Psoralen plus ultraviolet A (PUVA) soaks and UVB TL01 treatment for chronic hand dermatoses

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Abstract

Chronic eczematous hand dermatoses with and without contact allergies are complex diseases, which makes it a challenge to select the best treatment and obtain an optimal patient experience and a satisfactory treatment result. The aim of this study was to evaluate retrospectively the clinical effect and patient experience of local treatment with psoralen plus ultraviolet A (PUVA) soaks and TL01 phototherapy for severe chronic hand dermatoses, and also to evaluate the quality of life for the subgroup of patients with allergic contact dermatitis including *Compositae* allergy. A retrospective evaluation of results for 94 consecutive patients having received a total of 121 treatment courses with local PUVA soaks or TL01 phototherapy for one of the following diagnoses (n=number of treatment courses): psoriasis (n=19), hyperkeratotic hand eczema (n=27), Pustulosis Palmoplantaris (PPP) (n=22), vesicular eczema (n=16), *Compositae* dermatitis (n=24), and allergic contact dermatitis (n=13). Moreover, semi-structured interviews with 6 selected patients having multiple contact allergies including *Compositae* allergy were used to evaluate quality of life. As a result, we found that PUVA soaks has good effect in patients with psoriasis and hyperkeratotic hand eczema and local phototherapy for chronic hand dermatoses is a useful treatment option in selected cases.

Introduction

Chronic hand dermatoses, including eczema, psoriasis and palmar pustulosis are common, difficult to treat, and have a high impact on patients' quality of life. In Scandinavia the 1 year prevalence of hand eczema is 10-14%.[1,2] In spite of this only few and small treatment studies have been performed to document treatment effect. One explanation for the limited number of high quality treatment studies is the lack of agreement on classification of hand dermatoses and the fluctuation of disease severity.[1] Phototherapy is one treatment option used with questionable results.

Sezer and co-workers evaluated local (psoralen plus ultraviolet A) PUVA (administered as paint) compared to TL01 in patients with chronic hand dermatoses. The results showed that PUVA worked best in patients with PPP, and in patients with chronic hand eczema (dry and dyshidrotic) both treatment modalities had beneficial effect. Patients were assessed at week 0, 3, 6, 9 and 10 weeks after the last treatment, and 21 of 25 and 12 of 15 patients completed the studies respectively.[3,4] In an older study PUVA soaks (8-Methoxypsoralen) were given to 80 patients over a 5 year period; 56 patients completed the study, of these 16 (29%) cleared more than 90%.[5]

For nine years UVB TL01 and PUVA soaks (Trioxysalen) have been available as treatment modalities at the Department of Dermatology, Odense University Hospital for severe hand dermatoses. The treatment modalities were options for patients with difficult to treat dermatoses at the discretion of the dermatologist.

According to the Danish Contact Dermatitis Group hand eczema may turn into a chronic disease, if the patient is not offered examination, guidance and treatment within the first 3 months.[6] A study by Lerbaek *et al.* found that 68% (96/142) still suffer from hand eczema at a follow up study 8 years later.[7] Other studies show if the patient has got one contact allergy, his risk of getting more contact allergies, a more severe hand eczema and a worse prognosis is increased.[8,9] Agner *et al.* found that patients allergic to *Compositae* and rubber chemicals had the most severe hand eczema, and patients allergic to *Compositae*, cobolt or paraphenylendiamine (PPD) had the lowest quality of life.[9] This suggested that patients allergic to *Compositae* had the worst hand eczema and their life quality is severely affected. In another study, 2 patients allergic to *Compositae* were treated with PUVA (systemic) together with systemic Prednisolone to be able to tolerate the phototherapy and both needed maintenance treatment to prevent flares.[10] Hand eczema can have a great influence on patients' life and quality of life because of the physical, psychological and social consequences.[11,12]

This study evaluated retrospectively the experience and effect of PUVA soaks and TL01 phototherapy for the treatment of severe chronic hand dermatoses with the purpose to reveal the beneficial effects in balance with the duration of effect and resources involved in performance of the treatment. Further, a subgroup of patients suffering from multiple contact allergies and *Compositae* allergy was interviewed to explore how their quality of life was influenced by the allergies and hand eczema in order to optimize the service provided by health professionals (Table 1).

