

Impact of Sedative and Non-Sedative Antihistamines on the Impaired Productivity and Quality of Life in Patients with Pruritic Skin Diseases

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ABSTRACT

Background: The impairment that pruritic skin diseases have on patient productivity at work, in the classroom, and in daily activities is substantial and needs to be characterized. The objective of this study was to determine how pruritic skin diseases impact patient productivity and quality of life (QOL), in order to improve the measurement of these endpoints to allow the influence of treatment options including sedative and non-sedative antihistamines to be analyzed.

Methods: The impact of pruritic skin diseases and the effect of antihistamine therapy on work, classroom, and daily productivity were evaluated using the Work Productivity Assessment Index-Allergy Specific Questionnaire. The intensity of itch and patient QOL were assessed using a visual analogue scale and Skindex-16, respectively.

Results: Pruritic skin diseases resulted in significant impairment of work, classroom, and daily productivity. The severity of overall work impairment in atopic dermatitis (AD), urticaria, and prurigo was higher than for other diseases analyzed. However, classroom activity was more adversely affected in patients with urticaria relative to other diseases. All pruritic diseases in this study negatively impacted daily activity to a similar degree. Impaired productivity was significantly improved in patients taking non-sedative antihistamines for 1 month, and the improvements correlated with the alleviation of itch and improved QOL.

Conclusions: These results indicate that pruritic skin diseases reduce patient productivity at work, in the classroom, and during daily activities, and that non-sedative antihistamines may offer an advantage over sedative antihistamines for alleviating certain negative consequences of these skin diseases.

KEY WORDS

antihistamine, productivity, pruritic, quality-of-life, skin diseases, WPAI-AS

INTRODUCTION

The impaired quality of life (QOL) and diminished work and classroom productivity of individuals with pruritic skin diseases is a matter of public concern.^{1,2} Furthermore, estimates of the impact of pruritic skin diseases on the economic loss in businesses and school performance records have attracted a great deal of interest worldwide.^{3,4} Similar unfavorable impacts were identified for certain skin diseases, such

as chronic idiopathic urticaria, psoriasis, and chronic hand dermatitis.⁵⁻⁸ The Work Productivity Assessment Index (WPAI) is commonly used to determine the impact of health and disease on certain parameters related to patient productivity. According to the WPAI, the estimated percent of overall work impairment due to psoriasis, urticaria, and chronic hand dermatitis is 15%, 25%, and 29%, respectively.^{5,6,8}

Itching is a key characteristic of allergic skin diseases that dramatically affects a patient's quality of

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life.^{9,10} Thus, it is possible that itching alone would affect patient performance in the work place. The allergy specific WPAI (WPAI-AS) can be used to more effectively assess productivity in these patients as itching is a common symptom of allergy-related skin diseases. Recently, we reported the effect of antihistamines on productivity of patients with pruritic skin diseases using the WPAI-AS assessment questionnaire.^{11,12} On average, pruritic skin diseases impaired overall workplace productivity, classroom productivity, and daily activity by 39%, 45%, and 42% at baseline, respectively.¹² Furthermore, non-sedative antihistamines (mainly fexofenadine) reduced the intensity of itch and improved work productivity. In contrast, sedative antihistamines failed to improve work productivity, but significantly decreased itch intensity.¹² However, the relative impact of different pruritic diseases on work productivity has not been assessed. In this report, the WPAI-AS evaluation system was applied to each subgroup of patients with different diagnoses of pruritic skin diseases, and the degree of impairment for each disease at baseline was compared using a linear least-squares method. Furthermore, itch severity and patient QOL were assessed using a visual analogue scale (VAS) and Skindex-16, respectively. Finally, after validating the relationships between these parameters, we propose a method to approach the treatment of pruritic skin disease that will improve overall productivity in the workplace, in the classroom, and in daily activities.

METHODS

PATIENTS AND STUDY DESIGN

This study was conducted between April, 2008 and March, 2009. After obtaining approval from the Institutional Review Board (IRB), patients with pruritic skin diseases ($n = 216$) from Osaka University Hospital or its affiliated hospitals, gave informed consent to participate in this study. The final number of valid responses was $n = 206$ (male : female = 93 : 113; mean age $\pm$ SD: 52 ± 20 years). Patients with skin diseases associated with underlying systemic diseases (e.g., serious liver disease, renal dysfunction, and blood diseases), history of epilepsy, history of a previous drug allergy, or women who were pregnant or lactating were excluded from this study. Participants received no medical attention during the week before study initiation. The selection of therapy for each patient, such as oral antihistamines versus external medicine (e.g., steroid ointments, tacrolimus ointments, or certain moisturizers), was left to the physician's discretion (open-label trial). Fexofenadine ($n = 72$) and loratadine ($n = 2$), anti-histamines for which the package insert contained no cautionary statement regarding sedative actions, were categorized as "non-sedative". All other antihistamines were classified as "sedative".

STUDY INSTRUMENTS

The Skindex-16 quality-of-life instrument¹³ was used to measure the effect of pruritic skin diseases on QOL. The magnitude of the itch sensation was assessed using a VAS (0-100, "0" indicates no-symptom, and "100" indicates most severe symptom). Work and classroom productivity were assessed with the WPAI-AS instrument (score range, 0-100%; higher percentages indicate higher productivity).¹¹ Work productivity, classroom productivity, and daily activity impairment (%I) were calculated by the effects of the pruritic skin diseases on productivity while working/attending class or other daily activities during the past 7 days. The percentage of work/classroom time missed (%TM = TM/TW) was calculated by the number of work/classroom hours missed due to allergy (TM) and the usual number of hours worked/attending class (TW). Finally, the percentage overall impairment was calculated as follows: $\%TM + ([100 - \%TM] \times \%I) = \% \text{ overall impairment}$.¹¹ These instruments were patient-administered before (baseline) and 1 month after treatment initiation.

