in non-atopic patients with AA.

Patients and Methods

We surveyed prospectively 100 patients with AA having hair loss of more than 25% of the scalp in Razi hospital from January 2009 to January 2011. We excluded patients with pregnancy, lactation, history of atopy, patients who had received systemic corticosteroid or any other medication within 3 months before starting point of evaluation or for AA; also we excluded patients with cardiovascular disease and blood dyscrasia; we randomly divided the patients into two groups (A and B), their age varied between 6 to 47 years. In group A there were 50 patients who received topical diphenylcyclopropenone (DPCP) plus oral fexofenafine, who took fexofenafine (120 mg/day for adults or 60 mg/day for children); in group B there were 50 patients who received only topical DPCP, in group A we lost 6 patients due to headache (1 patient), vitiligo (1 patient) and discontinue to follow up (4 patients), in group B we lost 4 patients, one patient due to severe eczematous reaction and 3 patients due to discontinue follow up (Figure 1).

In group A there were 22 (44%) male and 28 (56%) female; in group B there were 26 (52%) male and 24 (48%) female the mean age was 25 ± 9.2 in group A and 24 ± 8.7 in group B. The severity of AA was evaluated using the Severity of Alopecia Tool (SALT) score proposed in the guidelines of the National Alopecia Areata Foundation [22,23]; S_0: no hair loss; S_1: 1-25% hair loss; S_2: 26-50% hair loss; S_3: 51-75% hair loss; S_4: 76-99% hair loss; and S_5: total is and universalis type AA. In group A severity of AA was S_2 in 9 patients (18%), S_3 in 9 patients (18%), S_4 in 8 patients (16%), 7 patients (14%) had alopecia total is and 17 patients (34%) had alopecia universalis (Figure 1) ; In group B severity of AA was S2 in 7 patients (14%), S_3 in 7 patients (14%), S_4 in 11 patients (22%), 7 patients (14%) had alopecia total is and 18 patients (34%) had alopecia universalis; 6 patients (12%) in group A and 7 patients (14%)

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in group B had ophiasis. 7 patients (14%) in group A and 13 patients (26%) in group B had a family history of Alopecia areata in first degree relatives; 9 patients (18%) in group A and 8 patients (16%) in group B had a family history of Alopecia areata in 2nd and 3rd degree relatives. 24 patients (48%) in group A and 25 patients (50%) in group B had nail involvement. 14 patients (28%) in group A and 11 patients (22%) in group B had autoimmune thyroid diseases.

All patients were sentisized with 2% DPCP solution in an area of scalp measuring 4×4 cm, the patients were treated by weekly contact immunotherapy using diphenylcyclopropenone (DPCP) until a tolerable level of itch and erythema appeared, the concentration of DPCP was gradually increased as follows: 0.001%, 0.01%, 0.1%, 0.2%, 0.5%, 1% and 2%. The applications were first performed in half of scalp and once hair regrowth noticed the patient was constructed to apply the solution to the whole scalp. The patients were visited in weekly or biweekly periods and effects and complications were monitored. The terminal hair regrowth score was estimated as weak response: Terminal hair growth of 1-25%; moderate response: Terminal hair growth of 26-50%; good response: Terminal hair growth: 51-75% and Excellent response: Terminal hair growth: 76-100%. Mean follow up was 12.04 ± 3.33 months in group A and 10.98 ± 2.72 months in group B.

Results

Terminal hair regrowth totally occurred in 44 patients (49%). The terminal hair regrowth response in group A was weak in 3 patients (7%), moderate in 3 patients (7%), good in 9 patients (20%) and Excellent in 11 patients (25%). The terminal hair regrowth response in group B was weak in 2 patients (4%), moderate in 1 patient (2%), good in 6 patients (14%) and Excellent in 9 patients (20%) (Table 1).

Discussion

Response rates of topical immunotherapy with DPCP widely range from 4% to 85% in literature and this may be due to the difference in number of patients, type, duration and severity of AA as well as time of treatment and methods of evaluation [10,24-30].

In one retrospective study, adding fexofenadine to conventional DPCP immunotherapy to enhance the therapeutic effects did not significantly alter the regrowth scores in non-atopic AA, but did improve the DPCP effect because the final concentration of DPCP was significantly lower in the fexofenadine group than the control [19].

