

Chapter 5

The effectiveness of integrated care for patients with hand eczema: results of a randomized, controlled trial



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Abstract

Objective

To evaluate the effectiveness of integrated, multidisciplinary care compared with usual care for patients with moderate to severe, chronic hand eczema after 26 weeks follow-up.

Design

This study was designed as a randomized, controlled trial.

Methods

Patients who visited one of the participating hospitals were randomized to integrated care (IC) or usual care (UC). IC was carried out by a multidisciplinary team and integrates clinical and occupational care to optimize treatment, the patient's quality of life and social functioning. Outcome variables were clinical assessment of hand eczema using the Hand Eczema Severity Index (HECSI) (primary outcome), quality of life, patient's global assessment of hand eczema and sick leave.

Results

Average improvement on the HECSI was 22.4 points in the intervention group and 11.7 points in the control group. The mean difference in improvement on the HECSI between both groups after 26 weeks was 10.7 points in favour of the integrated care group (SE 5.3, 95% CI 0.3-21.1, $P=0.044$). No differences in improvement between the groups were found for any of the other outcomes.

Conclusion

The integrated care program significantly improved clinical outcome measures compared with usual care and was effective for treating patients with chronic hand eczema.

Introduction

Occupational skin diseases are ranked first in prevalence of all occupational diseases in many countries and are considered to be in the top 3 of registered work-related disorders[1,2]. Hand eczema accounts for 90% of all occupational skin diseases[3,4]. Hand eczema often has a chronically relapsing course with a poor prognosis, resulting in a major burden for patients, their employers and society[2]. The physical and psychological burden for patients is comparable to patients with other chronic diseases, like multiple sclerosis and migraine, and even higher than patients with diabetes mellitus[5]. Medical consumption is high, and high costs are also related to productivity loss and sick leave[6].

Despite the major impact of hand eczema, usual care by a dermatologist is suboptimal. It does neither include consultation with the general practitioner nor with the occupational physician, and the people involved in the workplace to eliminate or accommodate allergen or irritating factors at home or work. In addition, due to limited time and expertise available at most outpatient clinics, treatment lacks the extensive counselling needed to change the patient's behaviour regarding the use of protective measures[7]. Integrated care has proved to be effective for patients on sick leave with low back pain[8]. However, integrated care is unique in the field of dermatology. For this reason, we developed an integrated care program based on the International Classification of Functioning, disability and health (ICF, [9]) for hand eczema. The program was carried out by a multidisciplinary team and aimed to integrate clinical and occupational care to optimize treatment and self management. The biopsychosocial model was used as the theoretical framework for this study[10]. With integrated care, we aimed to achieve behavioural change in the patient, by means of counselling using a cognitive-behavioural approach. Thereby, the patients' coping with hand eczema should improve, as well as self-management. Besides that, integrated care aimed at minimizing the patients' exposure to causal factors, for example by eliminating them or using the appropriate protection measures. The home situation as well as the workplace was taken into account. If the patient could not fulfil his daily work, the possibility of modified or alternative work was discussed. If indicated, the patient's relatives or colleagues and supervisors were included in the treatment. The ultimate goal of the intervention was to optimize the patient's quality of life and social functioning.

The aim of the present study was to assess the effectiveness of integrated care by a multidisciplinary team compared with usual care for patients with moderate to severe, chronic hand eczema at 26-week follow-up.

Methods

The present study was a randomized controlled trial. The Medical Ethics Committees of the participating hospitals (the VU University Medical Center, Radboud University Medical Centre, Groningen University Medical Centre, Canisius Wilhelmina Medical Centre and Jeroen Bosch Medical Centre) approved the study. All participants had signed an informed consent. A detailed description of the study design can be found elsewhere[11].

