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Efficacy of antihistamines in combination with topical corticosteroid and superficial cryotherapy for treatment of alopecia areata: A retrospective cohort study

To the Editor: Despite advancements in our understanding of the pathomechanism of alopecia areata (AA), optimal therapies and means to predict treatment responses remain elusive. Cases of AA with improvement after topical diphenylcyclopropenone (DPCP) immunotherapy and antihistamine treatment have been reported.[1] Hence, we investigated the role of adjuvant antihistamines in combination with a topical corticosteroid (TC) and superficial cryotherapy (SC) for AA.

We retrospectively analyzed patients with AA who visited our hospital from February 2012 to November 2018. At our hospital, we administer a treatment protocol consisting of TC and SC at 4- to 8-week intervals for patients with mild to moderate AA who are not candidates for topical DPCP immunotherapy and systemic corticosteroids. The patients included in the analysis were divided into 2 groups: those who were or were not treated with adjuvant antihistamines during the follow-up period. Notably, we did not consider whether the antihistamines were used intentionally for the treatment of AA or unintentionally for some other indication. The antihistamines included in the analysis were fexofenadine (180 mg/d for adults and 30 mg/d for pediatric patients) and ebastine (10 mg/d for adults). Demographic data and clinical progress were compared using the Kaplan-Meier method between both groups.

Twenty-four patients were treated with an adjuvant antihistamine—in combination with TC and SC—and 121 patients were not. There were no significant differences in sex, age, disease duration, type of episode, initial Severity of Alopecia Tool (SALT) score, history of atopy, or total follow-up period between groups (Table I). In the group treated with adjuvant antihistamines, the mean duration of antihistamine use within the AA treatment period was 6.29 months. A cumulative

Table I. Characteristics of patients treated with and without adjuvant antihistamines

Characteristics	TC + SC + AH	TC + SC	*P* value
Number of patients	24	121	
Age, y, mean ± SD	44.00 ± 13.74	39.31 ± 14.49	.147
Duration, mo, mean ± SD	8.71 ± 10.96	5.22 ± 10.80	.162
Sex, n (%)			.456
Male	9 (37.5)	50 (41.3)	
Female	15 (62.5)	71 (68.7)	
Type of current episode, n (%)			.315
First time	19 (79.2)	86 (71.7)	
Recurrent	5 (20.8)	34 (28.3)	
Initial SALT score, n (%)			.518
0-30	22 (91.7)	113 (93.4)	
31-50	2 (8.3)	8 (6.6)	
History of atopic diathesis,* n (%)			.399
Yes	3 (12.5)	21 (17.5)	
No	21 (87.5)	99 (82.5)	
Family history of AA, n (%)			.181
Yes	1 (4.2)	16 (13.3)	
No	23 (95.8)	104 (86.7)	
Total follow-up period, mo, mean ± SD	9.43 ± 8.03	7.28 ± 6.61	.229

AA, Alopecia areata; *AH*, antihistamine; *SALT*, Severity of Alopecia Tool; *SC*, superficial cryotherapy; *SD*, standard deviation; *TC*, topical corticosteroid.
*History of atopic diathesis included atopic dermatitis, asthma, allergic rhinitis, eosinophilic esophagitis, or anaphylactic reaction to food.

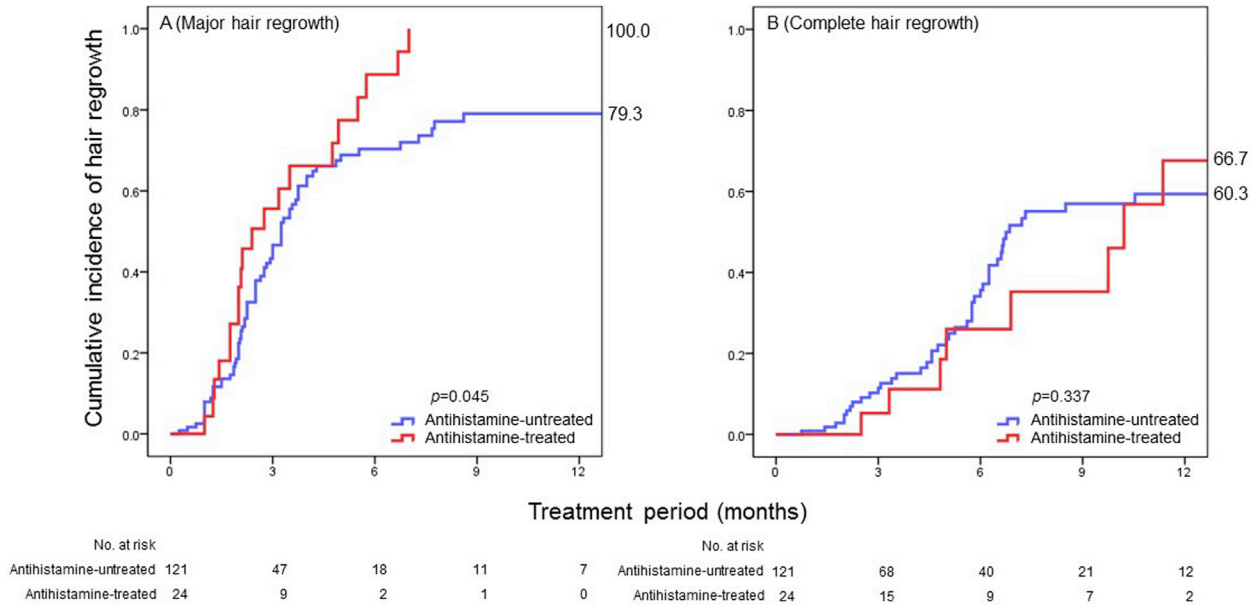

Fig 1. Cumulative incidence analysis of treatment response in patients with alopecia areata. There was a difference in the clinical prognosis of hair regrowth between the adjuvant antihistamine-treated and untreated groups. The survival analysis showed a significant difference between the 2 groups in major hair regrowth (major hair regrowth, 60% reduction in SALT score; complete hair regrowth, 90% reduction in SALT score). *SALT*, Severity of Alopecia Tool.

incidence analysis showed a significant difference in major hair regrowth (Fig 1). During the observation period, there were no instances of adverse effects that required discontinuation of antihistamines among patients treated with adjuvant antihistamines.