STATISTICAL ANALYSIS

The one-sample *t*-test was used for analysis of differences between two groups. Pearson's product-moment correlation coefficient was used to determine the significance of correlations between two parameters (Table 1, 2). To examine the significance of the contingency between the certain categorical data, Fisher's exact test (for evaluating the significance between the two kinds of classifications) and Cochran-Mantel-Haenszel general association statistics (for evaluating more than 3 kinds of classifications) were performed (Table 3). The bias of evaluative consequences to one variable was analyzed using univariate analysis (Table 4). A linear least-squares method was used to evaluate the degree of impairment in each disease at baseline. Because heterogeneity of starting values was inevitable, the effect measures illustrated in Figure 1 were evaluated using linear models. The results and confidence intervals for the improvement variations were compared visually for each parameter using a forest plot. Improvement variations (change ratios) were calculated as follows: $\text{change ratio} = (\text{evaluated value 1 month after the initiation of treatment} - \text{baseline value}) / (\text{baseline value})$. In all tests, values of $P < 0.05$ were considered statistically significant.

RESULTS

STUDY POPULATION CHARACTERISTICS

A total of 216 patients with pruritic skin disease entered the study, and data from 206 patients (average age of 52 ± 20 years) who completed the study were used for analysis. Company employees and part-time workers represented 48% of the patients ($n = 99$), and retired seniors and unemployed individuals ac-

Table 1 Correlations between baseline parameters and patient outcomes

	Correlations to baseline patient parameters [P-value, Pearson's coefficient of correlation (r), n]		
	Itch VAS	Skindex-16 score	Activity impairment
Allergic pruritic skin diseases (AD and urticaria)			
Overall work productivity impairment	NS (<i>r</i> = 0.2443, <i>n</i> = 52)	<i>P</i> < 0.001 (<i>r</i> = 0.5674, <i>n</i> = 51)	<i>P</i> < 0.001 (<i>r</i> = 0.6712, <i>n</i> = 52)
Overall classroom productivity impairment	NS (<i>r</i> = 0.1948, <i>n</i> = 14)	NS (<i>r</i> = 0.0915, <i>n</i> = 13)	NS (<i>r</i> = 0.1833, <i>n</i> = 14)
Activity impairment	<i>P</i> = 0.006 (<i>r</i> = 0.2893, <i>n</i> = 89)	<i>P</i> < 0.001 (<i>r</i> = 0.7051, <i>n</i> = 84)	-
Non-allergic skin diseases (All other excluding AD and urticaria)			
Overall work productivity impairment	NS (<i>r</i> = 0.2904, <i>n</i> = 44)	<i>P</i> < 0.001 (<i>r</i> = 0.4813, <i>n</i> = 46)	<i>P</i> < 0.001 (<i>r</i> = 0.8584, <i>n</i> = 47)
Overall classroom productivity impairment	NS (<i>r</i> = 0.2604, <i>n</i> = 4)	NS (<i>r</i> = 0.7963, <i>n</i> = 4)	<i>P</i> = 0.0014 (<i>r</i> = 0.9986, <i>n</i> = 4)
Activity impairment	<i>P</i> < 0.001 (<i>r</i> = 0.3332, <i>n</i> = 107)	<i>P</i> < 0.001 (<i>r</i> = 0.5170, <i>n</i> = 109)	-

NS, not statistically significant; vs., versus.

Table 2 Correlative relationships between antihistamine treatment groups and the improvement ratio of itch VAS scores to Skindex-16, overall work productivity impairment, and activity impairment

	Correlations to baseline patient improvement ratios by treatment group [P-value, Pearson's coefficient of correlation (r), n]	
	Non-sedative AH	Sedative AH
Skindex-16 score vs. itch VAS	<i>P</i> < 0.001 (<i>r</i> = 0.5769, <i>n</i> = 69)	NS (<i>r</i> = 0.2360, <i>n</i> = 99)
Overall work productivity impairment vs. itch VAS	<i>P</i> = 0.0042 (<i>r</i> = 0.4539, <i>n</i> = 38)	NS (<i>r</i> = 0.2462, <i>n</i> = 46)
Activity impairment vs. itch VAS	<i>P</i> = 0.0046 (<i>r</i> = 0.3448, <i>n</i> = 66)	NS (<i>r</i> = 0.1203, <i>n</i> = 92)

NS, not statistically significant; AH, anti-histamines; VAS, visual analogue scale.

counted for 43% (*n* = 89). Students made up a relatively small fraction of the study group (*n* = 18, 9%). Patients diagnosed with eczema/dermatitis had the highest representation (36%) among participants, followed in decreasing order by patients with urticaria, atopic dermatitis (AD), pruritus, prurigo, and psoriasis (Table 5).

ASSESSMENT OF WORK, CLASSROOM, AND ACTIVITY IMPAIRMENT

Table 6 shows the baseline work, classroom, and daily activity WPAI-AS productivity scores. Due to the relatively small sample size of each disease group, statistically significant differences in impairment between disease groups were not detected (Fig. 2). However, the results indicate that the overall impairment of work, classroom, and daily activity productivity tended to be larger in the atopic dermatitis, eczema/dermatitis, and urticaria disease groups (Fig. 2). There were also some interesting group-specific observations. Prurigo showed higher overall impairment of work productivity and daily activity. Individuals with urticaria had relatively higher percentages of

impairment of overall classroom productivity than that observed in other skin diseases. Daily activity was impaired at high percentages for individuals with AD.