Population

The population in this randomised controlled trial comprised patients aged 16 years and older with moderate to severe, chronic (>3 months) hand eczema who visited a dermatologist of one of the participating hospitals. The degree of hand eczema was determined using the Photographic Guide[12]. Patients with mild hand eczema who were on sick leave from work, or who scored at least 4 points on a Visual Analogue Scale (VAS) for perceived burden of disease in the last three months before inclusion were also eligible. We excluded patients who: had generalized eczema where hand eczema was not the main disease; used topical pharmacotherapy or phototherapy other than used in the study; used systemic treatment affecting hand eczema; were unable to complete questionnaires written in Dutch language. Patients received the information letter from their dermatologist and were contacted by the researchers by telephone. If the patient was willing to participate, the researchers planned a face-to-face appointment to sign the informed consent form. A detailed description of the design of this trial can be found elsewhere[11].

Interventions

Usual care

Patients allocated to the usual care group received allergological evaluation (intra-cutaneous tests and / or epicutaneous test with the European baseline series and additional series) delivered by their own dermatologist. The patient's own dermatologist was responsible also for further usual medical care, such as pharmacotherapy, provision of standard written information and advices.

Integrated care

The overall aim of the integrated care was to optimize the patient's quality of life and social functioning. The integrated care was provided by a multidisciplinary team consisting of a dermatologist, a specialized nurse / physician assistant and an occupational clinical physician.

Coordination

Integrated care was coordinated by a care manager, a role carried out by a member of the multidisciplinary team. The care manager was responsible for communication of the treatment plan with the patient. In addition, the care manager was responsible for the communication with all stakeholders, in the hospital (dermato-allergologist, occupational physician), as well as the relevant stakeholders in primary care (the patient's general practitioner and if applicable occupational physician and occupational hygienist). All patients were discussed weekly by the multidisciplinary team.

Content of the program

The program consisted of clinical and allergeo-dermatological evaluation by the dermatologist. The specialized nurse / physician assistant was responsible for counselling of the patient in the compliance to topical treatment and with regard to hand washing and care procedures, the use of protection measures such as protective gloves in general and the use of cotton gloves worn underneath. Topical treatment was standardized and consisted of dermatocorticosteroids and emollients, if needed supplemented with calcineurin-inhibitors. When the hand eczema was work-related or when there was a risk for (potential) absenteeism as a result of hand eczema, the clinical occupational physician was involved. If needed, materials derived from the workplace were tested. Workplace visits were organised if indicated, to gain relevant material for testing or information on work circumstances. The clinical occupational physician also gave advice about prevention and work procedures. If needed, provision of modified work was organized in communication with the employer's supervisor.

Measurements

Measurements took place at baseline and after 4, 12 and 26 weeks. Patients were sent questionnaires by mail, and were contacted in advance by telephone to schedule an appointment for the clinical scores in the outpatient clinic. Data on cumulative days of sick leave and patient's medical consumption were collected every month by means of a cost calendar.

The primary outcome measure in this study was the clinical severity score measured by a trained and blinded clinical assessor with the Hand Eczema Severity Index (HECSI)[13]. Secondary outcome measures were three categories of disease-specific quality of life (symptoms, emotion and function), measured using the Skindex [14], patients' global assessment, using Visual Analogue Scales (VAS) for itching, pain and fatigue, and sick leave. Risk profession, a history of atopic eczema and the presence of contact allergens were treated as a prognostic factor. Risk profession was investigated using the guideline of the Dutch Association of Occupational Physicians (NVAB)[15].

Sample size

The sample size calculation was based on a pilot study carried out in the Radboud University Medical Centre. In this pilot study, the Hand Eczema Area and Severity score (HEAS) was used. Because the HEAS and the HECSI only differ on minor aspects, we assumed that the results of the pilot study are applicable in the current study. In the pilot study, a reduction in HEAS of 50% was observed during the first six months after the intervention. A reduction of this percentage to 40% during the next six months was hypothesized. The standard deviation (on a logarithmic scale) of the HEAS was 1.2 and the correlation between measurements from 1 to 6 months apart was 0.5. The correlation did not depend on the length of the interval. Based on these findings, a two-sided type I error of 5% and a power of 80%, 85 evaluable patients with at least three follow-up assessments were required per treatment group. Taking into account 30 dropouts, 200 patients were to be included.