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Materials and Methods

A retrospective quantitative evaluation of the records of patients who in the years 2008-2010 had received a *minimum* of 10 treatments in one course[13] for treatment of one of the following diagnoses: Psoriasis, hyperkeratotic eczema, PPP, vesicular eczema, *Compositae* dermatitis, and allergic contact dermatitis. All patients also received topical treatment with varying amounts of topical corticosteroids and moisturisers with inadequate effect, therefore phototherapy was added as supplement.

Psoralen plus ultraviolet A soak

The patient placed hands for 10 min in 2 L water of 37°C mixed with 1.0 mL Tripsor 0.5 mg/mL (Trioxysalen). The patient then placed hands on UVA unit (Waldmann PUVA 180), body and face covered. Initially was given 0.10 Joule/cm^2, dose was raised 0.05 Joule/cm^2 at each treatment if tolerated by the patient. Max dose was 1.20 Joule/cm^2.

TL01

The patient placed hands on TL01 unit (Waldmann UV 181 BL), body and face covered. Initially was given 0.1 Joule/cm^2

(eczema) - 0.2 Joule/cm^2 (psoriasis), dose was raised 0.10 Joule/cm^2 (eczema) - 0.20 Joule/cm^2 (psoriasis) at each treatment if tolerated by the patient. Max dose was 2.90 Joule/cm^2.

The observation period after a treatment course was 24 weeks, or until the patient was discharged. The treatment effect was evaluated at the end of a treatment course by clinical evaluation of the severity of the hand dermatosis in relation to the severity prior to treatment. Good effect was defined as healing of the dermatosis (effect 4) or at least 75% improvement (effect 3). Inadequate treatment effect was defined as clinical improvement less than 75%. The effect was evaluated again at the end of the observation period (24 weeks) or before if the patient had a relapse. Some patients had more than one diagnosis and were included once with the most prominent diagnosis.

Semi structured interviews were done with a subgroup of 6 patients with multiple contact allergies (3 or more positive patch tests) and *Compositae* allergy.

The informants were 49-67 years of age (mean age 56.5 years), and they had hand eczema for 12-42 years (mean number of years 38.5).

An interview guide was developed for this investigation with questions about daily life events in relation to the contact allergies and hand eczema *e.g.* handling work, daily activities, leisure time, and patients' perspectives on these matters, and patients' experiences and views on relationship with family, colleagues, friends, and other people.[14]

Patients' signed informed consents before the interviews, which were conducted in a neutral office in the ward or in patients' home according to their preference. Patients' were offered compensation for transport expenses in due course. The interviews were tape-recorded (26-50 min, mean number of min 40), transcribed word-for-word and then analysed and interpreted according to Steinar Kvale's concepts.[14] At the time of transcription each patient was given a fictive name. Interviews were rewritten into a shorter exact language easier to read with respect to meaning and the patients' ways of expressing themselves. The text of each interview was then categorised in topics and subtopics and reorganized according to this. The patients' statements were translated from Danish into English by the author.

Interpretation was done by reporting patients' statements, rewriting them as the author understood them, and then compare them with the chosen theory by Heggdal.[15] Patients go through four stages from the first symptoms and until they have accepted their chronic disease: uncertainty, loss, learning, and living with the disease.

Results

A total of 107 patients received 138 treatment courses of PUVA soaks or TL01 treatment, and 94 (81%) had ≥10 treatments in one course and a total of 121 courses.

Figures 1 and 2 show that in 45/121 (37%) courses of PUVA soaks or TL01 the treatment was given with a good result, and in 76/121 (63%) the effect was inadequate.

Side effects

In 10 courses of PUVA soaks 8 patients experienced erythema and/or a burning sensation and 5 complained of pruritus and/or pain. In 2 courses of TL01 the patients had erythema and pruritus. In all cases the duration of side effects was short.

Patients having less than 10 treatments in one course

In 18 courses 16 patients had less than 10 treatments.

In 9 courses treatment was discontinued because of side effects/exacerbation, and in 9 courses treatment was discontinued because of no effect or because the patient decided to stop.

