Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis

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Authors' objectives
To evaluate the comparative efficacy and tolerability of topical calcipotriol in the treatment of mild to moderate chronic plaque psoriasis.

Searching
The authors searched (1987 to January 1999) the electronic databases of MEDLINE, EMBASE, the Cochrane Controlled Trials Register and the Index to Scientific and Technical Proceedings (via BIDS) using the textwords 'calcipotriol', 'MC903', 'calcipotriene', 'Dovonex', 'Daivonex', and 'Psorcutan'. The authors also searched the bibliographies of retrieved articles for additional relevant studies and contacted the manufacturer of calcipotriol for information.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs).

Specific interventions included in the review
Topical calcipotriol 0.005% cream or ointment versus placebo or other topical corticosteroid (grouped according to potency: moderate (cobetasone butyrate 0.05%), potent (betamethasone valerate 0.1%, betamethasone dipropionate 0.1%, desoxymethasone 0.25%, fluocinonide 0.05%, halobetasol 0.05%), and very potent (clobetasol propionate 0.05%, diflorasone diacetate 0.05%)).

Participants included in the review
Participants were patients with mild to moderate chronic plaque psoriasis.

Outcomes assessed in the review
The main outcome measure was the proportion of patients showing 'marked improvement' or better in patients' overall assessments and the mean percentage change in scores from baseline on the psoriasis area and severity index. The secondary outcome measure was the proportion of patients graded as 'marked improvement or better in the investigators' overall assessments of response. Adverse effects were also recorded regarding lesional or perilesional irritation, facial or scalp irritation, exacerbation of psoriasis, and the number of withdrawals due to adverse effects.

How were decisions on the relevance of primary studies made?
Two authors independently assessed the trials for inclusion. Disagreements were resolved by discussion.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two authors independently performed the data extraction. Disagreements were resolved by discussion.

Data were extracted for the categories of: study identification and year of publication, number of participants in treatment and control groups, duration of treatment, and individual mean difference calculations with 95% confidence intervals.

Adverse effects were also estimated with the rate ratio, the rate difference and the number needed to treat (NNT).
Topical steroids were grouped according to their potencies: moderate, potent or very potent.

Missing data were obtained by either contacting the principal author of the trial or the manufacturer.

**Methods of synthesis**

How were the studies combined?

Pooled rate ratios (RRs) were calculated for dichotomous outcomes with 95% confidence intervals (CIs).

Weighted pooled mean difference (WMD) was calculated for continuous outcomes with 95% confidence intervals (CIs).

How were differences between studies investigated?

The authors tested for heterogeneity using the chi-square test.

Trials were grouped and analysed according to the potency of the topical corticosteroids (moderate, potent and very potent).

The authors also performed sensitivity analyses of:

1. The effect of including one trial of only children treated.
2. The effect of excluding one trial of a once daily regimen of calcipotriol.
3. The effects of excluding those trials using half body comparisons or those with imputed variance.

**Results of the review**

Thirty-seven RCTs were included in the review with 6,038 participants.

Intention to treat (ITT) and remaining patient analyses led to the same conclusions.

Calcipotriol was at least as effective as potent topical corticosteroids, calcitriol, short contact dithranol, tacalcitol, coal tar, and combined coal tar 5%, allantoin 2%, and hydrocortisone 0.5%.

Calcipotriol versus placebo (8 trials, 1,185 participants) found that at six and eight weeks calcipotriol was more effective than placebo in adults. Based on the results of one trial calcipotriol was no better than placebo in children.

Calcipotriol caused significantly more skin irritation that potent topical corticosteroids (NNT to harm for irritation = 10, 95% CI: 6,34).

Calcipotriol monotherapy also caused more irritation than calcipotriol combined with a potent topical corticosteroid (NNT = 6, 95% CI: 4, 8).

The NNT for dithranol to produce lesional or perilesional irritation was 4 (95% CI: 3,5).

On average, treating 23 patients with short contact dithranol led to one more patient dropping out of treatment owing to adverse effects than if they were treated with calcipotriol. Significantly more patients withdrew from placebo compared with calcipotriol.

**Authors' conclusions**

The authors state that calcipotriol is an effective treatment for mild to moderate chronic plaque psoriasis, more so than calcitriol, tacalcitol, coal tar, and short contact dithranol. Only potent topical corticosteroids seem to have comparable efficacy at eight weeks. Although calcipotriol caused more skin irritation than topical corticosteroids this has to be balanced against the potential long-term effects of corticosteroids. Skin irritation rarely led to withdrawal of
calcipotriol treatment.

**CRD commentary**
The authors have stated their research question and inclusion and exclusion criteria. A reasonable literature search was performed although it is not stated whether there were any language restrictions on the search.

The authors do report how, and which of the authors, performed the selection of studies and the data extraction. There is no validity assessment of the included studies.

Data from the original studies and additional tables and graphs are contained on the BMJ website requiring additional searching to evaluate the included studies.

The statistical pooling was appropriate since no heterogeneity was found between those groups of studies which were pooled. Information on results of tests for heterogeneity and the type of pooling model is only found in the additional tables on the BMJ website. The authors' conclusions appear to follow from the results but these should be viewed with some caution because of the lack of a validity assessment of included studies.

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

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

**Research:** The authors state that longer term comparative trials (greater than six to eight weeks) of calcipotriol versus dithranol and topical corticosteroids are needed to see whether these short-term benefits are mirrored by long-term outcomes such as duration of remission and improvement in quality of life.

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