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Itching in Patients with Chronic Hand Eczema: Data from the CARPE Registry

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Key Words
Atopy · Chronic hand eczema · Dermatology Life Quality Index · Eczema · Itch · Pruritus · Quality of life · CARPE registry

Abstract
Background: Itching is a leading symptom of chronic hand eczema (CHE) having a great impact on patients. The determinants of itching in CHE are unclear. ***Objective:*** We performed a cross-sectional analysis investigating factors associated with the presence and severity of itch in CHE patients from the CARPE registry. ***Methods:*** We present baseline data on itch in relationship with sociodemographic factors, severity of CHE, atopy, contact allergy, treatment and patient-reported outcomes including health-related quality of life (HRQoL). ***Results:*** Of 1,051 patients with CHE, 78.1% reported itching. Significant positive associations with itching were observed for younger age groups (17–25 and 26–45 years), for moderate, severe and very severe CHE and for small/moderate impairment in HRQoL. Atopic skin diathesis, hardly being able to realize treatment recommendations and very or extremely large impairments in HRQoL were associated with itch severity. ***Conclusion:*** Taking the identified variables into account may help identify vulnerable groups most affected by (severe) itch.

Introduction

Hand eczema (HE) is a frequent and complex disease in terms of morphology, location, and especially of etiology [1, 2]. In contrast to acute HE, chronic hand eczema (CHE) is characterized by longer disease duration or recurrent episodes and is frequently refractory to topical anti-inflammatory treatment. Patients with CHE complain about a variety of symptoms such as itching, burning, stinging and pain. Often itching is the dominating symptom, but other dermatoses and diseases may also present with itching of the hands, requiring a precise diagnostic

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procedure of this symptom [3]. However, little is known about factors associated with the occurrence and severity of itching in CHE. Previous studies have focused on cofactors of itching in patients with various dermatological diseases [4, 5] or in samples drawn from the general population [6, 7]. An ongoing cross-sectional study in dermatological departments of 13 European countries investigates the prevalence and intensity of itch in dermatological patients. HE was reported to be among the most frequent diseases in patients suffering from (acute) itch [8].

The CARPE registry has been set up to evaluate sociodemographic and clinical characteristics as well as patient-reported outcomes and treatment modalities in patients affected by CHE. The aim of this data analysis was to identify factors associated with itch and itch severity using baseline data from all CHE patients included in CARPE.

Materials and Methods

The CARPE (German acronym: Chronisches Handekzem-Register zum Patienten-Langzeitmanagement, meaning chronic hand eczema registry on long-term patient management) registry was established in 2009 as a prospective observational patient cohort study. Eligible patients are patients diagnosed with CHE (defined as disease duration ≥3 months or >2 flares within the previous 12 months), with previous treatment with topical corticosteroids, no long-lasting healing under adequate topical treatment including corticosteroids and no other dominating active severe skin diseases or acute skin infection. Data are collected through dermatological examinations and patient questionnaires, e.g. through the Physician Global Assessment (PGA) and the Dermatology Life Quality Index (DLQI). The design and methodology of the CARPE registry have been previously described in detail [9, 10] (for further details see also http://carpe.dermis.net). Ethical approval was obtained from the University of Heidelberg, Germany (No. S-433/2008). The study was established according to the guidelines of good clinical practice. Patients gave their written informed consent.

This analysis is based on data from the physicians' documentation as well as patient data assessed at the first examination (baseline examination). We performed a cross-sectional analysis (n = 1,051) investigating factors associated with the presence and the severity of itch in patients with CHE.

Primary Outcome

Current itching was assessed by the physician by means of a verbal rating scale in four categories (none, mild, moderate and severe). Itching was evaluated once at baseline examination. 'Mild' and 'moderate' were collapsed into one category. The following two variables were used as outcome variables: (1) presence of itch (yes vs. no); (2) severity of itch (severe vs. mild/moderate).