Randomisation

The patients were assigned to either integrated care or usual care. Pre-stratification was applied for hospital and risk profession. Block randomisation (with blocks of four) was applied to ensure equal group sizes. Within each stratum a research assistant prepared sequentially numbered sealed envelopes containing a referral for either the intervention group or the control group.

Blinding

It was not possible to blind the patients for the treatment allocation. The care providers were also not blinded, but they were not involved in measuring the outcomes. Clinical scoring of the primary outcome measure was performed by an independent, trained clinical investigator, who was blinded for allocated treatment. A research assistant entered all data in the computer by the research code. Therefore, the analyses of the data by the researcher were blind.

Statistical analyses

All statistical analyses were performed on patient level, according to the intention-to-treat principle. To assess whether protocol deviations had caused bias, we compared the results of the intention-to-treat analyses with per protocol analyses. Student t-test and Chi square tests were performed to test for differences between baseline characteristics of patients in the IC group and the UC group. Non-response analyses were performed to assess differences between patients who completed follow up measurements and patients who were lost to follow-up.

The primary independent variable in the analyses was the treatment to which the patient was allocated. The primary dependent variable was the clinical severity score HECSI. Linear

mixed models were used to assess differences between the two groups in improvement on the HECSI score. A mixed model allows for patients within hospitals and measurements correlated within patients. To assess the effect over time, time was specified as a fixed factor with levels 0 (baseline), 4, 12 and 26 weeks. The effect of interest is the treatment by time interaction, thereby adjusting for baseline differences on HECSI between both treatment groups.

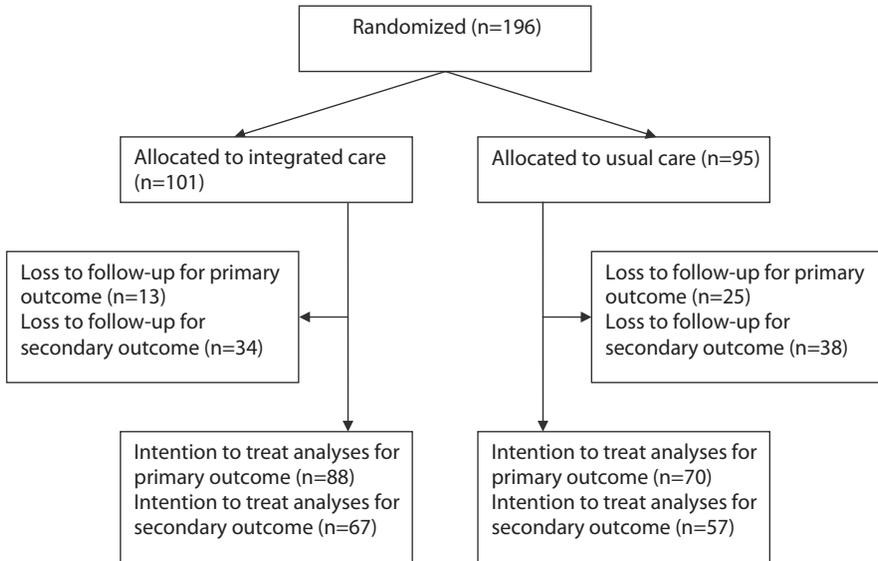
Linear mixed models were also applied to assess the differences between the groups in improvement on the secondary outcomes quality of life and patient's global assessment measures. An independent samples t-test was used compare the difference in cumulative days of sick leave between both groups.

First, an unadjusted linear mixed model analysis was performed. Second, in an adjusted analysis confounding and effect modification were assessed. The potential confounders or effect modifiers were predefined and were all measured at baseline: personal characteristics (age and gender); job characteristics (working in a risk profession), medical history (a history of atopic eczema and the presence of allergens) and HECSI score at baseline. Age was checked on linearity and HECSI score was dichotomized into low and high baseline score using the median in both groups; all other factors were dichotomous.

First, univariate tests for confounding and effect modification were performed for the primary outcome measure. Covariates were considered as confounders if there was a statistically significant or clinically relevant difference between the groups at baseline, and if the beta of the intervention variable changed more than 10% by adding the covariate to the mixed model. Effect modification was tested by performing the mixed model analyses separately for subgroups. For continuous variables (age, HECSI baseline), subcategories were defined based on the median score. When the results for the subgroups were relevantly different, the covariate was considered an effect modifier. For all effect modifiers, subgroup analyses were presented. We considered a p-value less than 0.05 as significant. The data were analysed with SPSS statistical software, version 15.0.

