

SHORT REPORT

Systemic antihistamines – a common outside the guidelines therapeutic strategy in hand eczema management

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Abstract

Background Hand eczema (HE) is the most common skin disease affecting hands. Although the current treatment guidelines do not recommend use of systemic antihistamines as routine therapy, they seem to be widely used by physicians handling with this problem.

Objective The aim of the study was to investigate the attitude to prescribe systemic antihistamines in HE.

Material and methods A 10-item questionnaire was distributed among physicians participating in regional dermatological conferences. 127 valid questionnaires were analysed.

Results A total of 127 physicians participated in the survey. 124 (97.6%) responders prescribe antihistamines in HE and 16 (12.6%) subjects declared routine use of oral antihistamines in the HE management. Significantly more dermatologists than other specialists used antihistamines in the treatment of HE accompanying atopic dermatitis (77.8% vs. 54.5%, $P < 0.01$) and dermatologists significantly more commonly used antihistamines in HE due to their anti-inflammatory properties (40.3% vs. 20.0%, $P = 0.02$). Regarding the type of eczema, antihistamines were prescribed most frequently in acute allergic HE ($n = 92$, 72.4%) and in HE accompanying atopic dermatitis ($n = 86$, 67.7%).

Conclusions Despite the lack of the large, randomized, controlled studies on the effectiveness of the systemic antihistamines in the treatment of HE, this type of therapy seems to be prevalently used among the physicians.

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Conflicts of interest

Adam Reich has been paid as a consultant or participated in clinical trials sponsored by following companies: Abbvie Laboratories, Actavis, Actelion, Amgen, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Novartis, Pierre Fabre Medicament, Regeneron. Jacek Szepietowski has been paid as an advisory board/consultant by following companies: AbbVie, Biogenetica International Laboratories, Leo Pharma, Merck-Serono, Novartis, Pierre-Fabre, Sandoz, Toray Corporation, and as speaker by AbbVie, Astellas, Actavis, Adamed, Berlin-Chemie Mennarini, Janssen-Cilag, Fresenius, Leo Pharma, Takeda, Mitsubishi Pharma, Vichy.

Introduction

Hand eczema (HE) is one of the most common skin diseases with an estimated prevalence of up to 10%^{1,2} and incidence set at approximately five patients/1000/year.³ The disease is a common reason for medical consultations and approximately 70% of patients with HE seek medical attention.^{4,5} Despite a multitude of therapeutic options, the treatment of HE, especially in respect of its' chronic and recurrent course, is often frustrating and unsatisfactory for patients and generates significant costs.^{6,7} This creates a therapeutic challenge for physicians dealing with the disease, which often look for alternative treatment options. In addition, HE is often accompanied by pruritus, which further impairs the patient's well-being. As antihistamines are the best known antipruritic agents, it seems, that these drugs are widely prescribed by dermatologists for patients with HE even though

convincing data about oral antihistamines in the treatment of HE are lacking and current treatment guidelines do not recommend use of systemic antihistamines as routine therapy because no controlled studies were performed to date on these drugs in HE. As we observed a significant discrepancy between the treatment recommendation and daily clinical practice in respect of antihistamine use in HE patients, we have undertaken a study to analyse the prescription profiles of these drugs in the treatment of HE.

Materials and methods

Characteristic of questioned physicians

A total of 127 physicians from Poland [108 (85.0%) women, 19 (15.0%) men] in the age between 25 and 80 years (mean age:

49.7 ± 14.0) participated in the study. The studied group consisted of 72 (56.7%) dermatologists, 13 (10.2%) internists, 10 (7.9%) paediatricians, 29 (22.8%) general practitioners, and 3 (2.4%) allergologists. The hospital was the main place of work for 32 (25.2%) physicians, the outpatient clinic for 75 (59.1%), and private office for the remaining 20 (15.7%) participants. Ninety one (71.7%) respondents declared over 10 years of professional experience, while 11 (8.7%) had lower than 2 years of professional experience, 17 (13.4%) ≥ 2 but <5 years, and 8 (6.3%) ≥ 5 but <10 years of clinical experience.

Study design

This was a cross-sectional questionnaire-based study. A 10-item semi-open questionnaire (Appendix 1) was distributed among physicians – participants of the regional dermatological conferences. Questionnaires were freely available during the meetings and willing doctors completed them anonymously. The scientific topics of the meetings did not cover the area of eczema diagnostic and treatment. In total, 127 valid questionnaires were received and analysed.