Sociodemographic and Clinical Data

The following variables were explored in correlational analyses (fig. 1): (1) sex (male, female); (2) age (grouped into four categories: 17–25 years, 26–45 years, 46–64 years, ≥65 years); (3) severity of CHE (assessed by PGA, supported by the use of a validated photographic guide [11] and rated on a five-point Likert scale: very severe, severe, moderate, almost clear, clear); (4) self-assessed severity of CHE, rated on a visual analogue scale ranging from 0 (clear) to 10 (very severe); (5) diagnosis of CHE (due to a frequent clinical overlap seen in CHE, multiple diagnoses were possible); (6) atopy (yes vs. no; documented according to the Erlangen Atopy Score [12]); (7) contact allergy (type IV allergy yes vs. no); (8) reported treatment of CHE in the 12 months prior to inclusion into the registry (topical treatment yes vs. no, UV phototherapy yes vs. no, systemic therapy yes vs. no); (9) patient-reported outcomes: (a) therapy perceived as burdensome, therapy being time-consuming and experience of unpleasant side effects, rated on a four-point Likert scale (not at all, a little, a lot, very much); (b) realization of treatment recommendations, rated on a four-point Likert scale (fully, mostly, hardly, not at all); (c) health-related quality of life (HRQoL), measured using the DLQI, ranging from no impairment to very severe impairment (0–30) and grouped into 5 categories according to Hongbo et al. [13] (0–1 = no effect on patient's life, 2–5 = small effect, 6–10 = moderate effect, 11–20 = very large effect, 21–30 = extremely large effect).

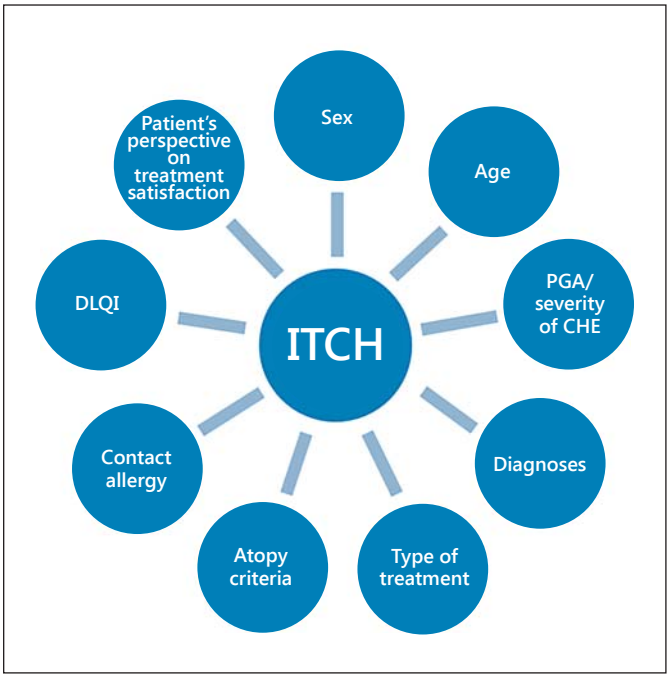

Fig. 1. Variables associated with itch in patients with CHE explored in correlation analysis.

Statistical Analyses

A Microsoft Access 2003 database was used for data entry. Statistical analyses were performed using SPSS (version 20) for Windows. Nominal and ordinal data were analyzed by computing absolute (n) and relative frequencies (%). Continuous variables were analyzed by computing mean and standard deviation (SD). Statistical analysis was done in two steps. First χ^2 statistics were used to iden-

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Table 1. Descriptive analysis of factors associated with itch in patients with CHE in the whole sample

Variable	%	n
Sex (n = 1,051)		
Male	46.4	488
Female	53.6	563
Age (n = 1,051)		
17–25	10.3	108
26–45	29.8	313
46–64	51.7	543
≥65	8.2	86
PGA (n = 1,049)		
Clear	2.0	21
Almost clear	9.5	100
Moderate	23.3	244
Severe	39.7	416
Very severe	25.5	268
Self-assessed severity (n = 1,032)		
0–1 (clear)	5.4	56
>1–3	23.9	247
>3–7	45.8	473
>7–9	17.3	179
>9–10 (very severe)	7.5	77
Itch (n = 1,049)		
None	21.9	230
Mild	29.6	311
Moderate	22.2	233
Severe	26.2	275
Diagnoses (n = 1,051)		
Irritant contact dermatitis	59.0	620
Atopic HE	36.3	382
Hyperkeratotic fissured eczema	36.5	384
Vesicular HE	29.3	308
Allergic contact dermatitis	17.4	183
Fingertip dermatitis	7.7	81
Other	2.0	21
Atopic skin diathesis (n = 1,045)		
No/unlikely/unclear	54.9	577
Yes	44.5	468
Contact allergy (n = 1,028)		
No	52.8	543
Yes	47.2	485
Treatment (n = 1,050)		
Systemic treatment		
No	50.8	533
Yes	49.2	517
UV phototherapy		
No	57.0	599
Yes	43.0	451
Patient's perspective on treatment		
Therapy perceived as burdensome (n = 1,011)		
Not at all	36.1	365
A little	38.0	384
A lot	16.7	169
Very much	9.2	93
Therapy being time-consuming (n = 1,009)		
Not at all	30.9	312
A little	38.9	393
A lot	20.8	210
Very much	9.3	94
Experience of unpleasant side effects (n = 988)		
Not at all	52.5	519
A little	26.8	265
A lot	14.3	141
Very much	6.4	63
Realization of treatment recommendations (n = 1,013)		
Fully	34.2	346
Mostly	58.5	593
Hardly	6.0	61
Not at all	1.3	13
DLQI (n = 1,027)		
No effect (0–1)	9.7	100
Small effect (2–5)	26.5	272
Moderate effect (6–10)	30.6	314
Very large effect (11–20)	27.8	285
Extremely large effect (21–30)	5.5	56

