Topical tacrolimus and pimecrolimus in the treatment of cutaneous lupus erythematous: an evidence-based evaluation

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CRD summary
This review evaluated the efficacy of topical pimecrolimus and tacrolimus in the treatment of cutaneous lupus erythematous. The authors reported that tacrolimus and pimecrolimus showed efficacy in the treatment of systemic lupus, erythematous cutaneous lesions, subacute cutaneous lupus erythematous and discoid lupus erythematous, although further research was necessary. The conclusions should be treated with caution due to poor-quality data and methodological flaws.

Authors' objectives
To evaluate the efficacy of topical pimecrolimus and tacrolimus in the treatment of cutaneous lupus erythematous.

Searching
MEDLINE, EMBASE and the Cochrane Database of Systematic Reviews were searched to August 2007 for studies in any language. Search terms were reported.

Study selection
Studies of topical pimecrolimus and tacrolimus for cutaneous lupus erythematous were eligible for inclusion. The included studies were of participants with discoid lupus erythematous, systemic lupus erythematous, subacute cutaneous lupus erythematous, lupus tumidus and facial cutaneous lupus erythematous. Pimecrolimus cream (1%) and tacrolimus ointment (0.1%) were applied (one controlled study used clobetasol propionate as the comparator); regimens varied and duration of treatment varied from three to eight weeks in the included studies.

Randomised, controlled trials (RCTs) and prospective uncontrolled studies were eligible for inclusion. Included studies had to be of a high level of evidence (level 4 or above). Retrospective studies, case series and unclear publications were excluded. Most included studies were uncontrolled. The outcomes reported from the included studies were response to treatment in systemic lupus erythematous, subacute cutaneous lupus erythematous and discoid lupus erythematous. Quality of life outcomes were reported for pimecrolimus.

It appeared that two independent reviewers selected the studies and that agreement was by consensus.

Assessment of study quality
Some aspects of study quality were reported, but the authors did not state that they assessed validity in a systematic way.

Data extraction
Data were extracted for the outcomes reported in the included studies. The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in a narrative synthesis by type of cutaneous lupus erythematous. A table of primary study details was available to examine differences between studies.

Results of the review
Five studies were included in the review (n was unclear but appeared to be 60): one randomised controlled trial (RCT) (n was unclear, but appeared to be 20); and four uncontrolled studies (n=40).

There was no significant difference between tacrolimus and clobetasol (one RCT), but there was a significantly higher occurrence of telangiectasia with clobetasol compared with tacrolimus (p<0.05).
Tacrolimus was effective for the initial skin lesions of systemic lupus erythematosus lesions with edematous or telangiectatic changes within two weeks of initiation of treatment (one uncontrolled study) and extensive photosensitive rash in systemic lupus erythematosus (one uncontrolled study). Pimecrolimus treatment was associated with significant improvement in skin lesions in systemic lupus erythematosus (one uncontrolled study).

Tacrolimus and pimecrolimus were reported to be efficacious for subacute cutaneous lupus erythematous to a lesser extent than for systemic lupus erythematosus (two uncontrolled studies, one RCT).

Pimecrolimus (two uncontrolled studies) and tacrolimus (one RCT and one uncontrolled study) were associated with improvement in discoid lupus erythematosus patients. Pimecrolimus-treated patients showed significant improvement in quality of life scores in two uncontrolled studies. The authors reported that patients with hyperkeratotic discoid lupus erythematous did not respond well to tacrolimus treatment (one uncontrolled study).

**Authors' conclusions**

The evidence suggested that tacrolimus and pimecrolimus were effective in the treatment of systemic lupus erythematosus cutaneous lesions, subacute cutaneous lupus erythematosus and discoid lupus erythematous. Further research was necessary.

**CRD commentary**

The review question was clear, but the inclusion criteria were not explicitly stated. Language restrictions were not applied to the search, thus reducing the possibility of language bias. The authors did not report any attempts to identify unpublished studies, which increased the possibility of publication bias. Validity of the primary studies was not thoroughly assessed, so it was not known whether the results and synthesis were reliable. The review process was not well reported, so it was not possible to tell whether steps were taken to minimise reviewer bias and error in study selection and data extraction. The included studies were small, generally appeared to be of poor quality and few study details were reported. The tables of study details were unclear as to which condition the outcomes referred.

This study had a several methodological flaws, was poorly reported and included few studies, which also appeared to be of poor quality. The authors' conclusions should be treated with caution.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that double-blind RCTs were needed to confirm data on efficacy and safety with long- and short-term usage. Further epidemiological studies with sufficient follow-up, systematic reviews and meta-analyses were needed to establish the risk of malignancy. Cost-effectiveness studies were also needed. Quality of life should be considered.

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