Evidence-based medicine for atopic eczema

Brown, S. J.

Published in:
British Journal of Dermatology

DOI:
10.1111/bjd.15247

Publication date:
2017

Document Version
Peer reviewed version

Editorial for BJD

Identifying the knowns and unknowns in eczema treatment

Linked article: Nankervis et al. What is the evidence-base for atopic eczema treatments? A summary of published randomised controlled trials. BJD-2016-0442.R1

Sara J Brown

Atopic eczema (atopic dermatitis; eczema[1]) is a condition very frequently encountered in clinical practice, but it can present considerable challenges in providing effective and holistic care. The patient perspective is also one of challenge and sometimes frustration with the multitude of different treatment options; these may be purchased or prescribed on a trial-and-error basis because of the lack of substantive evidence of efficacy or inefficacy. Many relatively inexpensive and low-risk treatments are used empirically, but the high population prevalence of atopic eczema combined with the chronically relapsing nature of this disease results in a large cumulative expense of treatment. The economic burden attributable to eczema was estimated to be £465 million/year in the UK as long ago as 1996[2] and in the USA a retrospective study in 2002 identified the annual cost of medical services and prescription drugs for the treatment of atopic dermatitis/eczema to be between $0.9 billion and $3.8 billion[3]. In the light of this economic burden and recent advances in evidence-based healthcare it is perhaps surprising that significant gaps in knowledge remain.

The summary presented by Nankervis *et al.* in the *BJD* this month[4] represents the result of a substantial amount of work conducted by a group from the Centre of Evidence Based Dermatology in Nottingham, UK. This well respected team of dermatologists and dermato-epidemiologists was commissioned by the UK's National Institute of Health Research (NIHR) to perform a comprehensive review to update a summary of evidence for eczema treatments that had been published in the year 2000. The NIHR is a UK government-funded body and part of the UK's National Health Service; its purpose is 'to conduct leading-edge research focused on the needs of patients and the public'[5]. The current work was requested and funded by the NIHR to provide an accessible evidence-base for healthcare professionals, patients, guideline writers and clinical researchers[4].

The authors have performed a 'scoping review' which is a strategy used to investigate a broad research question, in this instance the effectiveness of treatments for atopic eczema. A scoping review is designed to summarise the current knowledge-base and identify gaps in research for future systematic reviews and/or clinical trials[6]. In this piece of work, owing to a very large number of available publications, the review included only systematic reviews and randomised controlled trials (RCTs) since, as the authors state, these were likely to offer the most unbiased evidence. The review included a very broad range of interventions and outcomes, reflecting the diversity within eczema trials, and including patients of all ages. Treatments are helpfully categorised according to whether there is: evidence of benefit; evidence of no useful benefit; insufficient evidence; or absence of RCT evidence. Whilst a scoping review is primarily a qualitative study, trials were also assessed for risk of bias (using a Cochrane collaborator's tool) and inter-individual agreement in the review team was said to be 'good'[4].

The summary demonstrates that over the update period (*i.e.* 2000-2013 compared to pre-2000), the greatest increase in RCTs has been in testing emollients, topical immunomodulators and other topical treatments; interestingly the numbers of RCTs for dietary interventions and systemic treatments have also doubled. The authors highlight the

proactive use of twice-weekly topical corticosteroids or calcineurin inhibitors to maintain eczema remission[7] as a noteworthy addition and useful strategy in caring for patients with moderate-severe eczema. Equally important evidence that should prompt consideration of a change in clinical practice is the list of interventions for which there is 'reasonable evidence of no benefit in treating eczema'. This list includes: twice-daily as opposed to once-daily topical corticosteroids; antibiotic-containing corticosteroids for non-infected eczema; probiotics and dietary supplements for treating eczema; and ion-exchange water softeners for moderate-severe atopic eczema[4].