CORRELATION BETWEEN PRODUCTIVITY IMPAIRMENT AND SKINDEX-16, OR LOSS OF DAILY LIFE PRODUCTIVITY

To check the validity of the assessment procedures in this study, we looked for correlations between impaired productivity at work, in the classroom, and in daily activities. In addition, correlations between overall activity impairment, the magnitude of itch sensation as assessed by VAS, and QOL measures as assessed by Skindex-16 were analyzed (Table 1). As shown in Table 1, correlation analyses were divided between allergic (atopic dermatitis and urticaria) and non-allergic skin diseases (all other diagnosis groups). Results specific for allergic skin diseases indicated that impairment in overall work productivity showed a positive correlation with the itch VAS, Skindex-16, and the impairment in daily activity. A correlation between impairment in overall classroom

Table 3 Distribution of patient characteristics in the sedative and non-sedative antihistamine treatment groups

Background factors		Non-sedative AH		Sedative AH		P-value [†]
		<i>n</i>	%	<i>n</i>	%	
Age	<50	42	56.8	55	45.8	0.183
	≥50	32	43.2	65	54.2	
Gender	Male	37	50.0	48	40.0	0.183
	Female	37	50.0	72	60.0	
Disease	AD	20	27.0	22	18.3	0.515
	Ec/der	26	35.1	45	37.5	
	Urticaria	16	21.6	33	27.5	
	Other	12	16.2	20	16.7	
Occupation	Worker	45	60.8	51	42.5	0.017
	Student	8	10.8	10	8.3	
	Other	21	28.4	59	49.2	
Duration of disease	<5 years	46	62.2	74	61.7	1.000
	≥5 years	21	28.4	34	28.3	

[†]Differences in the distribution of patients between sedative and non-sedative antihistamine groups was determined by the Fisher's exact test for age, gender, and duration of disease and by the Cochran-Mantel-Haenszel general association statistic for disease diagnostic group and occupation. AH, antihistamines; AD, atopic dermatitis; Ec/der, eczema/dermatitis.

Table 4 Impact of background factors on the improvement of WPAI-AS score

Patient characteristics	Impact of patient characteristics on overall productivity impairment (P-value)		
	Overall work impairment	Overall classroom impairment	Daily activity impairment
Age	0.345	0.2986	0.3556
Gender	0.4454	0.5464	0.2615
Disease	0.0646	0.5349	0.4118
Duration of disease: <5 years, ≥5 years	0.0053	0.4793	0.2528
Occupation: worker, student, other	N/A	N/A	0.5097

N/A, not applicable.

productivity and itch VAS, Skindex-16 score, and activity impairment was not observed for the allergic skin diseases (Table 1). However, in the allergic skin disease subgroup there was a positive correlation between the impairment in daily activity and the magnitude of itch and Skindex-16 scores.

Similar analyses were performed on the subgroup of patients with all other skin disease diagnoses except atopic dermatitis and urticaria. This group was designated the non-allergic skin disease group even though varying causative conditions including allergic and non-allergic mechanisms could be responsible for symptoms related to eczema/dermatitis. As shown in Table 1, the correlation profile of this subgroup was very similar to that of the allergic skin disease subgroup with one major difference. There was a significant correlation between overall classroom productivity and activity impairment in the non-allergic skin disease subgroup (Table 1).