Five patients had vesicular hand eczema, 4 patients had PPP, 4 had hyperkeratotic hand eczema, 2 had *Compositae* allergy and 1 had psoriasis.

In 3 cases patients tolerated phototherapy in earlier courses, which meant they were not excluded from the study.

Discussion

Local phototherapy is often chosen as a supplement to patients' treatment with topical steroids, and to make it possible for patients to stop using steroids for a period in order to minimize possible side effects, for instance atrophy of the skin. Local phototherapy can also be used as a supplement to or instead of systemic therapies if the patient does not tolerate or wish to use systemic therapies.

Patients suffering from psoriasis and hyperkeratotic eczema had the best effect of PUVA soaks and TL01 (Figure 3). The effect was good for psoriasis in half of the treatment courses concerning PUVA soaks, and in one third of the courses with TL01. The effect of PUVA soaks are in accordance with results published by O'Kane and coworkers[16] and Schempp and coworkers.[17]

Among patients with PPP and a total of 21 courses of PUVA soaks the effect was of questionable value as it only lasted in more than 3

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Table 1. Patient distribution regarding sex, age, number of treatments in one course, single, and cumulative doses of UVA for each diagnosis. (J=Joule/cm^2)

	Psoriasis	Hyperkeratotic eczema	Pustulosis palmoplantaris	Vesicular eczema	*Compositae* dermatitis	Allergic contact dermatitis
Sex						
Women	5	10	16	9	18	7
Men	8	15	5	5	2	2
Age						
Range	29-82	34-74	39-76	29-57	46-79	33-69
Median	57	52	59	46.5	54.5	51
Number of treatments						
Range	13-35	10-33	14-33	10-46	10-37	10-33
Median	21	23	22	22	15	20
Max single UVA dose						
Range	0.65-1.20 J	0.35-1.20 J	0.65-1.20 J	0.40-1.20 J	0.35-1.20 J	0.45-1.10 J
Median	1.05 J	1.10 J	0.90 J	0.83 J	0.65 J	0.85 J
Cumulative UVA dose						
Range	4.85-23.70J	2.35-26.40J	5.95-19.85J	2.07-39.20J	2.70-28.48J	3.85-13.45J
Median	13.45 J	13.70 J	12.30 J	10.45 J	5.53 J	10.76 J

months in 4 patients. The effect could therefore be spontaneous remission. Layton *et al.*[18] conducted a placebo-controlled study, in which PUVA soaks (8-MOP emulsion) or placebo were used in 18 patients and there was no convincing effect of active treatment.

Concerning vesicular eczema, one study reported that PUVA soaks (8-MOP solution) had good effect in 9/12 patients.[19] The Behrens *et al.* study might be influenced by the exclusion criteria, as patients treated with systemic medication within the last 8 weeks and topical medication within the last 4 weeks were excluded, implying that patients included might have less severe hand eczema. In this study 5/14 (36%) of the patients obtained good effect.

When evaluating the effect of PUVA soaks in patients with *Compositae* dermatitis, it is necessary to take into consideration that one patient accounted for 4 courses of good effect (effect 4) and the treatment was combined with systemic steroid which might amplify the effect. TL01 also worked well in the patient but the effect did not last. If this patient was left out, only one patient had good effect of the treatment, meaning 1/15 (7%). In 14 courses (93%) the treatment was given with inadequate effect (effect 2, 1, 0). In 3/9 (33%) patients with allergic contact dermatitis PUVA soaks were given with good effect. The effect lasts for the observation period in 2 patients.

No direct relationship was found between effect and number of treatments given. The treatment effect often began after 10-12 treatments, and patients who do not experience effect after 1 month seldom do so later,[13] it seems reasonable to discontinue the treatment after 15 treatments if the patients have no effect. This corresponds to the Scottish treatment protocol from Photonet in which treatment is recommended discontinued if the patient does not experience more progress for 4 treatments in a row.[20] In patients, who had more courses of PUVA soaks and TL01 phototherapy, the pattern of effect might differ from course to course. Several factors might influence this *e.g.* the fluctuation of disease severity, the time of year and environmental exposures at work and at home.

A weakness in the study is the retrospective nature of data collection based on patient records with sometimes inadequate information.