However, despite a very thorough search of the research literature, the review sheds light on a field in which some findings are disappointing to say the least. The reporting of trials is said to be 'generally poor' and only 8% (22/287) of RCTs were defined by the team as having low risk of bias in randomisation, allocation concealment and blinding[4]. However it should also be bourn in mind that dermatological research presents some specific challenges in the blinding of participants and complex treatments, such as educational interventions, cannot effectively be concealed. In total 193 trials including more than 13,500 participants had been conducted to investigate treatments for which it is concluded that more research is required; a preponderance of small, poorly conducted trials is likely to have contributed to this waste of valuable resources. Lastly, there is a notable lack of RCTs conducted in primary care, despite evidence of clinical need in this setting.

It may be surprising to some readers to note that there is currently no RCT evidence for commonly used interventions including zinc or ichthammol medicated bandages. Furthermore, interventions that may appear to be common sense, *e.g.* soap avoidance, are also currently unproven by the very focussed methodology of RCT. The authors call for further, well-designed and adequately powered RCTs as the gold standard with which to assess these interventions and treatments. However, given the significant cost implications of undertaking what are likely to need to be large clinical trials, a detailed health economic assessment is warranted[8] to assess the balance of value, both financially and clinically, in further investigating these widely used empirical interventions.

The authors' entire review is freely available as an NIHR web-resource[9] and this includes important additional information on the dangers/drawbacks associated with some treatments. In addition, the Nottingham group have produced a publically-available online resource, the GREAT database (Global Resource of EczemA Trials)[10] which they plan to update 'to provide a comprehensive, easy to use resource that contains summary information about systematic reviews and randomised controlled trials of eczema treatments in order to facilitate the identification of published eczema research and to speed up future eczema research projects' [10].

The scoping review and accompanying GREAT database are relevant for practicing clinicians and should provide a valuable starting-point for any researcher considering performing a clinical trial in the treatment of atopic eczema. It will also be a powerful resource for clinical guideline-writers. Important gaps in knowledge have been highlighted for further work and we should all be mindful of the need for rigorous, carefully designed, adequately powered RCTs (where appropriate) to avoid future waste in research[11].

Acknowledgements

SJB's salary is supported by the Wellcome Trust (Senior Research Fellowship in Clinical Science ref 106865/Z/15/Z). I am grateful to Dr Matthew Ridd, Centre for Academic Primary Care, University of Bristol, for critically reading and commenting on this editorial.

Funding

Nil

Conflicts of interest

The author has submitted a patent application (GB 1602011.7) relating to a mechanism for *EMSY* in skin. SJB is currently collaborating with Prof Hywel Williams and Prof Kim Thomas on two NIHR-funded clinical trials in eczema (one is completed and one is on-going).

References

1 Johansson S, Bieber T, Dahl R *et al.* Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol* 2004; **113**: 832-6.

2 Herd RM, Tidman MJ, Prescott RJ *et al.* The cost of atopic eczema. *Br J Dermatol* 1996; **135**: 20-3.

3 Ellis CN, Drake LA, Prendergast MM *et al.* Cost of atopic dermatitis and eczema in the United States. *J Am Acad Dermatol* 2002; **46**: 361-70.

4 Nakervis H. What is the evidence-base for atopic eczema treatments? A summary of published randomised controlled trials. *Br J Dermatol* 2016.

5 NIHR. http://www.nihr.ac.uk/. In. 2016.

6 Armstrong R, Hall BJ, Doyle J *et al.* Cochrane Update. 'Scoping the scope' of a cochrane review. *J Public Health (Oxf)* 2011; **33**: 147-50.

7 Schmitt J, von Kobyletzki L, Svensson A *et al.* Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: systematic review and meta-analysis of randomized controlled trials. *Br J Dermatol* 2011; **164**: 415-28.

8 Sach TH, McManus E, McMonagle C *et al.* Economic evidence for the prevention and treatment of atopic eczema: a protocol for a systematic review. *Syst Rev* 2016; **5**: 90.

9 http://www.journalslibrary.nihr.ac.uk/pgfar/volume-4/issue-7 - abstract. In; NIHR Journals.

10 http://www.greatdatabase.org.uk/GD4/Home/Index.php : The Global Resource of Eczema Trials. In; Centre of Evidence Based Dermatology.

11 Ioannidis JP. Why Most Clinical Research Is Not Useful. *PLoS Med* 2016; **13**: e1002049.