Results

Between July 2008 and December 2009, 196 patients who had visited the dermatologist of one of the participating hospitals and signed informed consent, were randomized: 101 to the integrated care group (IC) and 95 to the usual care group (UC). Figure 1 shows the flow of patients through the study.

Figure 1. Flow of patients through the study

Loss to follow-up and compliance

Data on the primary outcome measure were complete for 196 patients and for 158 (81%) patients during 26 weeks of follow-up. Follow up data on secondary outcomes were complete for 124 patients (63%). Nine patients did not complete the intervention period for various reasons: no time (n=4), no perceived improvement (n=3) or perceived recovery (n=2).

Patient characteristics

Table 1 presents the baseline characteristics of the outcome measures and the prognostic variables for the integrated care and control group. A significant difference in history of atopic eczema was observed between the groups. The difference in risk profession between the groups was considered clinically relevant, although this difference was not significant. No differences were observed between patients with follow-up measurements and patients who were lost to follow-up.

Interventions

Usual care

Besides usual care by the patient's own dermatologist, health care use such as visits to their General Practitioner (GP) or Occupational Physician (OP) of all patients was collected using calendars to measure medical consumption. Data on number of visits is presented in table 2.

Table 1. Baseline characteristics and prognostic factors of outcome measures.

Variable	Integrated care (n=101)	Usual care (n=95)
Men	46 (46)	48 (52)
Women	54 (54)	47 (48)
Age (years) Mean (SD)	43.4 (13.8)	43.0 (13.9)
Risk profession	50 (50)	38 (40)
History of atopic eczema	34 (34)	18 (19)
Presence of allergens	65 (64)	66 (69)
HECSI Mean (SD)	43.9 (33.7)	36.5 (33.9)
Quality of life Mean (SD)		
- Symptoms	59.9 (16.0)	59.7 (18.2)
- Emotion	31.8 (19.7)	28.7 (18.6)
- Function	24.4 (18.8)	20.8 (18.2)
- Total	38.7 (15.9)	36.4 (15.5)
Patient's global assessment Mean (SD)		
- Pain	4.4 (2.7)	4.5 (2.4)
- Itching	4.2 (2.4)	4.1 (2.6)
- Fatigue	4.5 (2.9)	3.9 (2.7)

Values are expressed as number of patients (percentages) unless stated otherwise.

Integrated care

The median duration of integrated care from randomization was 84 days (interquartile range 82 – 91). The average number of visits to the specialized nurse was 3.9. In total, 29 patients had an indication to consult the clinical occupational physician (COP) and 18 patients (69%) did visit the COP. Additional treatment in this group applied by caregivers other than the multidisciplinary team was minimal, and is presented in table 2.

Table 2. Health care utilisation of study population during 26 weeks of follow-up.