For the study purpose, we have adopted the classification of HE proposed by Diepgen *et al.*⁸ In order to achieve consistent data, we have asked about the major subtypes of HE (i.e. irritant contact eczema, allergic contact eczema, and atopic hand eczema). However, as it is frequently not possible to indicate one possible cause of eczema in the routine daily practice, we have also decided to add more general terms (chronic hand eczema or acute hand eczema, not otherwise specified).

Statistical analysis

All results were analysed statistically using Statistica® 10.0 (Statsoft, Kraków, Poland). The significance of the observed differences between studied groups was determined by Student *t*-test, χ^2 test with Yates corrections or the two-sided Fisher exact test as well as with the multiple regression analysis, where appropriate. A *P*-value lower than 0.05 was considered as statistically significant.

Results

Antihistamines in hand eczema treatment

Only 3 (2.4%) persons have never used antihistamines to treat patients with HE among all 127 investigated physicians. In contrast, 16 (12.6%) subjects declared, that they have always applied antihistamines while treating patients with HE, for 51 (40.2%) physicians use of antihistamines depended on the eczema type, for 51 (40.2%) on pruritus severity and in remaining six persons, both eczema type and pruritus severity determined the necessity of antihistamine prescription. Twenty five (19.7%) physicians claimed that they have been using antihistamines in more than 75% of all HE patients, 58 (26.0%) have given antihistamines to ≥50–70% of patients, 37 (29.1%)

to ≥25–50% and the remaining 32 (25.2%) participants to less than one quarter of treated HE subjects. Regarding HE subtype, antihistamines were most often used in acute allergic HE (*n* = 92, 72.4%) and in HE accompanying atopic dermatitis (*n* = 86, 67.7%) (Table 1). The most important reason to prescribe antihistamines in HE was their anti-pruritic activity (*n* = 96, 75.6%) (Table 1). Physician's age did not influence the fact of prescribing antihistamines.

Analysing the type of antihistamine drugs, the newest medicines were used by majority of study participants (*n* = 69, 55.2%). First generation antihistamines were solely used by nine doctors (7.2%) and older antihistamines of the second generation were prescribed by 21 (16.8%) physicians. Other physicians (19.7%) used more than one different antihistamine class (e.g. first and second generation of antihistamines, two antihistamines of the second generation – older and newer, etc.). Usually one patient was treated with one antihistamine (*n* = 103, 81.7%), however, 22 (17.3%) doctors used more than one antihistamine to treat HE in some patients – they usually used a combined therapy with first- and second- class antihistamines. Eighty seven participants (68.5%) declared that they are using standard doses of antihistamines while treating patient with HE, whereas about one-third (*n* = 40) claimed, that they usually prescribe higher doses of antihistamines than registered ones (two or three times higher) to treat HE.

Factors determining the use of antihistamines in hand eczema

There were not many differences between dermatologists and other specialists regarding the use of antihistamines in HE. Significantly more dermatologists compared to other specialists used antihistamines for the treatment of HE in atopic dermatitis patients (77.8% vs. 54.5%, *P* < 0.01) (Table 1). In addition, dermatologists significantly more commonly than other specialists underlined that they used antihistamines in HE due to their anti-inflammatory properties (40.3% vs. 20.0, *P* = 0.02). Interestingly, length of professional experience (<10 years vs. >10 years) and place of work (hospital vs. outpatient clinic vs. private office) did not significantly influence the attitude of antihistamine use (Table 1). These findings were confirmed with multiple regression analysis (physicians' gender, age, specialty, length of professional experience and place of work were used as covariates) (Table S1).

Discussion

Over the last decade, the classification of HE has been a subject of numerous debates. Regarding the etiology, HE is divided into allergic contact dermatitis, irritant dermatitis, hand eczema in the course of atopic dermatitis and non-specific hand eczema.^{8,9} Recently published guidelines on the management of HE have taken into consideration both clinical appearance and etiological background of the disease and

Table 1 Use of antihistamines in hand eczema [results demonstrated as *n* (percentage)]