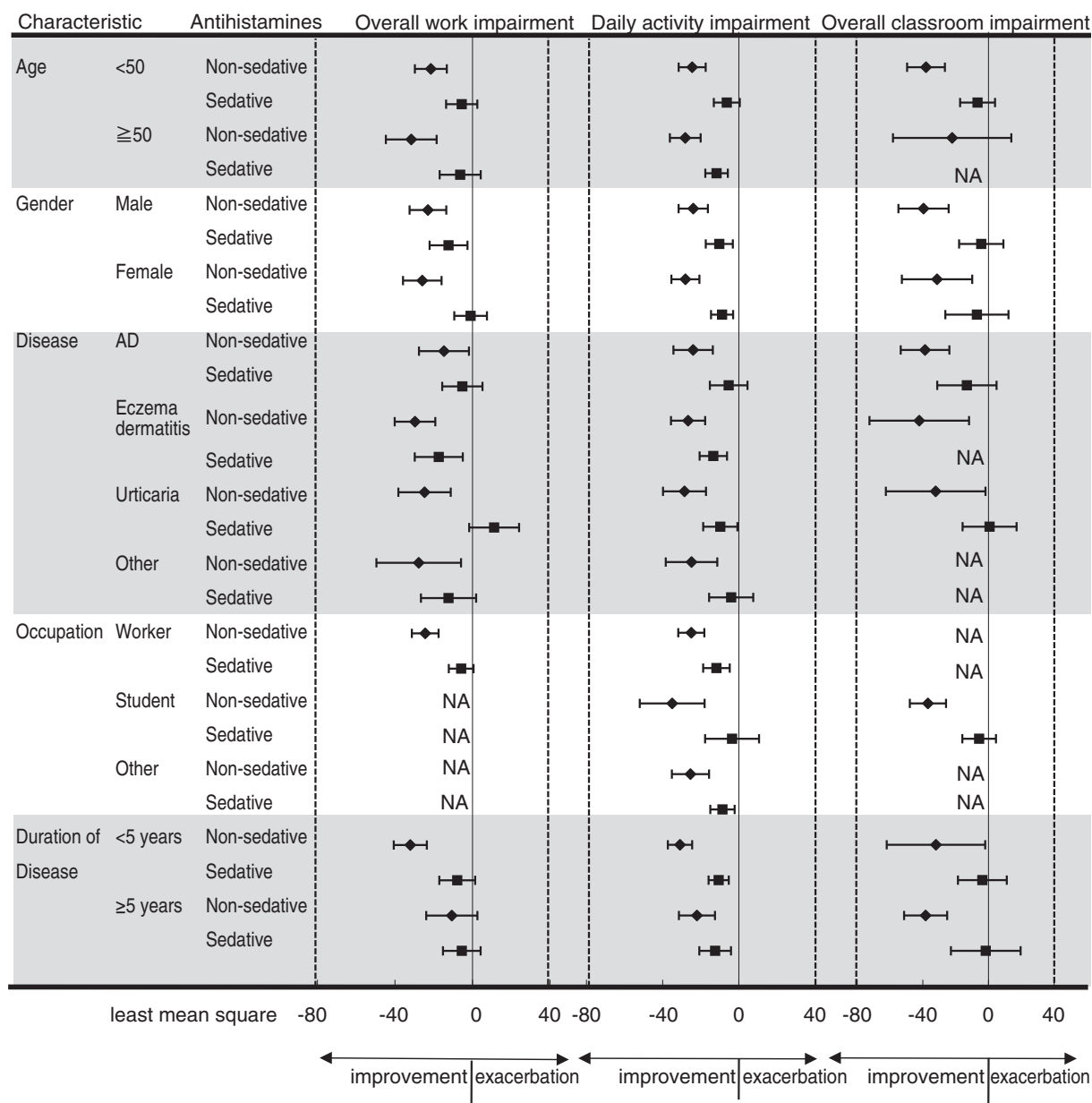
IMPACT OF ANTIHISTAMINES ON PATIENT OUTCOMES

Patients were treated with non-sedative antihistamines (*n* = 74), sedative antihistamines (*n* = 121), or

external medication (*n* = 11) for a duration of 1 month (Table 7). The patient characteristics in the physician-assigned treatment groups of sedative and non-sedative antihistamines were all well-matched with the exception of occupation (Table 3). We previously reported that the impaired productivity in pruritic skin diseases was significantly improved in patients taking non-sedative antihistamines.¹² Interestingly, for patients taking non-sedative antihistamines in this study, the improvement ratio as assessed using the VAS score showed a significant correlation with improvements in the Skindex-16 score, the reduction in overall work productivity impairment, and the reduction in daily activity impairment. No significant correlations were found among patients taking sedative antihistamines (Table 2).

To eliminate the bias for starting value dispersion, the effects of non-sedative and sedative antihistamines on overall work productivity, daily activity, and overall classroom productivity were corrected by grouping according to background factors or baseline value using the linear least-squares methods (Fig. 1A). Results indicated that non-sedative antihistamines produced greater overall improvements in pro-

A



B

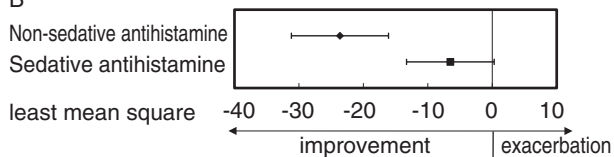


Fig. 1 A. The impact of antihistamines on overall work productivity impairment, activity productivity impairment, and overall classroom productivity impairment per-certain parameters of pruritic skin diseases. Changes in the evaluated value of certain parameters from baseline were adjusted with background factors and the initial value (a linear model). Results are shown in a forest plot. Horizontal lines indicate 95% confidence intervals. The rhomboid or square dot on center of the horizontal line indicates the point estimate. Significance is indicated by horizontal lines that do not overlap with the vertical line of least mean square = 0. NA, not applicable. **B.** Comparison of overall work impairment (amount of change) adjusted by background factor (disease duration).

Table 5 Characteristics of patient population by pruritic skin disease diagnostic group

Disease	(n)	Male	Female	Average age (yrs ± SD)	Average duration of disease (yrs ± SD)
Atopic dermatitis	43	21	22	33.7 ± 10.1	17.1 ± 13.2
Eczema/dermatitis	75	33	42	61.9 ± 17.8	3.1 ± 8.1
Urticaria	50	17	33	47.3 ± 16.3	5.4 ± 10.1
Pruritus	14	9	5	64.3 ± 18.1	3.4 ± 3.6
Prurigo	8	6	2	59.8 ± 16.6	2.1 ± 1.5
Psoriasis	7	4	3	49.3 ± 19.6	1.1 ± 1.4
Others [†]	9	3	6	54.7 ± 18.2	10.8 ± 14.9

[†]Includes patients with systemic lupus erythematoses, tinea pedis, toxicoderma, polymorphic light eruption, von Recklinghausen disease, tuberous sclerosis, scabies, bullous pemphigoid, and lupus erythematoses.

