A systematic review of adverse effects associated with topical treatments for psoriasis


CRD summary
This review aimed to compare the rates of adverse events associated with the various, currently available topical treatments for psoriasis. Reviewing adverse events is not easy, but unfortunately this review was poorly conducted and reported and the narrative synthesis was very superficial. Given these limitations, the authors' conclusions cannot be relied upon.

Authors' objectives
To compare the rates of adverse events associated with the various, currently available topical treatments for psoriasis.

Searching
MEDLINE (from 1966 to March 2003) and the Cochrane CENTRAL Register were searched for papers published in English; the search terms were stated. The retrieved articles were checked for further relevant studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials, or trials described as double-blind, were eligible for inclusion. Only trials of at least 50 patients were included. Trials in which the intervention treatment was administered after the designated assessment period were excluded from the review.

Specific interventions included in the review
The inclusion criteria for the interventions were not clearly specified. With the exception of experimental agents, any topical treatment for psoriasis was eligible for the review. Trials of maintenance therapy, as distinct from treatment, were not eligible.

The included studies were of: betamethasone dipropionate cream; betamethasone valerate cream or ointment 0.1%; butyrate cream (0.5 mg/g); calcipotriene ointment or cream (50 microg/g); calcipotriene cream (50 microg/g) plus betamethasone 17-valerate cream (1 mg/g) or clobetasone 17-butyrate cream or diflucortolone valerate ointment 0.1%; calcitriol ointment; clobetasol propionate 0.05% cream; coal tar (5%)-allantoin (2%)-hydrocortisone (0.5%) cream; desonide cream or lotion 0.05%; dithranol cream or stick; fluocinonide cream or ointment 0.05%; fluticasone propionate cream or ointment 0.05%; hydrocortisone buteprate 0.1% cream; mometasone furoate 0.1% ointment; mometasone furoate 0.1%-salicylic acid 5% ointment; salicylic acid 5%; tacalcitol ointment (4 microg/g); tazarotene gel 0.05, 0.1 or 0.5%. The active treatment had to be administered for a minimum of 14 days and for some pre-specified duration. It was unclear what comparators were used in the included studies.

Participants included in the review
The inclusion criteria for the participants were not clearly specified. Populations of patients with exclusively guttate, pustular or scalp psoriasis were excluded. The text states that most patients had mild to moderate psoriasis.

Outcomes assessed in the review
Studies that reported specific adverse events associated with each treatment were included in the review. Only treatment-related events and withdrawals due to treatment-related events were considered.

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

Assessment of study quality
There were no specific criteria for a validity assessment; the authors stated that they considered the trials valid if they met the inclusion criteria. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

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

The authors stated that all comparable data were extracted and tabulated. Details of treatment-related adverse events, the proportion of patients affected, and the proportion of patients who withdrew because of these events were extracted. Actual numbers were recorded; when only proportions were reported in the primary papers, the actual numbers were calculated.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
Differences between the studies were not discussed.

Results of the review
One study of each monotherapy or combination therapy was included unless variations in frequency or duration of treatment were reported. Twenty-three trials were included (70% double-blind, 70% comparison studies (presumably the authors mean active comparator rather than placebo control since only controlled trials were included)).

Monotherapy.
The lowest rate of treatment-related adverse events was reported for fluticasone propionate cream (3.2%). Among the non-corticosteroids, tacalcitol ointment 4 microg/g showed the lowest rate (4.8%), although the rate for calcitriol 3 microg/g was similar (5%). Dithranol was associated with the highest rate of treatment-related adverse events (72%). The rates for corticosteroid preparations ranged from 3.2 to 23%, for vitamin D analogues they ranged from 4.8 to 35%, and for tazarotene from 13 to 50%. Withdrawals due to treatment-related adverse events were generally lower with corticosteroids than with other therapies.

Combination therapy.
The rates of treatment-related adverse events ranged from 12% with mometasone furoate 0.1%-salicylic acid 5% to 24% with calcipotriene plus clobetasone 17-butyrate cream. The withdrawal rates were very low, ranging from 0% with mometasone furoate-salicylic acid to 5.3% with coal tar-allantoin-hydrocortisone cream.

Authors' conclusions
Topical treatments for psoriasis are usually well tolerated without severe adverse effects. Since clearance cannot usually be expected, the use of topical therapies should be limited as excessive use may increase the risk of both cutaneous and systemic adverse effects.

CRD commentary
Reviewing adverse events is not easy. This review attempted to review the adverse events of a large number of treatments. Unfortunately the inclusion criteria were not well defined and the decision to include only a single trial per specific intervention (presumably by dose and regimen and duration of treatment) was not an appropriate way to limit the extent of the review. There was no explanation of how the single trial was selected. Details of this and any other measures to limit bias within the review were missing. The details of the primary trials, but not participants, were...
tabulated, although it was unclear how the authors selected the data for inclusion in the tables. The narrative synthesis was very superficial. The treatments were compared indirectly rather than directly. Given the sources of potential bias in the review, the authors' conclusions are unlikely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that as clearance of psoriasis is not usually an attainable goal, the use of topical therapies should be limited as excessive use may increase the risk of both cutaneous and systemic adverse effects.

Research: The authors did not state any implications for further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.