Some patients were treated with systemic treatments *e.g.* Methotrexate or Neotigason before, during or after phototherapy. Most of the patients were treated with topical steroids (group 3 or 4), and all patients used moisturizers. The present results cannot be compared with the outcome of other studies due to characteristics of the selected patients material and possible differences in treatment protocols. However, the data are valuable as an audit for our department.

Reservations must also be taken due to the low number of patients included.

It was not possible to compare the effect of PUVA soaks and TL01 as only few patients received TL01. And as only few patients in the study had TL01 it was not possible to comment on the effect of the treatment to the included diagnoses.

To be able to judge the effect of the treatment it is recommended to document patients' symptoms at the 1st treatment and after 4 weeks. If the patients have no effect the treatment can be discontinued. If the patients have little effect treatment continues and the patients' symptoms and thereby effect are judged every 2 weeks. When no further progress is observed the treatment is discontinued.

Uncertainty and escaping the sick body

The informants did not understand why they got hand eczema. The hand eczema had great impact on them and their self esteem. At first they ignored the eczema, it got worse, and eventually they had to deal with it. One saw a doctor after 2 years.

I thought: It will disappear. It did, but then it got worse and worse... I have no idea what started it. (woman, 67 years old)

Reduced life, sorrow and sadness

Realizing having the eczema the informants felt depressed and tired. They needed to retreat to acquire peace and time to cope with the situation.

The following topics were found to be of significance: Affected state of mind, lack of energy, retreat from other people, and the importance of close relatives.

Afffected state of mind

Especially as the last allergy was Compositae, I almost ran from here crying. I dreaded this most. No, it is definitely not funny. (woman, 50 years old)

The garden was important to some informants. Working in the garden, being surrounded by plants and flowers, staying in the garden with friends and family, and participating in outdoor activities gave them quality of life.

The worst of my diseases is the eczema. It influences my quality of life the most. I feel I am no good. I can do nothing. (woman, 67 years old)

The informants felt sad and restricted by the hand eczema, and they felt less worthy as human beings. They were troubled by symptoms like severe itching, pain and bleeding.

Lack of energy

I am happy when it is not there. Honestly, I get much more energy. (woman, 59 years old)

When I get home from work there is no energy left to do anything, because it takes up so much room. It hurts, and I am finally at home and can relax a little. At such times not much is being done. (woman, 56 years old)

At times with severe hand eczema the informants only managed to carry out the most important duties. With those at work, the job was their priority, and with those at home likewise only the most important jobs were done.

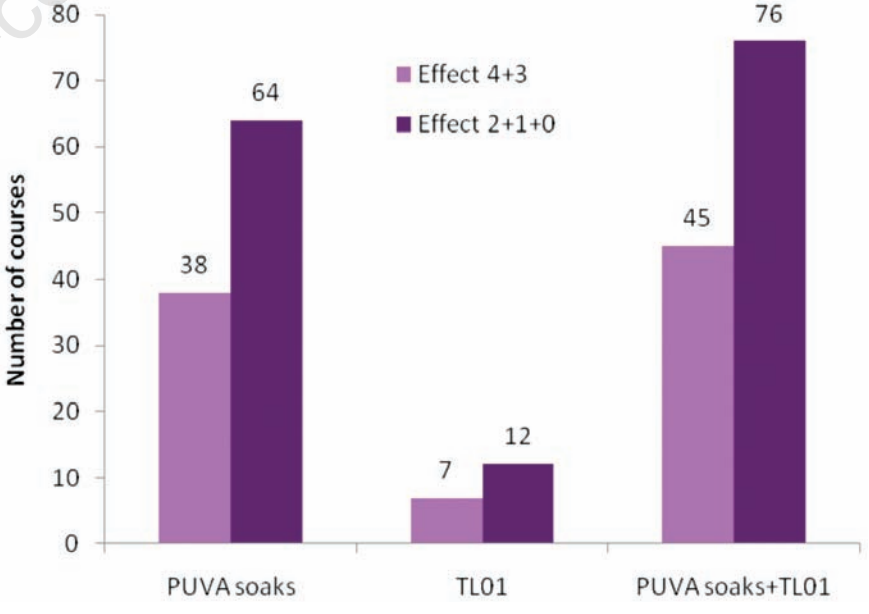

Figure 1. Good effect (effect 4, 3) and inadequate effect (effect 2, 1, 0) of PUVA soaks, TL01, and both treatment modalities together. Number of treatment courses stated.

