A pilot comparing ultraviolet modalities for hand eczema
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although less so initially to children and parents. It involves a general anaesthetic, surgical placement of a permanent device that can erode fragile skin, ongoing maintenance and a significant adjustment in body image. Is it worthwhile? The systematic review in the current issue of the British Journal of Dermatology by Zidorio et al.\(^1\) addresses this question.

Evaluation of therapy in this complex, heterogeneous, rare disease is difficult. There are no randomized controlled trials of GGT in EB: the seven suitable studies selected from a literature trawl of 641 were case series. Most involved children with RDEB and the authors included only studies providing anthropometric data and patient- or carer-reported outcomes. They conclude that nutritional status usually, but not always, improves. Interestingly, some patients report better life quality even when growth parameters have worsened, perhaps reflecting the extreme burden of maintaining oral intake.\(^3\) Effects on skin blistering, healing and activity levels are hard to quantify and are rarely documented. Complications led to GGT removal in 10% of patients. Unanswered questions include optimum diet and timing: should it be placed before or after malnutrition becomes a problem?

Surgical technique was not covered in this review, so failed procedures and immediate complications would not have been picked up. Endoscopic GGT placement risks mucosal damage, while placement via a laparotomy is invasive and likely to be complicated by chronic leakage. A laparoscopic approach has been used successfully.\(^3\)

Professionals managing EB need to share experience and collect consistent data on procedures, complications, nutritional status and EB-related quality of life. This can be achieved only if those managing patients with EB consult with expert centres, which in turn should collaborate.\(^4\) The organizations Debra International and EBClinet are leading the way in developing clinical practice guidelines.\(^5\) The U.K. has the unique advantage of a National Health Service and national Highly Specialized Service for EB: four of the seven studies came from U.K. centres but even these were not ideal. The newly established European Reference Network for Rare and Low Prevalence Complex Disease,\(^6\) with a specific sub-thematic group for EB, offers exciting opportunities for collaborative research, which patients and professionals sorely need.

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Conflicts of interest

None to declare.

References


Supporting Information

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A pilot comparing ultraviolet modalities for hand eczema: shedding light on feasibility

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In this issue of the BJD, Brass and colleagues report the results of a pilot study in which they explore the feasibility of performing a large randomized controlled trial (RCT) comparing psoralen–ultraviolet A (PUVA) and narrowband ultraviolet B (NBUVB) for the treatment of chronic palmar hand eczema.\(^1\)

It is very important that pilot studies are carried out, both financially and methodically. A full-scale RCT will ideally be performed only if its design proves feasible in a pilot. Potential flaws can be identified and dealt with, increasing the chance of performing a meaningful definitive study with practical implications. However, one should be very careful about the interpretation of efficacy data from pilot studies. Because pilot studies often contain the first structured assessment of the effect of an intervention, no robust sample-size calculation can be performed a priori. No sound conclusions can be made based on an insufficient sample size. One can often only really draw conclusions regarding feasibility.\(^2\)

Brass et al.\(^1\) venture to make some cautious statements on efficacy outcomes. They conclude that both PUVA and NBUVB improve the severity of chronic palmar hand eczema. However, few considerations put this conclusion in a different light.
The primary efficacy outcome measure used in the study is a Physician Global Assessment (PGA) that is used in a large placebo-controlled trial with the retinoid alitretinoin in hand eczema. This PGA incorporates not only objective signs like fissures and erythema, but also the subjective (patient-reported) items ‘pain’ and ‘itch’, which influence the severity score, making it hard to reproduce this outcome and making proper comparison between patients and between studies difficult. The authors argue that a more objective outcome like the Hand Eczema Severity Index (HECSI) might be a preferable alternative. Although true, it should be noted that this instrument needs to be validated more extensively before using it as primary efficacy outcome in trials. Furthermore, this pilot studied only patients with palmar hand eczema. A measurement instrument for the severity of solely palmar hand eczema has not yet been developed.

It is strongly recommended to patch test all patients with chronic hand eczema in routine daily practice. No patch testing was performed prior to this pilot. Because patients with hand eczema frequently have allergic contact dermatitis it is vital to take this into account. Patch testing will reduce the bias of inclusion of patients into studies while they still have major exposure to contact allergens that might be highly relevant for the severity of their hand eczema.

On the subject of feasibility, the authors see some issues. A large sample size will be needed for the definitive trial, while the rise of systemic therapy may lead to a reduced demand for phototherapy. Results of the ongoing ALPHA trial, comparing PUVA with alitretinoin for uncontrolled severe chronic hand eczema, will significantly influence whether there will be a need for a full-scale trial comparing PUVA with NBUVB. If such a need does arise, processing the issues mentioned above, along with the limitations that the authors state in their discussion will contribute to the design of a more comprehensive and meaningful clinical trial.

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Conflicts of interest
None to declare.

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References


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Aldara-induced dermatitis is associated with development of liver fibrosis in mice

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Liver fibrosis is a wound-healing response that occurs secondary to insults from hepatocyte lipid accumulation, inflammation and exposure to toxins, such as methotrexate and alcohol. A 2017 population-based study (people with psoriasis: n = 197 130) supported what other studies have previously shown: people with severe psoriasis are more likely to have liver fibrosis and cirrhosis than age-, sex- and BMI matched controls in the general population.

Liver fibrosis is a multifactorial disease; therefore, in human studies it will always be a challenge to disentangle the relative weighting of multiple potential risks (burden of inflammation, alcohol, obesity) on fibrosis development and progression. One strength of animal studies is the ability to investigate the impact of one risk alone.

Does psoriasis cause liver fibrosis? In this issue of the BJD, Vasseur et al. publish data to suggest that, in mice, cutaneous inflammation induced by repetitive applications of imiquimod-containing Aldara cream is associated with the development of hepatitis and liver fibrosis. (In mice both the vehicle in Aldara and imiquimod contribute to inflammation.)

Vasseur et al. compared two groups of mice (n = 10 mice/group). The first group were exposed to Aldara over 9 weeks;