tify variables that were significantly associated with itch and severity of itch in univariate analysis. p values <0.05 were considered significant. In a second step those variables that were significantly associated with the presence of itch and itch severity respectively were entered into multivariate logistic regression models. Adjusted odds ratios with corresponding 95% confidence intervals were computed.

Results

A description of the sample in terms of sociodemographic and clinical characteristics is provided in table 1. More than half of the patients were female. The mean age was around 48 years (SD 13.8). Around 78% (n = 819) of the patients were affected by itch. Of those affected by the symptom, 38% (n = 311) reported mild, 28% (n = 233) moderate and 34% (n = 275) severe itching.

Factors Associated with the Presence of Itch

Univariate Analysis. As shown in table 2, we found significant associations between the presence of itch and sex, age, PGA, self-assessed severity of CHE, atopic skin diathesis, therapy perceived as burdensome, experience of unpleasant side effects, realization of treatment recommendations and HRQoL.

Table 2. Presence of itch according to investigated variables (univariate analysis)

Variable	Itching, % (n)	p value
Sex (n = 1,049)		0.031
Male	75.1 (365)	
Female	80.6 (454)	
Age (n = 1,048)		0.001
17–25	91.7 (99)	
26–45	80.1 (250)	
46–64	75.3 (408)	
≥65	70.9 (61)	
PGA (n = 1,048)		<0.001
Clear	38.1 (8)	
Almost clear	51.0 (51)	
Moderate	71.2 (173)	
Severe	83.2 (346)	
Very severe	89.6 (240)	
Self-assessed severity (n = 1,030)		<0.001
0–1 (clear)	55.4 (31)	
>1–3	64.4 (159)	
>3–7	83.0 (391)	
>7–9	88.8 (159)	
>9–10 (very severe)	88.3 (68)	
Atopic skin diathesis (n = 1,043)		0.004
No/unlikely/unclear	74.7 (430)	
Yes	82.0 (383)	
Contact allergy (n = 1,026)		0.466
No	77.1 (417)	
Yes	79.0 (383)	
Diagnoses (n = 1,049)		
Irritant contact dermatitis	78.1 (336)	0.966
Atopic HE	85.3 (326)	<0.001
Hyperkeratotic fissured eczema	72.8 (279)	0.002
Vesicular HE	83.8 (258)	0.004
Allergic contact dermatitis	86.3 (158)	0.003
Fingertip dermatitis	79.0 (64)	0.832
Other	66.7 (14)	0.196
Systemic treatment		
12 months prior to inclusion (n = 1,048)		0.247
No	79.5 (423)	
Yes	76.6 (395)	
UV phototherapy		
12 months prior to inclusion (n = 1,048)		0.097
No	79.9 (477)	
Yes	75.6 (341)	
Therapy perceived as burdensome (n = 1,009)		0.001
Not at all	73.9 (269)	
A little	77.3 (296)	
A lot	84.0 (142)	
Very much	90.3 (84)	
Therapy being time-consuming (n = 1,007)		0.287
Not at all	78.8 (245)	
A little	76.0 (298)	
A lot	78.1 (164)	
Very much	85.1 (80)	
Experience of unpleasant side effects (n = 986)		0.038
Not at all	78.7 (407)	
A little	74.0 (196)	
A lot	83.7 (118)	
Very much	87.3 (55)	
Realization of treatment recommendations (n = 1,020)		<0.001
Fully	68.8 (161)	
Mostly	77.8 (360)	
Hardly	84.4 (217)	
Not at all	90.9 (60)	
DLQI (n = 1,025)		<0.001
No effect (0–1)	54.5 (54)	
Small effect (2–5)	70.2 (191)	
Moderate effect (6–10)	81.2 (254)	
Very large effect (11–20)	86.7 (247)	
Extremely large effect (21–30)	92.9 (52)	