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Retreat from other people

I did not have any social contacts, and I didn't want to be with my girlfriend either looking like this. (man, 49 years old)

The informant retreated from colleagues, friends, and girlfriend because he could not stand his symptoms and the way he looked. He also retreated to avoid further confrontation with the situation and thereby protected himself from any more pain.

If we were going to a party and I had to say hello to many people, I kept my gloves on, and that was hard on me to begin with. I wondered if people thought I was contagious. But in the end I realized that I had to think of myself, otherwise I could go nowhere. (woman, 57 years old)

Keeping up social activities took consideration and coming to terms with the situation before the informants could do so without strain *e.g.* using gloves and clothes also in warm weather. When the informants have come further in the process of living with hand eczema, they retreated from other people to protect themselves and because other people retreated from them. *E.g.* staying indoors or staying at home, explaining to people when they switched to another queue or ignoring them.

The significance of close relatives

Bent (husband) does not do housework, but he can peel onions for me and shape hamburgers. (woman, 56 years old)

I have a good family and a very good husband, he has been there for me the whole time. He is worth his weight in gold. He helps at home. He often says: Leave that. (woman, 67 years old)

The informants indicated how their close relatives helped to do practical housework, work in the garden, and offered support. Two informants described good support and help by relatives. With the other informants my impression was that they had to ask for help, which could be difficult.

Bodily learning and strengthened hope

The informants were eager to learn, but they also found it difficult to gather information on which plants and food were *Compositae*. Every time of success was a victory because they then knew more about how to prevent the eczema. They learnt to take care of their hands by using moisturizers and glove protection. They also learnt to be aware of limits in relation to skin tolerance *e.g.* in relation to housework, the use of gloves and staying outside.

The informants were vulnerable in respect to the way they were met by people *e.g.* informants who could see no pattern in their way of living, flares, and recovery gave up on it, their feeling of not being taken serious by health professionals accentuated this.

It is a science to find out, which plants are Compositae, you cannot look them up in a book, you can, but you will only find a few. (woman, 50 years old)

I get happy every time I find something that is no good for me. (woman, 67 years old)

I wrote a note, and when I could do no more... I continued the next day...I knew if I did too much, my hands would hurt. (woman, 57 years old)

Lately, especially after having phototherapy (TL01), it (the eczema) has changed, the itching has become different. (woman, 57 years old)

Almost all the time I think of and remember that I have to take care of my hands. (woman, 57 years old)

If only… but I can find no system. That is why I stopped coming here (dermatological clinic). I felt that I wasted my time, and I saw different doctors every time. (woman, 56 years old)

Embedded bodily knowledge, living with hand eczema

The informants indicated that they lived their lives with hand eczema and contact dermatitis in the way they wanted to in spite of limitations. They succeeded doing so by taking into account the knowledge and experience they had acquired and by being constantly alert. Limitations were of more or less nuisance according to the informants' individual interests.

In cases of flares they knew what to do, they were able to begin treatment or to ask for help *e.g.* in the department of dermatology. They were worried about the long-term effect of systemic steroid, but at the same time they were aware that they could not do without it in cases of severe flares.

I live with it in the way that I always try to be alert. I think of what I eat, what I do... If I don't, I know I will start flaring and I don't want that. (woman, 50 years old)

I feel it starting, my hands get rough. Then I start using ... (a topical steroid), I sleep with gloves on and so forth. (woman, 67 years old)

(PUVA soaks) is probably the best thing happened to me. I feel completely different after treatments. (woman, 59 years old)

I am a little worried that I get so many tablets (steroid). I am afraid they will damage me inside. I don't like that. (woman, 59 years old)