In our study, all patients with an obvious atopic diathesis were excluded to investigate the effects of fexofenadine in non-atopic individuals, regrowth in group A (DPCP with fexofenadine) was better than group B (DPCP without fexofenadine), but this was not statistically significant; also effective concentration of DPCP was lower in group A (DPCP with Fexofenadine) than in group B (DPCP without Fexofenadine) but this difference was not statistically significant either.

These results was in concordance with previous studies that found Fexofenadine effective for AA of atopic background [19,21]. Its effectiveness in patients with atopic background might be rather indirectly and due to the improvement of underlying dermatitis which serves as a condition making the Alopecia being resistant to therapies; therefore in patients with no underlying contributing situation Fexofenadine seems to be of no benefit.

Eczematous reaction and pruritus was significantly lower in group A (DPCP with fexofenadine) than in group B (DPCP without fexofenadine). This has been already shown in another study that Fexofenadine, an H1-receptor antagonist, rapidly inhibits the itch of contact dermatitis induced by diphenylcyclopropenone in the absence of topical corticosteroids, indicating that fexofenadine is an adequate concomitant drug at least for attenuating the pruritis complicating DPCP therapy [20].

Fexofenadine is not only an antihistamine drug with a reasonable safety profile but also easy to consume as a single daily dose with no marked sedation; therefore it can be added to conventional regimen in order to enhance the compliance of patients by reducing discomfort of DPCP treatment.

Figure 1: A 50 year old male patient with Alopecia universalis in group A (a and b); two months after treatment (c and d); 5 months after treatment (e and f).

GROWTH RATE GRADE	(group A)	(group B)	TOTAL
0	18 (39.1%)	28 (60.9%)	46 (51%)
1	3 (60%)	2 (40%)	5
2	3 (75%)	1 (25%)	4
3	9 (60%)	6	15
4	11 (55%)	9 (45%)	20

Regrowth in group A (25 patients=59%) was better than group B (18 patients=40%), but this was not statistically significant (*P* value=0.534). Eczematous reaction and pruritus was lower in group A (2 patients=4%) than in group B (18 patients=36%) which was statistically significant (*P* value=0.0001); the incidence of other complications such as posterior auricular lymphadenopathy and vitiligo was not statistically significant between two groups. Effective concentration of DPCP was higher in group B (0.28% ± 0.26) than in group A (0.17% ± 0.25) but this difference was not statistically significant (*P* value=0.1)

Table 1: Rate of regrowth in groups.