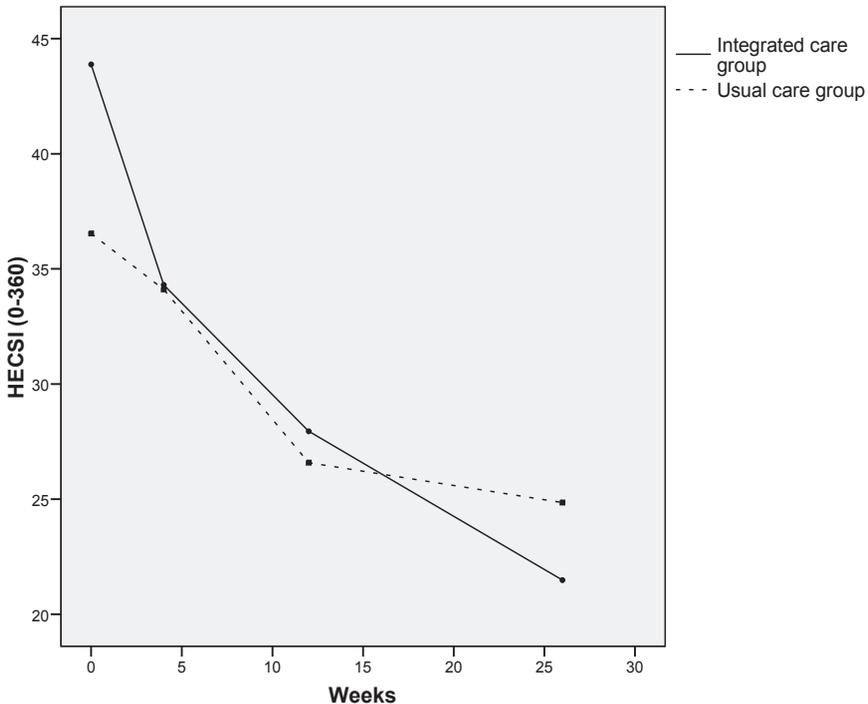
Health care	Integrated care	Usual care
Dermatologist	101 (347)	95 (222)
General practitioner	4 (4)	9 (13)
Clinical occupational physician	18 (18)	0 (0)
Specialized nurse	101 (398)	0 (0)
Occupational physician	9 (13)	7 (8)
Homeopath	2 (9)	0 (0)
Internist	0 (0)	2 (3)
Psychologist	1 (3)	0 (0)
Light therapy	4 (45)	1 (19)

Values are number of patients (number of consultations) unless stated otherwise

Primary outcome measure: HECSI

Patients in IC improved from 43.9 points at baseline (range 2 – 146) to 21.4 points after 26 weeks (range 0 – 110) on the HECSI. In UC, the average improvement was from 36.5 points at baseline (range 3 – 174) to 24.8 after 26 weeks (range 0 – 183). This means an improvement on HECSI of 22.5 points in IC and 11.7 points in UC. Figure 2 presents the graph of the fixed predicted values for the two groups. The mean difference in improvement on the HECSI between both groups after 26 weeks was 10.8 (SE 5.3, 95% CI 0.3-21.1, $P = 0.044$). The per protocol analysis results did not differ from the intention-to-treat analysis (mean difference 11.2 points, 95% CI 0,2-22,4).

Figure 2. Model based means of the primary outcome measure HECSI



No prognostic variables turned out to be confounders. Subgroup analyses showed that only baseline HECSI score was an effect modifier since the results relevantly differed between patients with a low or a high HECSI score at baseline. In patients with a low HECSI score, the difference in improvement on the HECSI between IC and UC was 3.2 (SE 4.2) points after 26 weeks. This difference was not significant. However, in patients with a high HECSI score at baseline a difference of 16.9 (95% CI 1.4-32.5) was found between IC and UC after 26 weeks. This difference was significant.

Secondary outcome measures

Table 3 presents the results of the effectiveness of integrated care on (three aspects of) disease-specific quality of life and patient's global assessment. In both groups, a relevant improvement was observed in the integrated care group on all aspects outcomes. No differences in improvement were observed between the integrated care group and the usual care group. Average cumulative days of sick leave was 9.2 days in the intervention group and 5.3 days in the control group. This difference was not significant ($p=0.27$).

Table 3. Differences in Quality of life and patient's global assessment at 4 measurements.