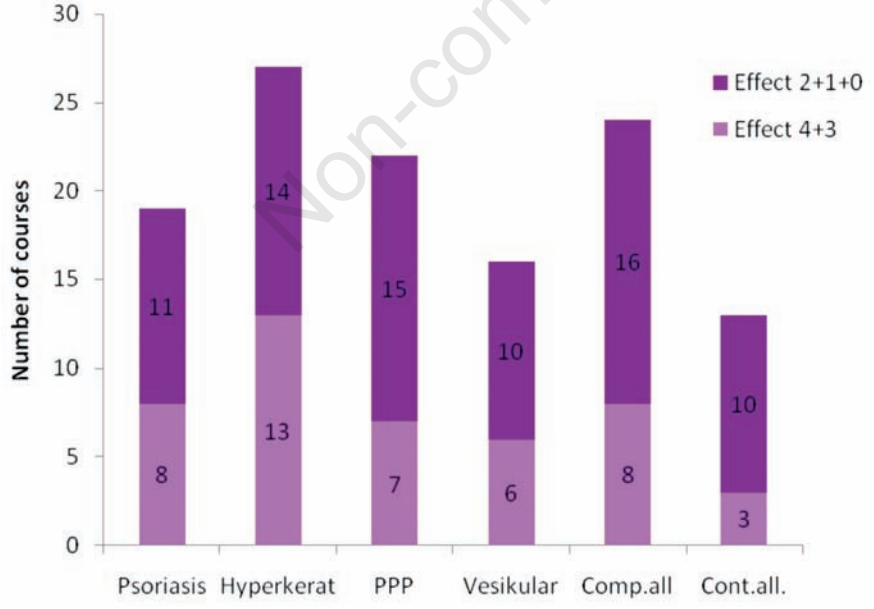

Figure 2. Effect of both treatment modalities divided on diagnoses. Good effect (effect 4, 3) and inadequate effect (effect 2, 1, 0). Number of treatment courses stated.

Conclusions

The informants agreed that hand eczema fiercely intruded their lives as it affected them physically, psychologically, socially, and existentially and thereby had great influence on their daily living and quality of life. *E.g.* the informants stated they had a lot of pain, they were very bothered by itching, they constantly had to be alert and perseverant in looking after and treating their hands, they were noticed by other people, they looked different and were different to touch, and other people kept a distance. This corresponds with Diepgen stating that patients are not satisfied if health professionals only focus on treating visible signs of disease as the burden of disease is even more important.[21] This is in accordance with Fowler who states that hand eczema is to be regarded as an impor-

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tant challenge in the health services.[22]

As reported by Cvetkovski other studies reveal that patients' quality of life improve when patch tested and positive reactions are found,[23] in this study the informants were relieved to know what they did not tolerate. With knowledge they were able to act in order to ease their eczema and regain control of their lives. Having a chronic disease includes the risk of recurrent relapses, which is trying for both patients and health professionals.[22,24] In such situations the informants might benefit from the self esteem and confidence gained when the eczema was at ease, situations with feelings of having knowledge and control. In the study one informant chose to be discharged from the clinic because of the lack of feeling in control.

Motivation and perseverance are important qualities having a chronic disease like hand eczema.[25] The informants living best with their hand eczema described this very well. All the time they were alert, taking care, beginning treatment and taking extra precautions as soon as they sensed a flare was on its way. *E.g.* they all used a moisturizer of a high content of fat, and one used different moisturizers according to the eczema and the informant's activities. All informants were worried about possible side effects to local or systemic steroid treatment. This is also referred to in Niemeier's study.[25] All the informants used gloves to varying degrees. They considered whether the gloves made them sweat, as this made their eczema worse, and they considered their activities. More studies emphasize the use of moisturizers and gloves as being the most important factors in the prevention of hand eczema, and also as important factors in the treatment of flares together with local steroids.[26,24] Concerning phototherapy two informants were very satisfied with the effect of this, one had recurrent good effect of PUVA soaks, and one experienced that treatment with TL01 made the eczema change into being milder. Another factor which is emphasised concerning allergic contact hand dermatitis is the importance of avoiding the allergen.[26,27] This may be extremely difficult with *Compositae* allergy as the plants in the family are widespread both as cultivated plants, weeds, and vegetables as well as the allergen being airborne.[28] The informants did their best to avoid *Compositae* taking their own experiences into account. They wore clothes, stayed indoors, and converted their gardens, which restricted their interests, activities, and social lives. Having to beware of their diet bothered them the least, as it was of no importance to them avoiding cosmetics containing *Compositae*.