Multivariate Analysis. Findings from multivariate analyses (table 3) revealed significant positive associations between age groups 17–25 years and 26–45 years, very severe, severe or moderately severe CHE as well as a moderate or very large impairment of QoL and itch. The association between presence of itch and DLQI clearly decreased after adjustment. A significant inverse association was found between experiencing unpleasant side effects 'a little' and itch.

Factors Associated with the Severity of Itch

Univariate Analysis. We found significant associations between the severity of itch and PGA, self-assessed severity of CHE, atopic skin diathesis, therapy perceived as burdensome, therapy perceived as time-consuming, realization of treatment recommendations and DLQI (table 4).

Multivariate Analysis. Multivariate logistic regression (table 5) revealed that the direction of association remained the same for the variables PGA, atopy, experience of unpleasant side effects and DLQI. However, only the presence of atopic skin diathesis, hardly any realization of treatment recommendation as well as a very and extremely large impairment of QoL were significantly associated with severity of itch.

Table 3. Results from multivariate logistic regression (outcome: presence of itch)

Variable	Adjusted OR (95% CI)
Sex (n = 1,049)	
Male	1.0
Female	1.29 (0.91–1.84)
Age (n = 1,048)	
17–25	**4.68 (1.76–12.46)**
26–45	**2.02 (1.05–3.87)**
46–64	1.65 (0.90–3.03)
≥65	1.0
PGA (n = 1,048)	
Clear	1.0
Almost clear	2.43 (0.81–7.31)
Moderate	**4.43 (1.51–13.02)**
Severe	**6.14 (2.07–18.16)**
Very severe	**9.34 (2.91–29.97)**
Self-assessed severity (n = 1,030)	
0–1 (clear)	1.0
>1–3	1.00 (0.50–2.00)
>3–7	1.70 (0.81–3.58)
>7–9	2.46 (0.97–6.24)
>9–10 (very severe)	2.08 (0.63–6.87)
Atopic skin diathesis (n = 1,043)	
No/unlikely/unclear	1.0
Yes	1.29 (0.90–1.86)
Therapy perceived as burdensome (n = 1,009)	
Not at all	1.0
A little	1.16 (0.76–1.78)
A lot	1.47 (0.77–2.80)
Very much	2.48 (0.92–6.67)
Experience of unpleasant side effects (n = 986)	
Not at all	1.0
A little	**0.51 (0.33–0.79)**
A lot	0.58 (0.30–1.14)
Very much	0.51 (0.18–1.44)
Realization of treatment recommendations (n = 1,020)	
Fully	1.0
Mostly	1.18 (0.82–1.71)
Hardly	2.68 (0.76–9.41)
Not at all	0.44 (0.12–1.63)
DLQI (n = 1,025)	
No effect (0–1)	**1.0**
Small effect (2–5)	**1.39 (0.80–2.41)**
Moderate effect (6–10)	**1.87 (1.03–3.41)**
Very large effect (11–20)	**2.05 (1.02–4.10)**
Extremely large effect (21–30)	**2.84 (0.83–9.79)**

CI = Confidence interval; OR = odds ratio. Bold indicates $p < 0.05$.

Discussion

To our knowledge this is the first study investigating the prevalence and severity of itch in patients affected by CHE. The CARPE registry provides data on sociodemographic, clinical and treatment-related characteristics of patients with CHE, which allows the investigation of cofactors of itch in CHE patients.