All physicians		Specialty		Length of professional experience				Place of work			
		Dermatologists	Non-dermatologists	P	<10 years	≥10 years	P	Hospital	Outpatient clinic	Private office	P
N	127	72	55	–	36	91	–	32	75	20	–
Indication											
Acute HE, not otherwise specified	46 (36.2)	31 (43.1)	15 (27.3)	0.1	11 (30.6)	35 (38.5)	0.53	14 (43.7)	26 (34.7)	6 (30.0)	0.55
Acute allergic HE	92 (72.4)	50 (69.4)	42 (76.4)	0.51	27 (75.0)	65 (71.4)	0.85	22 (68.7)	57 (76.0)	13 (65.0)	0.54
Acute irritant HE	31 (24.4)	16 (22.2)	15 (27.3)	0.65	9 (25.0)	22 (24.2)	0.9	8 (25.0)	17 (22.7)	6 (30.0)	0.79
Chronic HE	38 (29.9)	19 (26.4)	19 (34.6)	0.42	13 (36.1)	25 (27.5)	0.46	10 (31.2)	19 (25.3)	9 (45.0)	0.23
HE in the course of atopic dermatitis	86 (67.7)	56 (77.8)	30 (54.5)	<0.01	22 (61.1)	64 (70.3)	0.43	23 (71.9)	50 (66.7)	13 (65.0)	0.84
Other type of HE	3 (2.4)	3 (4.2)	0 (0)	0.26	0 (0)	3 (3.3)	0.56	0 (0)	2 (2.7)	1 (5.0)	0.49
Reasons for antihistamine use											
Sedation	20 (15.7)	8 (11.1)	12 (21.8)	0.16	3 (8.3)	17 (18.7)	0.24	4 (12.5)	14 (16.7)	2 (10.0)	0.54
Anti-itching	116 (91.3)	67 (93.1)	49 (89.1)	0.64	36 (100)	80 (87.9)	0.07	32 (100)	66 (88.0)	18 (90.0)	0.13
Anti-inflammatory	51 (40.2)	33 (45.8)	18 (32.7)	0.19	11 (30.6)	40 (44.0)	0.24	14 (43.7)	31 (41.3)	6 (30.0)	0.58
Anti-allergic	73 (57.5)	38 (52.8)	35 (63.6)	0.3	21 (58.3)	52 (57.1)	0.94	17 (53.1)	45 (60.0)	11 (55.0)	0.78
Antihistaminic	69 (54.3)	37 (51.4)	32 (58.2)	0.56	19 (52.8)	50 (54.9)	0.98	16 (50.0)	42 (56.0)	11 (55.0)	0.85
Primary reasons for antihistamine use											
Sedation	10 (7.9)	4 (5.6)	6 (10.9)	0.44	4 (11.1)	6 (6.6)	0.63	3 (9.4)	6 (8.0)	1 (5.0)	0.85
Anti-itching	96 (75.6)	57 (79.2)	39 (70.9)	0.39	29 (80.6)	67 (73.6)	0.56	28 (87.5)	54 (72.0)	14 (70.0)	0.19
Anti-inflammatory	40 (31.5)	29 (40.3)	11 (20.0)	0.02	8 (22.2)	32 (35.2)	0.23	12 (37.5)	21 (28.0)	7 (35.0)	0.58
Anti-allergic	64 (50.4)	35 (48.6)	29 (52.7)	0.78	18 (50.0)	46 (50.5)	0.89	17 (53.1)	38 (50.7)	9 (45.0)	0.85
Antihistaminic	63 (49.6)	33 (45.8)	30 (54.5)	0.43	17 (47.2)	46 (50.5)	0.89	17 (53.1)	37 (49.3)	9 (45.0)	0.85
Tradition	2 (1.6)	1 (1.4)	1 (1.8)	0.6	1 (2.8)	1 (1.1)	0.92	1 (3.1)	1 (1.3)	0 (0)	0.66
Applied doses of antihistamines											
Registered dose	85 (66.9)	48 (66.7)	37 (69.8)	0.58	24 (66.7)	63 (69.2)	0.95	19 (59.4)	54 (72.0)	14 (70.0)	0.43
Doubled dose	37 (29.1)	23 (31.9)	14 (26.4)		11 (30.6)	26 (28.6)		11 (34.4)	20 (26.7)	6 (30.0)	
Quadruple dose	3 (2.4)	1 (1.4)	2 (3.8)		1 (2.8)	2 (2.2)		2 (6.2)	1 (1.3)	0 (0)	

