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Title:

Treatment of severe, chronic hand eczema. Results from a UK-wide survey.

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Running Head: Treatment of Hand Eczema in the UK

Learning Points:

- Currently, treatment pathways for severe hand eczema in the UK are diverse
- PUVA and Alitretinoin are both widely used as first choice treatment for severe hand eczema
- The majority of UK dermatologists are very concerned with the potential side effects of long term or repeated use of Ciclosporin A
- Further studies reflecting standard practise are needed to guide treatment pathways.

Abstract

Treatment of severe hand eczema (HE) which is resistant to topical potent corticosteroid treatment is challenging. In 2013 we surveyed 194 UK dermatologists to obtain information about usual treatment pathways to inform the choice of the comparator in a trial of alitretinoin in severe HE (ALPHA trial); the results indicate that treatment approaches differ among UK dermatologists. Psoralen combined with ultraviolet A (PUVA) and alitretinoin were identified as the most frequent first line treatment options for hyperkeratotic HE, whereas oral corticosteroids were identified as frequent first line treatment for vesicular HE, followed by PUVA and alitretinoin. In terms of potential side effects of long-term or repeated use, oral steroids and ciclosporin A were reported to cause most concerns. There is uncertainty about which treatment gives the best short and long-term outcome due to a lack of definitive randomised controlled trials evaluating the effectiveness of different treatment pathways in severe HE.

Introduction

Hand Eczema (HE) is common with up to 10% of the population reporting the presence of HE at least once in a single year[1-3]. HE has an average disease duration of over 10 years. It is estimated that 5-7% of all HE patients may develop severe, chronic HE[4] (CHE) which is resistant to treatment with potent topical corticosteroids. CHE has a poor prognosis and can cause considerable impairment of patients' quality of life. The overall socioeconomic impact is also high due to prolonged sick leave, job changes and unemployment[1,4].

Treatment of severe CHE resistant to topical treatment with potent corticosteroids is challenging and treatment response is often unsatisfactory. There is a knowledge gap as to what is the most effective short and long-term treatment for severe CHE due to a lack of randomised controlled trials (RCTs) that directly compare first line HE treatments on which therapy recommendations could be based. Previously published studies are difficult to compare due to heterogeneous patient populations with different HE subgroups or severity, duration of treatment and outcomes used[5].

As data on current treatment pathways for severe CHE in the UK were lacking, we distributed a survey via the UK Dermatology Clinical Trials Network and British Association of Dermatologists to inform the choice of comparator arm in the ALPHA trial. A total of 194 dermatologists responded

to the survey consisting of 8 questions (supplementary Table S1) on the treatment of severe hyperkeratotic or vesicular CHE. The treatment options included: PUVA, alitretinoin (9-cis retinoic acid), narrowband UVB, ciclosporin A, oral steroids, methotrexate, azathioprine, mycophenolate mofetil and acitretin.

Report

PUVA and alitretinoin were considered as first choices for the treatment of hyperkeratotic CHE by 40.2% and 30.9% of the dermatologists surveyed, whilst narrowband UVB and mycophenolate mofetil would never be used by 45.4% and 38.1% (Figure 1A). The first choice of treatment for vesicular CHE differs to hyperkeratotic CHE; 37.6% of those surveyed would consider oral steroids first with PUVA and alitretinoin considered as first line treatment by 26.3% and 15.5% respectively. Narrowband UVB, acitretin and mycophenolate mofetil would never be used for the treatment of vesicular CHE by 43.3%, 37.1% and 35.1% respectively (Figure 1B). The survey results also indicated that, 58.2% and 41.2% were very concerned about the potential side effects of long-term (e.g. 3 months or longer) or repeated use of oral steroids and ciclosporin A respectively (Table 1).

The surveyed dermatologists had diverse opinions on the most effective treatment for severe HE in terms of long-term outcome (e.g. stable 3-6 months after cessation of therapy) with alitretinoin and PUVA considered to be most effective by 42.3% and 28.9% respectively (Table 2).

The survey results indicated that topical steroids are frequently recommended for use in conjunction with systemic treatment for the management of severe CHE. Most frequently used topical steroids belong to the "very potent" and "potent" class including clobetasol propionate 0.05% (Dermovate; N=101 (52.3%)), mometasone furoate 0.1% (Elocon; N=55 (28.4%)) and betamethasone valerate BP 0.1% (Betnovate; N=32 (16.5%)). The majority of emollients recommended by those surveyed were non-urea containing and it was acknowledged that patients' preferences are important.