Table 6 Baseline WPAI-AS productivity scores (Mean ± SD)

	AD	Ec/Der	Urticaria	Pruritus	Prurigo	Psoriasis	Others
	(n = 31)	(n = 31)	(n = 21)	(n = 2)	(n = 5)	(n = 3)	(n = 6)
Work							
Work productivity impairment	38.7 ± 26.3	41.0 ± 24.8	33.8 ± 25.8	20.0 ± 0	36.0 ± 18.2	26.7 ± 25.2	23.3 ± 29.4
Work time missed	4.9 ± 11.4	2.6 ± 10.3	10.6 ± 26.8	0	12.2 ± 21.7	2.2 ± 3.8	0
Overall work productivity impairment	40.4 ± 26.8	41.3 ± 25.2	41.8 ± 29.5	20.0 ± 0	42.9 ± 24.8	28.9 ± 21.7	23.3 ± 29.4
Classroom	(n = 8)	(n = 1)	(n = 6)	(n = 1)	(n = 0)	(n = 1)	(n = 1)
Classroom productivity impairment	41.3 ± 25.3	50.0	63.3 ± 15.1	0	-	0	10
Classroom time missed	0	0	14.5 ± 17.8	0	-	0	0
Overall classroom productivity	41.3 ± 25.3	50.0	70.1 ± 10.5	0	-	0	10
Activity	(n = 43)	(n = 72)	(n = 46)	(n = 14)	(n = 8)	(n = 7)	(n = 9)
Activity impairment	50.2 ± 26.9	41.8 ± 23.0	37.6 ± 26.4	37.9 ± 20.1	46.3 ± 22.0	44.3 ± 28.8	34.4 ± 29.2

AD, atopic dermatitis; Ec/Der, Eczema/Dermatitis; SD, Standard deviation.

ductivity in patients with skin diseases than sedative antihistamines (Fig. 1A). Non-sedative antihistamines significantly improved work productivity under almost all background conditions with the exception of disease duration. Sedative antihistamines only had a significant impact on the subpopulation of patients that were male or those that had a diagnosis of eczema/dermatitis (Fig. 1A).

The duration of disease was the only baseline patient characteristic that could significantly influence or bias the outcomes seen from administration of antihistamines (Table 4). Therefore, we compared the amount of change in the overall work impairment in the sedative and non-sedative antihistamine treatment groups after adjusting for the baseline duration of disease (Fig. 1B). These results confirmed that non-sedative antihistamines significantly improved the overall work impairment, while sedative antihistamines did not (Fig. 1B). Evaluation of impact of antihistamines on daily activity impairment and overall classroom impairment also demonstrate the superiority of non-sedative antihistamines over sedative antihistamines (Fig. 1A). Interestingly, sedative antihistamines failed to improve overall classroom productivity in all the patient population groups analyzed (Fig. 1A).

THE EFFECT OF ANTIHISTAMINES ON ATOPIC DERMATITIS

The effect of antihistamines on atopic dermatitis is still controversial.^{14,15} Therefore, the treatment effects specifically for patients with atopic dermatitis (*n* = 43) were analyzed independently from other diagnostic groups (Fig. 3). As expected, treatment with antihistamines significantly reduced itch intensity in atopic dermatitis, while external medicines were ineffective (Fig. 3A). No differences were found between patients taking non-sedative versus sedative antihistamines (Fig. 3A). The impact of all treatments on the Skindex-16 QOL measure was similar to that for the itch VAS, with a significant effect for all antihistamines, but not for topical medications (Fig. 3B). Both non-sedative, and sedative antihistamines improved overall work impairment without statistical significance (Fig. 3C). Alternatively, the non-sedative antihistamine significantly reduced activity productivity impairment, whereas the trend towards improvement seen with sedative antihistamines did not reach statistical significance (Fig. 3D). These patients were prescribed concomitant external medications, but there were no remarkable differences between the non-sedative and sedative antihistamines treatment groups (Fig. 3E).

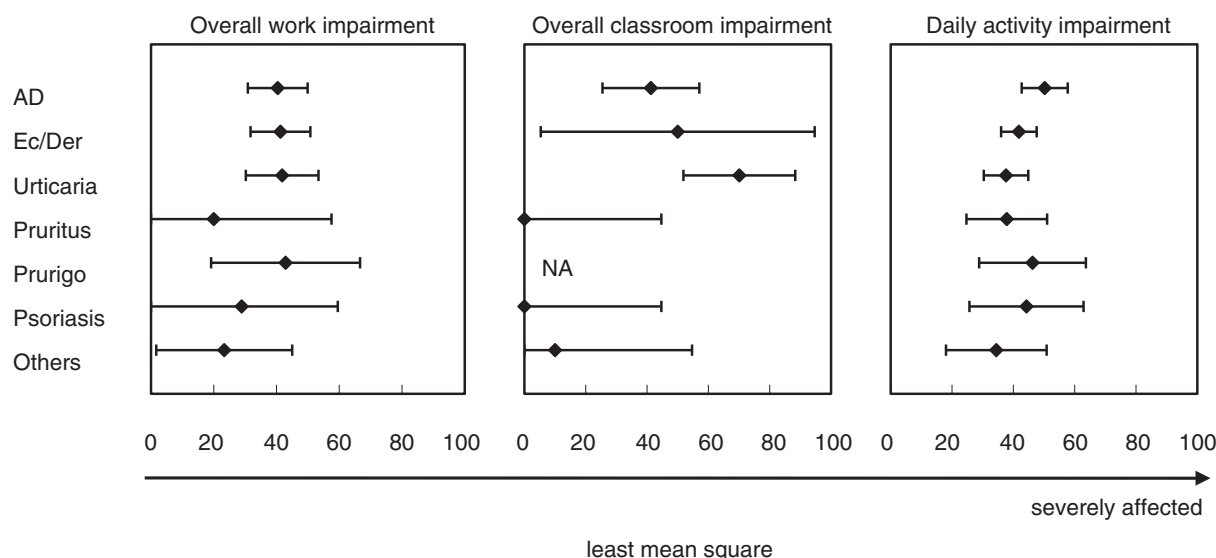


Fig. 2 Forest plots demonstrating the degree of impairment in each disease at baseline was evaluated using a linear least-squares method. Horizontal lines represent 95% confidence intervals. The rhomboid dot on the center of horizontal line indicates the point estimate. NA, not applicable.