References

1. Safavi KH, Muller SA, Suman VJ, Moshell AN, Melton LJ 3rd (1995) Incidence of alopecia areata in Olmsted County, Minnesota, 1975 through 1989. Mayo Clin Proc 70: 628-633.
2. Whiting DA (2003) Histopathologic features of alopecia areata: a new look. Arch Dermatol 139: 1555-1559.
3. Gilhar A, Ullmann Y, Berkutzki T, Assy B, Kalish RS (1998) Autoimmune hair loss (alopecia areata) transferred by T lymphocytes to human scalp explants on SCID mice. J Clin Invest 101: 62-67.
4. Gilhar A, Etzioni A, Assy B, Eidelman S (1993) Response of grafts from patients with alopecia areata transplanted onto nude mice, to administration of interferon-γ. Clin Immunol Immunopathol 66: 120-126.
5. Ito T, Ito N, Bettermann A, Tokura Y, Takigawa M, et al. (2004) Collapse and restoration of MHC class-I-dependent immune privilege: exploiting the human hair follicle as a model. Am J Pathol 164: 623-634.
6. Agarwal A, Nath J, Barua K (2006) Twice weekly 5 mg betamethasone oral pulse therapy in the treatment of alopecia areata. J Eur Acad Dermatol Venereol 20: 1375-1376.
7. Tosti A, Iorizzo M, Botta GL, Milani M (2006) Efficacy and safety of a new clobetasol propionate 0.05% foam in alopecia areata: a randomized, double-blind placebo-controlled trial. J Eur Acad Dermatol Venereol 20: 1243–1247.
8. Ricciardi A, Ruberto A, Garcia-Hernandez MJ, Kotzalidis GD, Trevisi M, et al. (2006) Alopecia areata with comorbid depression: early resolution with combined paroxetine-triamcinolone treatment. J Eur Acad Dermatol Venereol 20: 1000-1001.
9. Cotelessa C, Peris K, Caracciolo E, Mordenti C, Chimenti S (2001) The use of topical diphenylcyclopropenone for the treatment of extensive alopecia areata. J Am Acad Dermatol 44: 73-76.
10. Happle R (2002) Diphencyprone for the treatment of alopecia areata: more data and new aspects. Arch Dermatol 138: 112-113.
11. Toyoda M, Makino T, Kagoura, Morohashi M (2001) Expression of neuropeptide-degrading enzymes in alopecia areata: an immunohistochemical study. Br J Dermatol 144: 46-54.
12. Giustizieri ML, Albanesi C, Fluhr J, Gisondi P, Norgauer J, et al. (2004) H1 histamine receptor mediates inflammatory responses in human keratinocytes. J Allergy Clin Immunol 114: 1176-1182.
13. Ashenager MS, Grgela T, Aragane Y, Kawada A (2007) Inhibition of cytokine-induced expression of T-cell cytokines by antihistamines. J Investig Allergol Clin Immunol 17: 20-26.
14. Paolieri F, Battifora M, Riccio AM, Bertolini C, Cutolo M, et al. (1998) Terfenadine and fexofenadine reduce in vitro ICAM-1 expression on human continuous cell lines. Ann Allergy Asthma Immunol 81: 601-607.
15. Ogawa H, Imai R, Nishiyama S (1994) The effect of an anti-allergic drug on the disease activity of alopecia areata. Skin Res 36: 60-68.
16. Ogawa H, Ueki R, Nishiyama S (1995) The effect of an anti-allergic drug (azelastine) on alopecia areata. Nishinihon J Dermatol 57: 1206-1211.
17. Yoshizawa Y, Kawana S (2005) Efficacy of ebastine in the treatment of Alopecia Areata. Jpn J Dermatol 115: 1473-1480.
18. Inui S, Nakajima T, Itami S (2007) Two cases of alopecia areata responsive to fexofenadine. J Dermatol 34: 852-854.
19. Inui S, Nakajima T, Toda N, Itami S (2009) Fexofenadine hydrochloride enhances the efficacy of contact immunotherapy for extensive alopecia areata: Retrospective analysis of 121 cases. J Dermatol 36: 323-327.
20. Asano K (2007) Inhibition by of fexofenadine hydrocloride on substance P production from dorsal root ganglion cells. Skin Allergy Frontier 5: 58-59.
21. Katagiri K, Arakawa S, Hatano Y, Fujiwara S (2006) Fexofenadine, an H1-receptor antagonist, partially but rapidly inhibits the itch of contact dermatitis induced by diphenylcyclopropenone in patients with alopecia areata. J Dermatol 33: 75-79.
22. Fiedler VC, Alaiti S (1996) Treatment of alopecia areata. Dermatol Clin 14: 733-737.
23. Olsen E, Hordinsky M, McDonald-Hull S, Price V, Roberts J, et al. (1999) Alopecia areata investigational assessment guidelines. National Alopecia Areata Foundation. J Am Acad Dermatol 40: 242-246.
24. Olsen EA, Hordinsky MK, Price VH, Price V, Roberts J, et al. (1999) Alopecia areata investigational assessment guidelines – Part II. National Alopecia Areata Foundation. J Am Acad Dermatol 51: 242-226.
25. McDonald Hull S, Norris JF (1988) Diphencyprone in the treatment of long-standing alopecia areata. Br J Dermatol 119: 367-374.
26. Wiseman MC, Shapiro J, MacDonald N, Lui H (2001) Predictive model for immunotherapy of alopecia areata with diphencyprone. Arch Dermatol 137*:* 1063-1068.
27. Firooz A, Bouzari N, Mojtahed F, H Pazoki-Toroudi2, M Nassiri-Kashani *et al*. (2005) Topical immunotherapy with diphencyprone in the treatment of extensive and or long lasting alopecia areata. J Eur Acad Dermatol Venereol 19**:** 393-394.
28. Galadari I, Rubaie S, Alkaabi J, Galadari H (2003) Diphenylcyclopropenone (diphencyprone, DPCP) in the treatment of chronic severe alopecia areata (AA). Eur Ann Allergy Clin Immunol 35: 397-401.
29. van der Steen PH, Happle R (1993) Topical immunotherapy of alopecia areata. Dermatol Clin 11: 619–622.
30. Hull SM, Pepall L, Cunliffe WJ (1991) Alopecia areata in children: response to treatment with diphencyprone. Br J Dermatol 125: 164-168.