Presence of Itch

Our study showed that younger patients were more likely to report itching than older participants, with patients aged 17–25 years being most affected by itch, followed by the age group 26–45 years. This is in contrast to most findings from previous studies on itch, where older people (especially those between 50 and 60 years) tended to be more affected by itch [4, 6, 7, 14]. One population-based study on chronic itch from Germany found a significant positive association between itch and the age group 31–40 years [7]. Results from our multivariate analysis did not show a significant difference between the presence of itch and sex, meaning that women and men with CHE are equally affected by itch. This is in contrast to results from most of the studies on itch considering sex [4, 5, 15–17]. A cross-sectional study with adults on self-reported skin morbidity in Oslo, Norway showed that women reported itching more often than men throughout all age groups [15].

Dermatologist-assessed severity of CHE was significantly associated with the presence of itch in a linear manner. Since no studies focusing on the presence and severity of itch in patients with HE have yet been conducted, further evidence is needed to confirm our results.

Our results show that the experience of unpleasant side effects indicated by the patients as 'a little' was associated with less itch. Patients reporting little experience of unpleasant side effects may be on effective treatment not imposing a heavy burden on them. If this is the case, itch may also be well controlled or not present. However, this remains speculative and the finding needs to be verified in future studies.

Moderate and extremely large effects on QoL, measured by the DLQI, were significantly associated with the presence of itch in patients with CHE. A study analyzing different dermatological diseases found a significant correlation between the presence of itch and a lower QoL measured by DLQI [18]. A Turkish study investigated a significant relationship between itch and DLQI scores ≥10 in psoriasis patients [19]. Patients affected by pemphigus vulgaris showed significantly increased DLQI scores when itching was reported [20]. Similar results

Table 4. Severity of itch according to the investigated variables (univariate analysis)

Variable	Severe itching, % (n)	p value
Sex (n = 819)		0.155
Male	31.0 (113)	
Female	35.7 (162)	
Age (n = 818)		0.781
17–25	36.4 (36)	
26–45	33.6 (84)	
46–64	32.4 (132)	
≥65	37.7 (23)	
PGA (n = 818)		<0.001
Clear	25.0 (2)	
Almost clear	17.6 (9)	
Moderate	19.7 (34)	
Severe	30.1 (104)	
Very severe	52.5 (126)	
Self-assessed severity (n = 808)		<0.001
0–1 (clear)	16.1 (5)	
>1–3	18.2 (29)	
>3–7	32.2 (126)	
>7–9	42.1 (67)	
>9–10 (very severe)	63.2 (43)	
Atopic skin diathesis (n = 813)		0.004
No/unlikely/unclear	28.8 (124)	
Yes	38.4 (147)	
Contact allergy (n = 800)		0.580
No	32.6 (136)	
Yes	34.5 (132)	
Systemic treatment		
12 months prior to inclusion (n = 818)		0.131
No	31.2 (132)	
Yes	36.2 (143)	
UV phototherapy		
12 months prior to inclusion (n = 818)		0.385
No	32.3 (154)	
Yes	35.2 (120)	
Therapy perceived as burdensome (n = 791)		<0.001
Not at all	34.9 (94)	
A little	26.7 (79)	
A lot	28.9 (41)	
Very much	53.6 (45)	
Therapy being time-consuming (n = 787)		0.010
Not at all	35.5 (87)	
A little	25.8 (77)	
A lot	39.6 (65)	
Very much	36.2 (29)	
Experience of unpleasant side effects (n = 776)		0.037
Not at all	29.7 (121)	
A little	33.7 (66)	
A lot	32.2 (38)	
Very much	49.1 (27)	
Realization of treatment recommendations (n = 792)		<0.001
Fully	27.2 (70)	
Mostly	32.8 (154)	
Hardly	52.6 (30)	
Not at all	66.7 (6)	
DLQI (n = 798)		<0.001
No effect (0–1)	14.8 (8)	
Small effect (2–5)	20.9 (40)	
Moderate effect (6–10)	27.2 (69)	
Very large effect (11–20)	45.3 (112)	
Extremely large effect (21–30)	65.4 (34)	

were found in psoriatic patients with itch, who had significantly decreased HRQoL compared to patients not affected by itch [21]. A cross-sectional study with patients affected by systemic sclerosis from Canada measured QoL according to the 36-Item Short Form Health Survey. Patients suffering from pruritus had a significantly greater negative impact on QoL than patients without pruritus [22]. A cross-sectional study in 13 European countries with 250 consecutive patients and 125 healthy controls demonstrated that patients reporting itch were more depressed than those without itch, had more anxiety and a larger impact on QoL measured by the DLQI [23].