	Group	Baseline	4 weeks	12 weeks	26 weeks	p Value
Specific QoL						
- Symptoms	IC	59.8 (1.73)	53.1 (2.12)	46.4 (2.18)	40.8 (2.62)	0.83
	UC	60.1 (1.88)	51.3 (2.26)	46.6 (2.32)	41.5 (2.84)	
- Emotion	IC	31.6 (1.94)	28.2 (2.01)	22.6 (1.89)	17.4 (1.85)	0.51
	UC	29.0 (2.10)	23.7 (2.15)	20.1 (2.03)	16.5 (2.00)	
- Function	IC	24.8 (1.88)	20.9 (1.87)	17.4 (1.75)	15.3 (1.63)	0.76
	UC	21.2 (2.03)	18.0 (2.00)	14.9 (1.88)	10.7 (1.76)	
- Total	IC	38.6 (1.58)	34.1 (1.72)	28.8 (1.67)	24.5 (1.78)	0.29
	UC	36.8 (1.72)	31.0 (1.84)	27.2 (1.79)	22.9 (1.93)	
Global assessment						
- Itching	IC	5.5 (0.27)	4.2 (0.27)	3.5 (0.28)	2.8 (0.29)	0.94
	UC	5.6 (0.30)	4.1 (0.30)	3.7 (0.31)	2.8 (0.32)	
- Pain	IC	4.4 (0.28)	3.2 (0.28)	2.7 (0.29)	2.5 (0.31)	0.93
	UC	4.5 (0.30)	3.3 (0.30)	2.7 (0.31)	2.5 (0.34)	
- Fatigue	IC	4.5 (0.29)	4.4 (0.30)	3.6 (0.28)	3.7 (0.34)	0.99
	UC	3.9 (0.31)	3.8 (0.32)	3.1 (0.31)	3.0 (0.37)	

Results of the mixed models analysis. Means and standard errors of both groups at baseline and after 4, 12 and 26 weeks. IC, integrated care; UC, usual care. IC baseline: $n=95$; 4 weeks $n=84$; 12 weeks $n=75$; 26 weeks $n=66$. UC baseline: $n=84$; 4 weeks $n=71$; 12 weeks $n=65$; 26 weeks $n=58$

Discussion

Integrated care for patients with chronic hand eczema had a positive effect on improving the clinical severity score HECSI after 26 weeks. Patients in the integrated care group showed significantly more improvement than patients in the control group. Disease-specific quality of life and patient's global assessment were significantly improved after 26 weeks, but this improvement was not different between the integrated care group and the control group. No differences were observed between both groups in sick leave.

Comparison with other studies

The present study is not the first to demonstrate the effectiveness of integrated care. Integrated care has proved to be effective for patients with chronic low back pain on work-related outcomes[16,17]. In this study, we did not find effects on work-related outcomes such

as sick leave. This may have been caused by the fact that not only patients with work-related hand eczema or on sick leave were included in this study. Only a low number of patients were on sick leave compared to all in the LBP study. Secondly, our process evaluation showed that the clinical occupational physician (COP) was only consulted by 22.8% of patients compared to 100% in the mentioned study[8]. This may explain the lack of effect on work-related outcomes for patients with work-related hand eczema or on sick leave.

The results of the secondary outcome measures in our study are comparable to those of a systematic review on nurse-led services[18]. The researchers of that review reported that only marginal improvements on quality of life have been identified in nurse-led services. They also reported patient education by a nurse could reduce severity of eczema and could improve more appropriate use of topical therapy. A study of Held et al. also reported a reduction of clinical severity. They found that an educational programme for workers in wet work occupations had a significant effect on reducing clinical skin symptoms within the intervention group, as well as compared to a usual care group[19]. Despite the effect on reducing HECSI score, we could not find any differences in improvement on disease-specific quality of life and patient's global assessment between the integrated care group and the usual care group. This may indicate that improvement in clinical scores is not leading to an improvement on disease-specific quality of life and patient's global assessment.

Interpretation of results

A significant effect of the intervention was found on the primary outcome measure, the HECSI score. Our study showed a reduction in HECSI of 51% in the integrated care group, compared with 32% within the control group. This reduction in the integrated care group was statistically significant.

During the first four weeks of the intervention, a larger improvement in HECSI score can be seen in the integrated care group compared to the control group. This short-term improvement can possibly be subscribed to the effects of the use of prescribed corticosteroids and emollients. An essential part of the intervention was proper instruction on how to effectively apply them by the specialized nurse[18,20]. This is an advantage over people in the control group, who were only informed through written information.

Another explanation for the improvement in the first weeks could be the difference in baseline HECSI score, which was by coincidence higher in the integrated care group. A relatively larger improvement could thus be expected in the integrated care group compared to the usual care group, since there is more space to improve in this group.

