An evidence-based review of the efficacy of antihistamines in relieving pruritus in atopic dermatitis

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Authors' objectives
To assess the efficacy of antihistamines in relieving pruritus in patients with atopic dermatitis.

Searching
The authors searched MEDLINE (1966 to March 1999) using the keywords: 'dermatitis', 'atopic/therapy' or 'eczema/therapy' and 'histamine H1 antagonists/therapy', with publication types 'randomized controlled trial' or 'clinical trial'.

The authors also searched the Cochrane Database of Systematic Reviews and Best Evidence databases using the keywords 'atopic dermatitis' and 'eczema'.

Study selection
Study designs of evaluations included in the review
The authors stated that randomised controlled trials (RCTs) were to be included. However, only case reports and case series were included in this review.

Specific interventions included in the review
Antihistamines as treatment and active placebo including: terfenadine, chlorpheniramine alone or plus cimetidine hydrochloride, LN2974, promethazine hydrochloride, astemizole, cetirizine hydrochloride (10, 20, or 40 mg), loratadine, acrivastine, hydroxyzine hydrochloride (0.7 or 1.4 mg/Kg), cyproheptadine hydrochloride or clemastine fumarate. The non-antihistamine ketotifen fumarate was included as an intervention in one trial.

Participants included in the review
Patients with atopic dermatitis.

Outcomes assessed in the review
The relief of pruritus (itching).

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The authors assessed the quality of each trial by applying a modified version of Sackett's criteria for technical evidence, ranking trials as either grade A, B or C (A = best, C = worst) (see Other Publications of Related Interest no.1). Quality criteria included: sample size, method of randomisation, blinding and use of a placebo control group. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Data were extracted for the categories of: study identification, quality grade, intervention used, numbers of participants in the treatment group and the placebo group, numbers of participants completing the study, and details (yes or no) as to whether trials were double-blind, randomised, placebo-controlled, and crossover.
Methods of synthesis
How were the studies combined?
The studies were combined in a narrative review.

How were differences between studies investigated?
The authors do not state any test for heterogeneity.

Results of the review
Sixteen studies were included in the review with 803 participants (641 intervention and 162 placebo). Six of the trials were not placebo-controlled and, in addition, one of those did not state the number of participants in the study.

Large, RCTs with definitive conclusions (grade A studies) have not been performed.

Two grade B studies (small, rigorous, randomised trials with uncertain results due to moderate to high alpha or beta error) refuted the use of antihistamines in relieving pruritis. Only one trial at grade B supported the efficacy of antihistamines in relieving pruritis.

All remaining trials (grade C) lacked placebo controls or randomisation, or contained fewer than 20 participants in each treatment group. Of these trials, four supported the use of antihistamines and nine studies refuted the use of antihistamines for the relief of pruritis.

Cost information
The average wholesale price per 25-mg tablet of generic diphrenhydramine hydrochloride equals $0.04 (1998 dollars). A 1-month supply for a 50-mg daily dose of diphrenhydramine hydrochloride equals $2.40. The average wholesale price per tablet of prescription loratadine is approximately $2.14 (1998 dollars) and a 1-month supply for 1 daily dosage equals $64, approximately 27 times more expensive than over-the-counter.

Authors' conclusions
The authors state that although antihistamines are often used in the treatment of atopic dermatitis, little objective evidence exists to demonstrate relief of pruritis. The majority of trials are flawed in terms of the sample size of study design. Based on the literature alone, the efficacy of antihistamines remains to be adequately investigated. Anecdotally, sedating antihistamines have sometimes been useful by virtue of their soporific effect and bedtime use may be warranted. There is no evidence to support the effectiveness of expensive non-sedating agents.

CRD commentary
The authors have stated their research question and some inclusion and exclusion criteria. The literature search was limited and it is not clear whether there were any language restrictions. It is therefore possible that additional relevant studies may have been missed. The authors do not report who, or how many of the authors, performed the selection of studies or the data extraction. There is a quality assessment of the included studies based on randomisation, blinding and withdrawals.

The review was a narrative discussion with no statistical pooling. Only the grade B studies were described in any detail. There was a more general summary of the remaining grade C studies.

The authors’ conclusions appear to follow from the results but these should be viewed with caution because of the lack of details about how the review was performed.

Implications of the review for practice and research
Practice: The authors state that in patients with co-morbid conditions, such as allergic rhinitis, allergic conjunctivitis,
allergen-induced asthma and chronic urticaria, nonsedating agents may be useful.

Research: The authors do not state any implications for research.

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