Table 7 Number of patients from each skin disease diagnostic group assigned to indicated treatments

	Sedation	<i>n</i>	AD	Ec/Der	Urticaria	Pruritus	Prurigo	Psoriasis	Others
Fexofenadine	NS	72	20	26	14	5	1	1	5
Loratadine	NS	2	0	0	2	0	0	0	0
Olopatadine	S	53	8	18	18	2	3	3	1
Epinephrine	S	8	3	3	0	0	0	2	0
Cetirizine	S	9	2	6	0	0	1	0	0
Ebastine	S	11	1	7	1	1	0	0	1
Other 2 nd generation	S	19	5	5	7	1	0	0	1
1 st generation	S	21	3	6	7	2	2	1	0
External medicine	-	11	1	4	1	3	1	0	1
Total	-	206	43	75	50	14	8	7	9

AH, anti-histamines; NS, non-sedative; S, sedative; AD, atopic dermatitis; Ec/Der, Eczema/Dermatitis.

DISCUSSION

This study demonstrates that allergic skin diseases may have detrimental effects on productivity at work, in the classroom, and during daily activity. Previous reports demonstrated that allergic rhinitis impaired mean overall productivity at work, in the classroom, and in daily activity by ratios of 27-48%, 33-47%, and 42-51%, respectively.¹⁶⁻¹⁹ In the present study, work performance and daily activities were highly and similarly impaired in patients with allergic skin diseases. However, WPAI-AS baseline scores in our study were slightly high relative to previous reports of WPAI (unidentified version) baseline scores for chronic idiopathic urticaria, psoriasis, and chronic hand dermatitis.^{5,6,8} It is not currently clear why the present study generated different WPAI baseline scores, but further investigation is warranted.

According to the WPAI-AS values for the various pruritic skin diseases, the impairments in classroom productivity and overall classroom productivity were higher for patients with urticaria (Fig. 2). To clarify the reason why urticaria affected classroom productivity, cases of students with urticaria were analyzed independently for correlations with certain parameters (data not shown). Only the Skindex-16 was significantly associated with classroom impairment in this group ($P = 0.0075$, $r = 0.9282$, $n = 6$). Presumably, urticaria may impair a student's classroom productivity by negatively impacting their QOL.

In previous reports, WAPI scores of overall work impairment in patients with psoriasis were lower than those for patients with chronic idiopathic urticaria and chronic hand dermatitis.^{5,6,8} Pearce and colleagues⁶ discussed the observation that QOL measures did not exhibit the same trend as WPAI score in