Given that the infiltration of mast cells and eosinophils around hair follicles is noted in AA and that a subset of AA shares some aspects of atopic dermatitis, the role of antihistamines can be suggested in the treatment of AA.[2] Aside from the ability of antihistamines to reduce the irritation caused by DPCP, several studies on fexofenadine and ebastine have shown decreased expression of serum cytokines or substance P and reduced T-cell infiltration around hair follicles histologically in experimental setting.[3] Notably, the role of antihistamine treatment—specifically, T helper (Th) type 17 or Th1/Th2 axis regulation—has been evaluated in various autoimmune diseases.[4,5] However, a well-designed comparative clinical trial is needed to determine if the efficacy of antihistamines in AA is derived from their ability to act as intrinsic histamine H1-receptor antagonists and also to demonstrate their efficacy as a monotherapy (Supplementary Table I available via Mendeley at https://doi.org/10.17632/fkfx7dmysy.1).

This study has several limitations that warrant consideration. First, this was a retrospective, single-center study with a relatively small cohort and deviation of sample size between both groups. Additionally, we did not determine the cumulative dose-dependent relationship between antihistamine use and disease prognosis. In conclusion, this study attempted to expand the role of antihistamines as an adjuvant treatment for patients with AA in combination with TC and SC.

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Trends in Medicare utilization and reimbursement for electronic brachytherapy following 2016 billing code changes

To the Editor: Electronic brachytherapy (EBT) has emerged in the last decade as a nonsurgical treatment option for nonmelanoma skin cancer. Prior studies documented a sharp increase in the use of EBT from 2012 to 2015.[1,2] Before 2016, EBT was billed under the 0182T Healthcare Common Procedure Coding System (HCPCS) billing code, regardless of anatomic location. However, in 2016, the Centers for Medicare & Medicaid Services replaced the 0182T code with 2 new billing codes: 0394T (skin sites) and 0395T (nonskin sites). The aim of this study is to characterize trends in use of and Medicare expenditure on EBT after replacement of the 0182T code.

The Medicare Physician and Other Supplier Public Use File (POSPUF) provides reimbursement and use data on all services and procedures provided to Medicare fee-for-service beneficiaries.[3] Using the Medicare POSPUF, we aggregated the volume of services, average Medicare reimbursement, and the number of providers for the HCPCS billing codes 0182T, 0394T, and 0395T from 2012 to 2017. For each billing code, we estimated total Medicare expenditure by multiplying the average reimbursement by the volume of services. We restricted our analysis to physician office claims, because physician offices accounted for more than 99% of EBT claims.[1]

The volume of EBT administrations increased 978%, from 4611 in 2012 to 49,684 in 2015. During this time period, average Medicare reimbursement was $1,673.58 per administration in 2012 and $1,380.73 in 2015. From 2012 to 2015, total annual Medicare expenditure on EBT increased 807%, from $9,648,655 to $87,590,904, with a peak of $121,579,588 in 2014. Over this time period, the number of providers filing claims for EBT increased 872%, from 25 to 243 (Table I).

After the HCPCS billing code 0182T was replaced by 0394T (skin) and 0395T (nonskin) in 2016, the average Medicare reimbursement for EBT administration on skin sites decreased 90%, to $132.96. Concurrently, the overall volume of EBT administrations (volume of 0394T plus volume of 0395T) decreased 48%, from 49,684 in 2015 to 25,866 in 2016. In 2016, 25,811 of 25,866 (99.7%) total EBT administrations were administered on skin sites, and in 2017, 36,111 of 36,169 (99.8%) were on skin sites. As a result, total annual Medicare expenditure on EBT (expenditure on 0394T plus expenditure on 0395T) decreased 95%, from $87,590,904 in 2015 to $4,415,809 in 2016 (Fig 1).

Our study is the first to show more than $80 million in Medicare cost savings after the 90% decline in physician reimbursement rate associated with replacement of the 0182T EBT billing code. The American Society of Radiation Oncology and American Brachytherapy Society recently cautioned against the use of EBT, citing uncertainty over efficacy and safety.[4,5] Therefore, our results suggest that the steep reduction of EBT use in 2016 may have

Table I. Electronic brachytherapy services and expenditures, 2012-2017

Year	HCPCS code	Number of services	Number of providers	Average Medicare payment amount	Total Medicare expenditure
2012	0182T	4611	25	$1673.58	$9,648,655.83
2013	0182T	24,126	91	$1473.49	$45,266,407.50
2014	0182T	66,577	193	$1430.10	$121,579,588.55
2015	0182T	49,684	243	$1380.73	$87,590,904.64
2016	0394T (skin)	25,811	106	$132.96	$4,385,030.79
2016	0395T (nonskin)	55	12	$432.59	$30,778.55
2017	0394T (skin)	36,111	121	$127.55	$5,945,315.04
2017	0395T (nonskin)	58	10	$431.15	$32,196.96

HCPCS, Healthcare Common Procedure Coding System.