discuss a wide range of medications used in the therapy, while they have devoted little concern to the role of antihistamines or ignore them completely.^{10–12} However, the use of antihistamines in the management of HE seems to be an integral part of the HE therapy. Updated data from the CARPE registry (Chronisches Handekzem-Register zum Patienten-Langzeitmanagement; meaning: chronic hand eczema registry on long-term patient management) indicates that 25.6% of the patients with HE have used oral antihistamines in the past 12 months.¹³ The authors of the report suggest that the main reason for the oral antihistamines administration is the management of itch, but they also underline that there is no evidence-base for such proceedings. Our study has clearly shown that antihistamines are widely used in the treatment of HE. Moreover, in many patients they are one of the major drugs administered in HE. The tendency to prescribe antihistamines in HE was unrelated to the specialization, years of professional experience or sex of prescribers, indicating that these drugs are unanimously believed to be of help for patients with HE. The antihistamines are administered not only in the management of HE accompanying atopic dermatitis but also in allergic contact dermatitis and even in irritant HE or chronic HE, regardless of their etiology. What is even more important, according to our study more than 10% of physicians declare a routine use of antihistamines in every subjects with HE and the majority of clinicians used them in most HE patients. However, results obtained in only one country may be biased as they could reflect local habits and, therefore, it would be very interesting to perform similar studies in other countries.

Focusing on the administration reason of antihistamines, we found out that these drugs were used not only for their antihistamine action, but also for their anti-pruritic and anti-inflammatory properties. Interestingly, anti-inflammatory properties of antihistamines was mainly a prescription for dermatologists, but not for other specialists. Physicians who used antihistamines in the treatment of HE considered these drugs as an adjunct therapy to other treatment modalities, mainly to topical corticosteroids, emollients and keratolytics.

In our study, we did not find any correlation between the variant of HE and the prescribed type of antihistamines administered dose of the antihistamines and combination therapy with antihistamines of two generations. The way of the prescription, the type of preparation, the use of antihistamines in particular types of eczema seems to be based on beliefs rather than supported by evidence-based medicine. The lack of an uniform standard profile for the use of antihistamines in HE may be linked to disregard them in the guidelines on the treatment of hand eczema in Poland and worldwide. Taking into account, how often these drugs are given to patients with HE, we would like to underline an urgent need for performing control studies to confirm or neglect their efficacy in this disease, especially regarding various HE subtypes.

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Appendix 1

Oral antihistamines in the treatment of hand eczema – a survey

- (1) Do You administer oral antihistamines in the treatment of hand eczema?
 - a) yes, always
 - b) yes, it depends on the type of eczema
 - c) yes, it depends on the itch intensity
 - d) no, never.
- (2) If You use antihistamines in patients with hand eczema, in how many patients they are prescribed?
 - a) in 76–100%
 - b) in 51–75%
 - c) in 26–50%
 - d) in 0–25%.
- (3) In what kind of hand eczema do You prescribe antihistamines most frequently (you can select more than one answer)
 - a) in acute eczema, regardless of the cause
 - b) in acute allergic contact dermatitis
 - c) in acute irritant contact dermatitis
 - d) in chronic eczema

- e) in hand eczema in the course of atopic dermatitis
 - f) another hand eczema (what kind?.....)
- (4) For what reason do you prescribe antihistamines in hand eczema? (you can select more than one answer)
- a) because of their sedative effects
 - b) due to their anti-pruritic effect
 - c) due to their anti-inflammatory activity
 - d) due to their anti-allergic properties
 - e) due to their antihistamine activity
 - f) I do not know, but traditionally I use
 - g) for other reasons (which?.....)
- (5) According to You, what is the main reason for the use of antihistamines?
- a) their sedative effects
 - b) the anti-pruritic properties
 - c) the anti-inflammatory activity
 - d) the anti-allergic effect
 - e) the antihistamine activities
 - f) traditional use
 - g) other reasons.
- (6) What preparations do You prescribe the most frequently?
- a) first-generation drugs (e.g. clemastine)
 - b) second-generation drugs (e.g. cetirizine)
 - c) the latest generation of drugs (e.g. desloratadine, levocetirizine, fexofenadine)
 - d) other.
- (7) How do You usually apply antihistamines in hand eczema?
- a) only one antihistamine preparation
 - b) more than one antihistamine at the same time in one patient.
- (8) If you prescribe more than one antihistamine in the treatment of hand eczema, the most common combination is:
- a) two-first-generation drugs (e.g. clemastine + hydroxyzine)
 - b) first-generation drug + classic second-generation drug (e.g. cetirizine)
 - c) first-generation drug + modern second-generation drug (e.g. levocetirizine, desloratadine)
 - d) classic second-generation drug + modern second-generation drug.
- (9) If You prescribe antihistamines in hand eczema, which dose do You choose:
- a) registration dose
 - b) at twice
 - c) a dose four times higher.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Multiple regression analysis for analysed parameters

Multiple regression analysis for analyzed parameters.

[illegible]