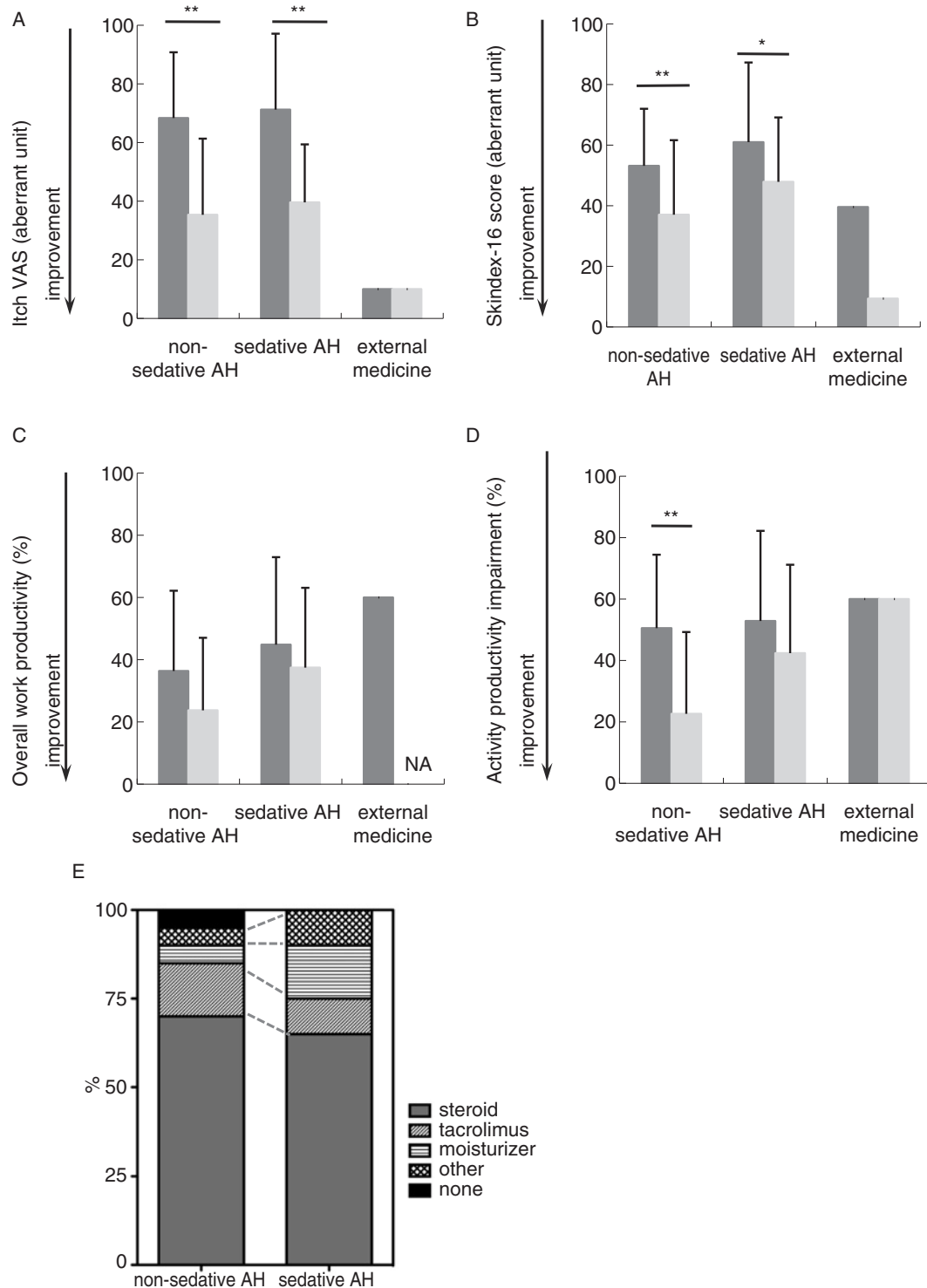


Fig. 3 The impact of antihistamines on (A) itch VAS, (B) skindex-16 score, (C) overall work productivity impairment, and (D) daily activity productivity impairment in atopic dermatitis. The data of baseline assessment (dark gray bar) and post treatment assessment (light gray bar) are shown as mean $\pm$ SD. **Statistically significant improvement compared with the data of baseline assessment ($P < 0.001$), * $P < 0.01$. NA, not applicable; AH, antihistamines. (E) Concomitant external medicine for cases with atopic dermatitis. "Other" includes vitamin D3 or non-steroidal anti-inflammatory ointment.

patients with psoriasis, and indicated that estimating the impact of psoriasis on social life seemed to be difficult. Indeed, as the number of patients with psoriasis was low in this study, which may indicate that our data are not representative of the general population of patients with psoriasis.

Concerning WPAI-AS scores in patients with atopic dermatitis, the total loss of daily activities was relatively higher than for patients with other skin diseases (Table 6, Fig. 2). It has been said that the intensity of itch might be increased in a relaxed environment, such as coming home or at nighttime.²⁰ In support of this, daily activity in patients with atopic dermatitis or pruritus was severely impaired compared with the impairment in overall work productivity (Table 6). Thus, daily activity may be highly susceptible to impairment in patients with atopic dermatitis and pruritus.

The differences between patients taking non-sedative versus sedative antihistamines was also addressed. As previously reported, sedative antihistamines failed to reduce work productivity impairment despite decreasing itch VAS values and Skindex-16 measures.¹² Impaired performance as an adverse effect of sedative antihistamines may be a major factor in these divergent results. In fact, in patients treated with sedative antihistamines, the improvement ratio for itch VAS scores did not significantly correlate with either the Skindex-16 QOL measure, the reduced impairment in overall work productivity, or the reduced impairment in daily activity (Table 2). Additionally, the extent of impairment in overall work productivity can be predicted by the Skindex-16 measures (Table 1). Nevertheless, clinicians should keep in mind that they could overestimate the effect of sedative antihistamines to improve on work productivity by relying solely on patient itch-intensity and QOL values. For these reasons, non-sedative antihistamines have substantial value in the treatment of patients with pruritic skin diseases.

However, the criteria for selecting antihistamines differ from disease to disease and vary worldwide. It is well known that non-sedative antihistamines, but not sedative antihistamines, are recommended as first-line agents for urticaria treatment.²¹⁻²⁵ In contrast, many previous published reviews, guidelines, and position papers on the care of atopic dermatitis state that the antihistamines are no more than a supportive management for pruritus, and their sedative properties offer an advantage for reducing the magnitude of itch in atopic dermatitis.^{14,15,26,27} Thus, there is a tendency worldwide to recommend sedative antihistamines for the treatment of atopic dermatitis with intense itch or sleep disturbance.^{14,15,26} Our data challenge this trend, since non-sedative antihistamines reduced the impairments in daily activity in patients with atopic dermatitis, while sedative antihistamines were ineffective (Fig. 1A, 3). Accordingly, the criteria

for selecting antihistamines in certain skin diseases should be reconsidered.

Limitations of this study include the number of patients in each group and the potential influences of the adverse global economic conditions. Nonetheless, this report may highlight a new goal in the treatment of pruritic skin diseases and provide a rationale for shifting the choice of treatment options to non-sedative antihistamines.