Severity of Itch

Our study demonstrates that patients with atopy seem to be more likely to suffer from a severe form of itching than patients with no or an uncertain atopy. It is well known that atopic hand dermatitis is very frequently accompanied by itch, but so far there are no studies that specifically address this issue. A web-based questionnaire study on itch characteristics showed that atopic dermatitis responders experienced itch more frequently and more intensely when compared to subjects suffering from psoriasis [24]. In patients with occupational CHE, those with irritant contact dermatitis reported significantly less intense itching than patients with irritant-induced atopic HE [16]. Patients with severe CHE reported more intense itching than patients with non-severe CHE, and individuals with atopic dermatitis had higher visual analogue scale scores for itch than patients with exclusive HE [16]. This confirms our results showing a significant association between atopic diathesis and severe itch.

Table 5. Results from multivariate logistic regression (outcome: severe itching)

Variable	Adjusted OR (95% CI)
PGA (n = 818)	
Clear	1.0
Almost clear	0.99 (0.10–10.27)
Moderate	0.89 (0.09–8.74)
Severe	1.26 (0.13–12.24)
Very severe	2.16 (0.22–21.06)
Self-assessed severity (n = 808)	
0–1 (clear)	1.0
>1–3	0.96 (0.28–3.29)
>3–7	1.40 (0.41–4.79)
>7–9	1.37 (0.38–4.50)
>9–10 (very severe)	2.49 (0.62–10.01)
Atopic skin diathesis (n = 813)	
No/unlikely/unclear	1.0
Yes	**1.43 (1.01–2.03)**
Therapy perceived as burdensome (n = 791)	
Not at all	1.0
A little	0.73 (0.45–1.17)
A lot	0.54 (0.28–1.04)
Very much	1.15 (0.52–2.57)
Therapy being time-consuming (n = 787)	
Not at all	1.0
A little	0.65 (0.41–1.04)
A lot	0.76 (0.42–1.40)
Very much	0.33 (0.15–0.73)
Experience of unpleasant side effects (n = 776)	
Not at all	1.0
A little	1.31 (0.82–2.11)
A lot	0.83 (0.44–1.56)
Very much	1.36 (0.56–3.29)
Realization of treatment recommendations (n = 792)	
Fully	1.0
Mostly	1.20 (0.82–1.77)
Hardly	**2.03 (1.01–4.06)**
Not at all	1.98 (0.40–9.79)
DLQI (n = 798)	
No effect (0–1)	1.0
Small effect (2–5)	1.26 (0.52–3.02)
Moderate effect (6–10)	1.53 (0.64–3.65)
Very large effect (11–20)	**3.00 (1.21–7.37)**
Extremely large effect (21–30)	**7.06 (2.30–21.64)**

CI = Confidence interval; OR = odds ratio. Bold indicates $p < 0.05$.

Difficulties in the realization of treatment recommendations were associated with severe itching, suggesting that the previous treatment of CHE had not sufficiently addressed itching. Another explanation may be that severe CHE is associated with more intense itch [16], which can complicate its treatment. One may also speculate that physicians tend to underestimate itch in CHE, leading to a reduced awareness and recording of this symptom, also in clinical studies.

Severity of itch in patients with CHE was significantly associated with impaired QoL (assessed by the DLQI) in a linear manner. Similar results were shown in patient populations affected by other skin diseases accompanied by itch, such as urticaria [25] and psoriasis [21, 26, 27]. One study investigating psychological factors associated with hand dermatoses showed that high stress responders stated significantly higher values for itch [28].

Limitations

In the CARPE registry, itch is only measured as one variable. As solely the presence of itch was asked, the results presented here refer to current itch. Details like course, localization and accompanying sensations like pain, burning or stinging would have been of interest as well. An assessment of itch according to the visual analogue scale is recommended for studies on itch [29, 30], but we relied on itch measured by a verbal rating scale. All findings presented in this paper are only representative for patients with CHE refractory to topical treatment. Because of the cross-sectional design of our study, caution needs to be exercised concerning suggestions about a causal relationship between the presence or severity of itch and the investigated variables. Further prospective and longitudinal studies may permit to establish a causal relationship. Our current analyses should be considered exploratory in nature. Nevertheless, these are the first findings on a variety of factors associated with the presence and severity of itch in patients with CHE.

Disclosure Statement

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