Efficacy and safety of treatments for childhood psoriasis: a systematic literature review

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CRD summary
The authors concluded that calcipotriene with or without corticosteroids was the treatment of choice for childhood psoriasis, followed by dithranol. Methotrexate was the systemic treatment of choice. Evidence on specific treatments was limited: based at most on one randomised controlled trial of unknown quality plus studies of less reliable design. This means that the conclusions should be interpreted with caution.

Authors' objectives
To evaluate the efficacy and safety of treatments for childhood psoriasis.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials were searched from 1980 to September 2008. The main search terms were reported. The full search strategy was available from the authors. Reference lists of all identified articles were searched. Studies published in English, German or Dutch were eligible.

Study selection
Any study that evaluated the efficacy of any clearly described treatment for any type of childhood (<18 years) psoriasis was eligible for inclusion. Studies with subgroups of children were included if results for children were reported separately. Studies had to describe an outcome measure such as Psoriasis Area and Severity Index (PASI), Physician global Assessment and total severity score for erythema, scaling and thickness or subjective measures such as percentage of clearance. Studies were excluded if they were in children with psoriatic arthritis or used combinations of treatments apart those that included low-to-moderate potency topical corticosteroids. Studies of treatments that were only evaluated in a single study were excluded.

The included studies varied in design from randomised controlled trials (RCTs) to single-person case reports. Studies evaluated a range of treatments that included topical corticosteroids, vitamin D analogues, calcineurin inhibitors, dithranol, phototherapy, antibiotics, retinoids, cyclosporine, methotrexate and biologics. Treatment duration ranged from once-only administration to 30 months. Types of psoriasis varied between (and sometimes within) studies and included plaque, pustular, guttate, palmoplantar and erythrodermic psoriasis. Participant ages ranged from three months to 17 years.

Two reviewers independently selected studies

Assessment of study quality
The authors did not state that they assessed validity. However, two reviewers independently extracted information on blinding and graded studies using a hierarchy of study design based on the Oxford Centre Evidence-Based Medicine Levels of Evidence (level one for RCTs, level two for cohort studies, level three for case-control studies, level four for case series and level five for case reports and expert opinions). Disagreements were resolved through consensus or by consultation with a third reviewer.

Data extraction
Two reviewers independently extracted outcome data onto a pre-designed form. The authors classified clearance as more than 90% improvement from baseline. Other levels of improvement were marked (70% to 90%), moderate (50% to 70%), slight (30% to 50%) and poor (<30%). Disagreements were resolved through consensus or by consultation with a third reviewer.

Methods of synthesis
Studies were grouped by intervention and combined in a narrative synthesis. The overall level of evidence for each intervention was graded A (consistent RCTs), B (generally cohort or case-control studies), C (generally case series) and
D (case reports, expert opinion or any type of inconsistent studies).

**Results of the review**

Sixty-four studies were included.

**Topical corticosteroids:** Halobetasol cream 0.05% and clobetasol propionate emulsion 0.05% cream seemed to be effective for childhood plaque psoriasis; grade C evidence came from one open-label study (n=11), one poor-quality RCT (n=9) and one case report (n=1).

**Vitamin D analogues:** Calcipotriene (mostly 50µg/g) was effective and reasonably well-tolerated for plaque psoriasis; grade A evidence came from one double-blind RCT (n=77), four open-label studies (n=110) and two case reports (n=2). Calcitriol seemed effective with mild side effects; grade B evidence came from one RCT (n=10) and one placebo-controlled study with the same four patients as one case series.

**Calcineurin inhibitors:** Tacrolimus seemed effective and safe for short-term treatment of facial and intertriginous psoriasis, but there was no evidence on long-term safety; grade C evidence came from two open-label studies (n=19) and one case report (n=1). No conclusions could be reached on pimecrolimus (two case reports, n=2) due to insufficient evidence. Dithranol was effective with a good short-term side-effect profile; grade C evidence came from two open-label studies (n=99) and one case report (n=1).

**Phototherapy:** Narrow-band ultraviolet B radiation (NB-UVB) results were good for plaque and guttate psoriasis and side effects were reasonably mild over the treatment period; grade C evidence came from two open label studies (n=30) and two case series (n=55). No conclusion could be reached on photochemotherapy UVA radiation (PUVA) due to insufficient evidence from one case series (n=2) and two case reports (n=2).

**Antibiotics:** The authors stated that the efficacy of antibiotics remained controversial; grade C evidence came from one RCT (n=4), one open-label study (n=3), two case series (n=6) and one case report (n=1).

**Retinoids:** Etretinate was effective for pustular and erythrodermic psoriasis, but side effects were common; grade C evidence came from three case series (n=17), one open-label study (n=3) and one case report (n=1). No conclusion could be reached on acitretin due to insufficient evidence (one case report, n=1). The authors stated that the efficacy of cyclosporine was ambiguous; grade C evidence came from two case series (n=7) and two case reports (n=2). Methotrexate was effective in moderate to severe psoriasis. Most evidence on methotrexate was about plaque psoriasis. Short-term side effects were generally mild and treatable. Grade C evidence on methotrexate came from four case series (n=45) and four case reports (n=4).

**Biologics:** Etanercept was effective for plaque psoriasis. Short-term side effects were generally infections. Grade A evidence came from one RCT (n=211), two case series (n=7) and four case reports (n=4). No conclusion could be reached about infliximab due to insufficient evidence (four case reports, n=4).

**Authors’ conclusions**

Calcipotriene with or without corticosteroids was the treatment of choice for childhood psoriasis followed by dithranol; methotrexate was the systemic treatment of choice.

**CRD commentary**

The review question was clearly stated. Inclusion criteria were broad. Three relevant databases were searched. Some attempts were made to minimise language bias. No attempts were made to minimise publication bias. Appropriate methods were used to minimise reviewer error and bias during the review process. Apart from blinding, study validity was not assessed and so results from these studies and any synthesis may not have been reliable. Given the diversity among studies, a narrative synthesis was appropriate. Evidence on specific treatments was limited: based at most on one RCT of unknown quality plus other studies of less reliable design. The conclusions should be interpreted with caution.

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

Database of Abstracts of Reviews of Effects (DARE)
**Practice:** The authors stated that the treatment of choice for childhood psoriasis was calcipotriene (if required combined with mild to moderate topical corticosteroids). Tacrolimus 0.1% could be added for treatment resistant flexural and/or facial psoriasis. For non-responders or patients with moderately to severe psoriasis, dithranol was recommended. Should the above be ineffective, short-term NB-UVB could be considered for adolescents. Antibiotics could be considered for guttate psoriasis and where streptococcal infection was suspected. The systemic treatment of choice was methotrexate with retinoids considered for pustular and erythematous psoriasis; cyclosporin should be considered only in exceptional cases. Etanercept should be considered as a third-line drug.

**Research:** The authors stated that placebo-controlled RCTs were required to evaluate treatments for childhood psoriasis. They also stated that specialist centres should co-operate in developing a database to record all treatments.

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