Concerning work one informant was able to keep the job, one was able to make arrangements to stay employed, one found a new job, and three had pension. This contradicts to a study mentioned by Diepgen in which 15% leave work because of hand eczema.[21] It might have been of some importance that all the informants in this study had wet work, which could have made it more difficult for them to take necessary precautions.

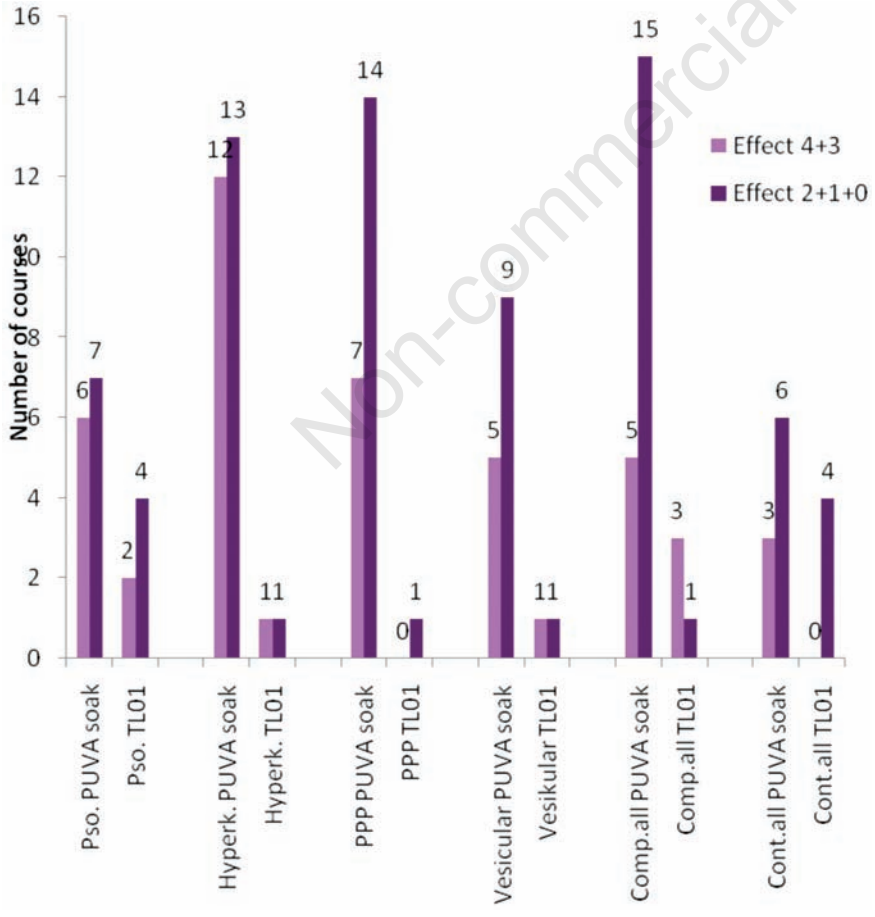

Figure 3. Good and inadequate effect of PUVA soaks and TL01 shown for each diagnosis. Number of treatment courses stated.

Recommendation

To be able to help future patients in carrying and possibly ease their burden of living with chronic hand eczema and allergic contact dermatitis health professionals are suggested to support patients in finding joy and experiencing victory of finding out what they do not tolerate and what works in their situation. This means helping them to find their individual limits and solutions according to limits and preferences. Our task as health professionals is to make our theoretical and experience based knowledge available to the patient, *e.g.* about hand eczema, allergy, treatment, and prevention. The information must be adapted to the patient's capability at the time. The patient's task is to transform the knowledge presented into practical knowledge in the patient's current life situation. Health professionals must continuously be ready to offer more knowledge or to challenge the patient to consider the situation.

In order to optimize the learning situation it is proposed that the patient is connected with a team of doctors and nurses having the necessary knowledge, also as the patient might be coming back over some time.

Health professionals are also suggested to visit patient's home and work in order to gather more information and inspiration for the education of this and other patients.[29]

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