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REFERENCES

1. Carr WW, Nelson MR, Hadley JA. Managing rhinitis: Strategies for improved patient outcomes. *Allergy Asthma Proc* 2008;**29**:349-57.
2. Szeinbach SL, Seoane-Vazquez EC, Beyer A, Williams PB. The impact of allergic rhinitis on work productivity. *Prim Care Respir J* 2007;**16**:98-105.
3. Lamb CE, Ratner PH, Johnson CE *et al*. Economic impact of workplace productivity losses due to allergic rhinitis compared with select medical conditions in the United States from an employer perspective. *Curr Med Res Opin* 2006;**22**:1203-10.
4. Walker S, Khan-Wasti S, Fletcher M, Cullinan P, Harris J, Sheikh A. Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in United Kingdom teenagers: case-control study. *J Allergy Clin Immunol* 2007;**120**:381-7.
5. Thompson AK, Finn AF, Schoenwetter WF. Effect of 60 mg twice-daily fexofenadine HCl on quality of life, work and classroom productivity, and regular activity in patients with chronic idiopathic urticaria. *J Am Acad Dermatol* 2000;**43**:24-30.
6. Pearce DJ, Singh S, Balkrishnan R, Kulkarni A, Fleischer AB, Feldman SR. The negative impact of psoriasis on the workplace. *J Dermatolog Treat* 2006;**17**:24-8.
7. Reilly MC, Lavin PT, Kahler KH, Pariser DM. Validation of the Dermatology Life Quality Index and the Work Productivity and Activity Impairment-Chronic Hand Dermatitis questionnaire in chronic hand dermatitis. *J Am Acad Dermatol* 2003;**48**:128-30.
8. Fowler JF, Ghosh A, Sung J *et al*. Impact of chronic hand dermatitis on quality of life, work productivity, activity impairment, and medical costs. *J Am Acad Dermatol* 2006;**54**:448-57.
9. Amaty B, Wennersten G, Nordlind K. Patients' perspective of pruritus in chronic plaque psoriasis: a questionnaire-based study. *J Eur Acad Dermatol Venereol* 2008;**22**:822-6.
10. Holm EA, Wulf HC, Stegmann H, Jemec GB. Life quality assessment among patients with atopic eczema. *Br J Dermatol* 2006;**154**:719-25.
11. Reilly MC, Tanner A, Meltzer EO. Work, classroom and activity impairment instruments: validation studies in allergic rhinitis. *Clin Drug Invest* 1996;**11**:278-88.

12. Murota H, Kitaba S, Tani M, Wataya-Kaneda M, Katayama I. Effects of nonsedative antihistamines on productivity of patients with pruritic skin diseases. *Allergy* 2009; **65**:929-30.
13. Chren MM, Lasek RJ, Sahay AP, Sands LP. Measurement properties of Skindex-16: a brief quality-of-life measure for patients with skin diseases. *J Cutan Med Surg* 2001; **5**:105-10.
14. Akdis CA, Akdis M, Bieber T *et al*. Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL Consensus Report. *Allergy* 2006; **61**:969-87.
15. Hanifin JM, Cooper KD, Ho VC *et al*. Guidelines of care for atopic dermatitis, developed in accordance with the American Academy of Dermatology (AAD)/American Academy of Dermatology Association "Administrative Regulations for Evidence-Based Clinical Practice Guidelines". *J Am Acad Dermatol* 2004; **50**:391-404.
16. Meltzer EO, Casale TB, Nathan RA, Thompson AK. Once-daily fexofenadine HCl improves quality of life and reduces work and activity impairment in patients with seasonal allergic rhinitis. *Ann Allergy Asthma Immunol* 1999; **83**:311-7.
17. Fairchild CJ, Meltzer EO, Roland PS, Wells D, Drake M, Wall GM. Comprehensive report of the efficacy, safety, quality of life, and work impact of Olopatadine 0.6% and Olopatadine 0.4% treatment in patients with seasonal allergic rhinitis. *Allergy Asthma Proc* 2007; **28**:716-23.
18. Kim LS, Riedlinger JE, Baldwin CM *et al*. Treatment of seasonal allergic rhinitis using homeopathic preparation of common allergens in the southwest region of the US: a randomized, controlled clinical trial. *Ann Pharmacother* 2005; **39**:617-24.
19. Okubo K, Gotoh M, Shimada K, Ritsu M, Okuda M, Crawford B. Fexofenadine improves the quality of life and work productivity in Japanese patients with seasonal allergic rhinitis during the peak cedar pollinosis season. *Int Arch Allergy Immunol* 2005; **136**:148-54.
20. Patel T, Ishiuiji Y, Yosipovitch G. Nocturnal itch: why do we itch at night? *Acta Derm Venereol* 2007; **87**:295-8.
21. Grattan CE, Humphreys F. Guidelines for evaluation and management of urticaria in adults and children. *Br J Dermatol* 2007; **157**:1116-23.
22. Powell RJ, Du Toit GL, Siddique N *et al*. BSACI guidelines for the management of chronic urticaria and angioedema. *Clin Exp Allergy* 2007; **37**:631-50.
23. Zuberbier T, Bindslev-Jensen C, Canonica W *et al*. EAACI/GA2LEN/EDF guideline: management of urticaria. *Allergy* 2006; **61**:321-31.
24. Tedeschi A, Girolomoni G, Asero R. AAITO Position paper. Chronic urticaria: diagnostic workup and treatment. *Eur Ann Allergy Clin Immunol* 2007; **39**:225-31.
25. Joint Task Force on Practice Parameters. The diagnosis and management of urticaria: a practice parameter part I: acute urticaria/angioedema part II: chronic urticaria/angioedema. *Ann Allergy Asthma Immunol* 2000; **85**:521-44.
26. Klein PA, Clark RA. An evidence-based review of the efficacy of antihistamines in relieving pruritus in atopic dermatitis. *Arch Dermatol* 1999; **135**:1522-5.
27. Leung DY, Nicklas RA, Li JT *et al*. Disease management of atopic dermatitis: an updated practice parameter. Joint Task Force on Practice Parameters. *Ann Allergy Asthma Immunol* 2004; **93**:S1-21.