Systematic review of treatments for atopic eczema

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Authors' objectives
To produce an up-to-date coverage 'map' of randomised controlled trials (RCTs) of treatments for atopic eczema, and to assist in making treatment recommendations by summarising the available RCT evidence using qualitative and quantitative methods.

Searching
MEDLINE (from 1966 to the end of 1999), EMBASE (from 1980 to end of 1999), the Cochrane Controlled Trials Register, and the Cochrane Skin Group's Specialised Register were searched using the search terms provided in the report. These searches were supplemented by handsearches of atopic eczema conference proceedings, a follow-up of the references in retrieved articles, contact with atopic eczema researchers, and requests to pharmaceutical manufacturers with an interest in the area of atopic eczema.

Study selection
Study designs of evaluations included in the review
RCTs were included.

Specific interventions included in the review
Therapeutic agents used in the prevention or treatment of atopic eczema. These included: oral cyclosporin; topical corticosteroids; psychological approaches; ultraviolet light therapy; maternal allergen avoidance; oral antihistamines; Chinese herbs; dietary restriction; homeopathy; house dust mite reduction; massage therapy; hypnotherapy; evening primrose oil; emollients; topical coal tar; topical doxepin; the avoidance of enzyme-based washing powders; cotton versus synthetic clothing; biofeedback; the frequency of steroid application; topical antibiotic and steroid combinations; and antiseptic bath additives.

Participants included in the review
Babies, children or adults who have atopic eczema or atopic dermatitis according to the diagnostic criteria of Hanifin and Rajka (see Other Publications of Related Interest No.1), or as diagnosed by a physician.

Outcomes assessed in the review
Changes in patient-rated symptoms of atopic eczema, such as itching (pruritis) or sleep loss, were used where possible. Global severity as rated by patients or their physician were also sought. If these were unavailable, then global changes in the composite rating scales using a published named scale were used, or where not possible, existing scales modified by the authors or new scales developed within the study were summarised. Adverse events were also included if reported. The selection of the outcome measures was explored in more detail in a focus group of consumers held by one of the authors.

The secondary outcome measures were changes in the individual signs of atopic eczema, as assessed by a physician. Studies that only reported changes in blood tests or cellular mechanisms were excluded.

How were decisions on the relevance of primary studies made?
Not all the references had abstracts, and therefore, 'titles only' had to be included as possible trials to avoid premature judgement. Where doubt existed from the abstract or title, the full paper was requested and scrutinised further by two of the authors. The papers labelled as 'rejects' were categorised with another label to specify why they were unsuitable for inclusion. This was carried out by one reviewer and checked by a second reviewer in any cases of possible uncertainty.
**Assessment of study quality**
The methodological quality of each study was assessed using a scheme where the three potential sources of bias were evaluated (see Other Publications of Related Interest No.2): the quality of the randomisation procedure; the extent to which the primary analysis included all participants initially randomised (i.e. an intention to treat analysis); and the extent to which those assessing the outcomes were aware of the treatments of those being assessed (blinding). The authors of the review were not blinded to the identity of the RCT authors when rating the studies for quality. The authors do not state how many of the reviewers performed the quality assessment.

**Data extraction**
Data abstraction forms were developed and used for those treatment groups where pooling appeared likely. The data to be pooled were abstracted by two authors, and any discrepancies were checked by a third if required. The data for the qualitative summary were abstracted by one author and checked by a second. The data abstractors were not blinded to the identity of the RCT authors. The following data were extracted: interventions; study population and sample size; trial design; description and follow-up; outcome measures; main reported results; and the quality of reporting.

**Methods of synthesis**
How were the studies combined?
Where pooling made sense clinically in terms of the interventions, study participants and common clinical outcomes, a meta-analysis was performed using both fixed-effect and random-effects models depending on whether there was evidence of statistical heterogeneity. The odds ratios of improvement, compared with the comparison intervention, were used in the pooling exercises. The inverse of the variance of the outcome measures was used as a weight for pooling the data from different trials.

Where pooling was deemed to be inappropriate, detailed descriptions of the study characteristics and main reported results were presented, along with comments on study quality.

How were differences between studies investigated?
Sources of heterogeneity, such as differences in patients or formulation of interventions, were explored within the meta-analysis.

**Results of the review**
There were 283 RCTs of atopic eczema included in the review. These covered at least 47 different interventions, which could be broadly categorised into ten main groups.

The quality of reporting was generally poor. Limited statistical pooling was only possible for oral cyclosporin, and only then after considerable data transformation.

There was reasonable evidence from the RCTs to support the use of oral cyclosporin, topical corticosteroids, psychological approaches and ultraviolet light therapy.

There was insufficient evidence to make recommendations with regards to maternal allergen avoidance for disease prevention, oral antihistamines, Chinese herbs, dietary restriction in established atopic eczema, homeopathy, house dust mite reduction, massage therapy, hypnotherapy, evening primrose oil, emollients, topical coal tar and topical doxepin.

There was no evidence from the RCTs to support any clear clinical benefit with regards to the following: the avoidance of enzyme-based washing powders; the use of cotton clothing rather than soft-weave synthetics; biofeedback; twice-daily as opposed to once-daily topical corticosteroids; topical antibiotic and steroid combinations versus topical steroids alone; and antiseptic bath additives.

There was complete absence of any RCT evidence on short bursts of potent versus longer-term weaker topical steroids, dilution of topical corticosteroids, oral prednisolone and azathioprine, salt baths, impregnated bandages, wet-wrap bandages, water softening devices, allergy testing, and different approaches to the organisation of care.
Authors' conclusions
The evidence base for the prevention and treatment of atopic eczema has many limitations. It is characterised by a profusion of short-term trials of 'me too' products, a lack of common outcome measures which measure things that are important to patients, poor standards of clinical trial reporting, and a lack of data on questions that physicians and people with atopic eczema deem to be important. Little research has evaluated commonly used treatments compared with each other or in combination. This mismatch is probably due to a combination of the questions not being asked, coupled with a lack of independent investment in primary atopic eczema research.

CRD commentary
The authors stated their review question and the inclusion criteria clearly. The literature search was clearly described and thorough, and attempts were made to identify grey literature. Foreign language RCTs were included in the review.

The quality of the individual studies was assessed adequately. The data abstraction was undertaken by two authors where pooling appeared likely, and undertaken by one author and checked by another where the data were likely to be summarised qualitatively. The reviewers were not blinded to the source. The studies were selected by one author and checked by another in cases of uncertainty.

Details of the studies were adequately reported in tables and in the text. The majority of the studies were synthesised narratively rather than statistically.

This review appears to be relevant to the topic area. The authors’ results and conclusions appear justified.

Implications of the review for practice and research
Practice: The authors state that there was reasonable evidence from RCTs to support the use of oral cyclosporin, topical corticosteroids, psychological approaches and ultraviolet light therapy.

Research: The authors state that urgent primary research priorities include RCTs of wet-wrap treatments, the clinical benefit of allergy testing, the use of water softeners, the role of specialist nurses, comparisons of tacrolimus and ascomycin against topical corticosteroids, studies of disease prevention, and the use of emollients in preventing disease relapse. This review suggests that there is some scope for further secondary research by systematically reviewing some of the major treatment groups (e.g. antihistamines and essential fatty acids) in more detail; some of these are already underway within the Cochrane Skin Group. Future methodological research is needed to increase the clinical relevance and reliability of outcome measures for atopic eczema.

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