Discussion

Existing evidence on systemic treatment options with special focus on alitretinoin has been summarised in the Evidence Review Group's Report[6] on alitretinoin for the treatment of severe CHE. The report highlighted that although alitretinoin has been demonstrated to be efficacious for the treatment of severe CHE that is unresponsive to potent topical corticosteroids, data are lacking in terms of comparison to other treatment approaches, and longer term (>48 weeks) outcomes including relapse.

The benefits of emollient therapy are widely accepted. The survey indicated that dermatologists recommended the use of emollients and topical steroids in conjunction with systemic treatment and PUVA. However, none of the published RCTs on alitretinoin permitted the use of topical steroids concomitantly or during follow-up, and the results of these trials are therefore not directly applicable to standard NHS practice.

The combination of 5- or 8- methoxypsoralen followed by broad-band UVA exposure is frequently used for conditions including psoriasis and eczema affecting hands and feet. Although this survey did not distinguish between systemic and topical PUVA (where methoxypsoralen is applied in form of immersion, cream or gel) clinical experience in a number of UK centres suggests that systemic PUVA is effective, however it can show systemic side effects, and has been replaced in many dermatology centres in Europe and the UK by topical PUVA treatment as a well-tolerable alternative[1,7]. The effectiveness of topical PUVA has not been compared to other treatment approaches for severe CHE and available studies on PUVA treatment in CHE are all based on small numbers of patients. Further, these studies used different HE severity subgroups and outcome measures compared to the alitretinoin studies thus preventing a comparison of both treatments across studies.

In summary, when patient education[10], allergen/irritant avoidance and topical treatment are insufficient to control the disease, UV therapy or systemic immune-modifying drugs are used[1,8,9]. Despite alitretinoin being the only licensed systemic agent for severe CHE unresponsive to potent topical corticosteroids, these survey results indicate that treatment approaches for severe CHE differ among UK dermatologists. Some comments provided were that: "Alitretinoin is new and expensive so limited use in practice so far", "UVB very helpful but logistically very difficult to persuade patients into thrice weekly visits for 2-3 months". The survey results demonstrated uncertainty about which treatment gives the best long-term outcomes and additional comments provided indicated that this is due to limited evidence comparing treatment pathways in severe CHE indicating a need for RCTs. The survey identified alitretinoin and PUVA as popular first treatment choices for both severe hyperkeratotic and vesicular CHE. These results were used to inform the design of the ALPHA trial which will compare alitretinoin with immersion PUVA as used in standard practice for the treatment of severe CHE which is unresponsive to treatment with potent topical corticosteroids. The trial will evaluate outcomes at short (12 weeks) and longer term (up to 52 weeks) timepoints using various outcomes for comparability with other studies and will describe second line treatments in patients with a poor response to first line therapy.

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References

1. Coenraads, P.J. Hand eczema. N Engl J Med 367, 1829-1837 (2012).
2. Hald, M., Berg, N.D., Elberling, J. & Johansen, J.D. Medical consultations in relation to severity of hand eczema in the general population. Br J Dermatol 158, 773-777 (2008).
3. Meding, B. & Jarvholm, B. Hand eczema in Swedish adults - changes in prevalence between 1983 and 1996. The Journal of investigative dermatology 118, 719-723 (2002).
4. Diepgen, T.L., et al. Management of chronic hand eczema. Contact Dermatitis 57, 203-210 (2007).
5. Weistenhofer, W., Baumeister, T., Drexler, H. & Kutting, B. An overview of skin scores used for quantifying hand eczema: a critical update according to the criteria of evidence-based medicine. Br J Dermatol 162, 239-250 (2010).
6. Paulden, M., et al. Alitretinoin for the treatment of severe chronic hand eczema. Health Technol Assess 14 Suppl 1, 39-46 (2010).

7. Halpern, S.M., et al. Guidelines for topical PUVA: a report of a workshop of the British photodermatology group. Br J Dermatol 142, 22-31 (2000).
8. English, J., et al. Consensus statement on the management of chronic hand eczema. Clin Exp Dermatol 34, 761-769 (2009).
9. Van Coevorden, A.M., et al. Overview of studies of treatments for hand eczema-the EDEN hand eczema survey. Br J Dermatol 151, 446-451 (2004).
10. Ibler, K.S., et al. Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: randomised clinical trial. BMJ 345:e7822 (2012).

Legends

Figure 1

Treatment choice for hyperkeratotic (A) and vesicular (B) HE.

The graph depicts the percentage of responses of all dermatologists surveyed for each category given.

Table 1

Concern about potential side effects of long term (e.g. longer than 3 months) or repeated use of treatment

The table shows the number and percentage of responses received for each treatment option.

Table 2

Long-term treatment outcome and concomitant topical corticosteroids

The table gives number and percentage of responses received for each treatment option.