After 12 weeks, almost no further improvement is accomplished in the usual care group whereas in the integrated care group, patients still improved with almost 6.5 points. The continuation of reduction in HECSI score could be as a result of education by the specialized nurse, which aimed at increasing self-management and better coping of the patients. The

goal of those consultations was to establish behavioural change. Since it takes time to effectively embed advices and instructions in the long run, a lasting effect can be expected after the intervention period was completed at 12 weeks after the start of the program. However, since per protocol analysis results did not differ from the intention-to-treat analysis, a Hawthorne effect can not be excluded.

Different effects were found for patients with high and low HECSI scores at baseline. An explanation for these differences is that patients with mild hand eczema are often benefiting from topical treatment only. This implies that the urge of those patients to comply with the complete study protocol may be diminished. As a result, the difference between the intervention and usual care is minimal for patients with low HECSI baseline score. On the other hand, patients with a high HECSI score at baseline probably did not benefit as much from topical treatment only, and thus were more motivated to comply with study protocol. This hypothesis is supported by the per protocol analysis, where a baseline HECSI score of 46.7 points is observed for patients who complied with the complete study protocol, compared to 43.9 points in the complete integrated care group.

Limitations and strengths of the study

Some limitations of this study need to be discussed. Unfortunately, some patients were lost to follow up. This could be explained by the fact that patients had to visit the hospital for the primary outcome, i.e. the HECSI score. We could not offer any compensation for this effort, which could have been the major reason for the loss to follow-up, especially in the control group. Non-response analyses showed however no differences at baseline between patients who were completed follow up measurements and patients who were lost to follow up. Although the number of patients lost to follow-up was not excessively high (19%), selection bias cannot be ruled out. This may have resulted in a selection of the more motivated patients in the study.

Another point worth mentioning is the severity of hand eczema symptoms at the moment of inclusion. The range of HECSI scores at baseline is high. This can be explained in two ways: the timing of inclusion and the inclusion criteria. Before a patient visits the dermatologist, it is likely that he has already visited his general practitioner. This visit may have resulted in treatment. By the time the patient visits the dermatologist, the treatment may have had an effect on the symptoms. This implies that the HECSI score at baseline is not necessarily taken at the worst clinical stage of symptoms, which may have resulted in a lower HECSI score at baseline. For this group, it is more difficult to demonstrate an effect of integrated care, because HECSI scores may have already been lowered. This could have been solved by adaptation of the inclusion criteria. However, we have chosen to add the patient's self-perceived burden of disease to the inclusion criteria. For patients with low HECSI scores at baseline, the effect of integrated care may be prevention of relapse and maintenance of the

lower scores. Second, the inclusion criteria for participation in this study were rather broad, since we not only focussed on severe hand eczema, but also on (risk for) sick leave and patient's global assessment. This may have led to inclusion of patients with relatively mild hand eczema. It can be expected that integrated care is more effective in patients with more severe clinical scores. Indications for this can be found in the subgroup analyses based on baseline HECSI score, showing that integrated care was more effective in the subgroup with high baseline HECSI scores. Hence, the found difference in improvement between groups may be diminished by the broad inclusion criteria for the study population.

The strength of this study is the unique integrated care approach, in which all factors that may cause or maintain hand eczema are taken into account were evaluated in a randomized controlled trial, which is to our knowledge the first time in the field of dermatology. An objective, reliable and simple scoring method by a blinded assessor was used to assess the primary outcome measure[13], alongside subjective outcome measures. Due to the broad inclusion criteria, the effectiveness of integrated care was evaluated in a wide variety of patients with different degrees of hand eczema in a wide range of hospitals with varying expertise. For this reason, the external validity of the study results is high.

Conclusion

Integrated care improved clinical severity of hand eczema significantly more than usual care during a follow-up period of 26 weeks. This applies to a broad group of patients with different degrees of hand eczema. The integrated care intervention was not effective in improving quality of life since no differences were observed in quality of life scores between both groups. No effect has been found on cumulative days of sick leave. Based on the improvements in clinical severity of hand eczema, this study shows that integrated, multidisciplinary care is a promising treatment for patients with hand eczema.

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