Efficacy of systemic treatments for moderate to severe plaque psoriasis: systematic review and meta-analysis

Bansback N, Sizto S, San H, Feldman S, Willian MK, Anis A

CRD summary
This generally well-conducted review compared a number of different treatments for psoriasis based solely on the outcome of PASI response criteria. Despite the limitation of using only this outcome, the authors’ conclusion that TNF inhibitors were more effective than T-cell agents and systemic non-biologics seems reasonable.

Authors’ objectives
To compare the efficacy of psoriasis treatments.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and ISI Science and Technology Proceedings were searched from inception to January 2007. Reference lists of identified studies and conference proceedings were handsearched. No language restrictions were initially placed on the search, but only papers in English were included.

Study selection
Randomised controlled trials (RCTs) that compared any potential treatment for psoriasis approved by the US Food and Drug Administration against a placebo or with any other active agent and placebo were eligible for inclusion. Trials had to have a primary endpoint of between eight and 16 weeks and have been conducted in a developed country. Participants were restricted to those with moderate to severe psoriasis who had an inadequate response to topical treatments alone and had received (or were candidates for) systemic therapy or phototherapy. The primary outcome was the Psoriasis Area Severity Index (PASI).

Participants had a mean age of 44 years and mean disease duration of 19 years. All trials contained a greater percentage of male participants. Interventions included biologics acting as tumour necrosis factor (TNF) inhibitors (adalimumab, etanercept, infliximab) or T-cell agents (alefacept, efalizumab), non-biologic systemics (retinoids, methotrexate, cyclosporine) and non-systemic therapies (phototherapy, combination therapy).

Inclusion criteria were applied by one reviewer and independently verified by another. Discrepancies were resolved by discussion.

Assessment of study quality
Quality of included studies was assessed using the Jadad scoring system of randomisation, blinding and an adequate description of withdrawals and drop-outs. The maximum possible score was 5.

Quality ratings were applied by one reviewer and independently verified by another. Discrepancies were resolved by discussion.

Data extraction
Data on study and patient characteristics and primary endpoint efficacy data were extracted by one reviewer and independently verified by another. Data from one trial that reported in several publications were combined into one record and reported as a single trial. PASI 50, PASI 75 and PASI 90 (defined as ≥50%, 75% and 90% reduction from baseline PASI) were extracted. Χ² or Fisher exact tests were used to compare PASI response rates of different dosages of the same treatments. Unlicensed dosages that achieved statistically significant differences from those at licensed dosages were excluded.

Methods of synthesis
A mixed treatment comparison meta-analysis was conducted to determine the comparative efficacy of the different treatments using PASI 50, 75 and 90 response rates to give a probability of response and relative risk for each treatment. If all three PASI response rates were not available, the missing response was grouped with another.

A hierarchical Bayesian model was used with uninformative prior distributions for each treatment.

Number needed to treat was calculated and sensitivity analyses performed using different trials and dosages and compared to base results.

**Results of the review**

Twenty-two RCTs were included in the analysis (n=9,917): 20 RCTs (n=9,704) of biologics versus placebo and two RCTs (n=213) of comparators. The quality of the included trials was high: mean Jadad score 4.3 and no trial less than 3.

**Probabilities of response:** TNF inhibitors generally gave rise to the greatest probability of response. Infliximab (5mg/kg every eight weeks following doses at zero, two and six weeks) produced the greatest probability of response in all PASI response categories. Probabilities of response were 93% (PASI 50), 81% (PASI 75) and 54% (PASI 90). T-cell agents were estimated to have the lowest probability of response compared with all other treatments analysed.

**Relative risk:** TNF inhibitors were most likely to achieve a response at all PASI response levels. When combined (for PASI 75) the relative risk for systemic non-biologics was 9.24 (95% CI 5.33 to 13.95), for T-cell agents the relative risk was 5.65 (95% CI 3.74 to 7.97) and for TNF inhibitors the the relative risk was 15.57 (95% CI 12.46 to 19.25).

Number needed to treat and sensitivity analyses were reported. Sensitivity analysis identified dosage as an important determinant of outcome whereas quality of study was not.

**Authors’ conclusions**

Based on PASI response criteria, treatment with TNF inhibitors was superior to that with T-cell agents and treatment with adalimumab or infliximab was superior to conventional systemic therapies and to etanercept.

**CRD commentary**

This review addressed a clear question and was supported by appropriate inclusion criteria. Several relevant sources were searched to identify potential studies and some attempt was made to search out unpublished studies. It appeared that the authors restricted included studies to those in English, which may have introduced language bias. The authors attempted to minimise bias and error during the review process by carrying out study selection, validity assessment and data extraction in duplicate. As the authors pointed out, limiting the outcome measure to the PASI response criteria was associated with some known limitations and potentially important criteria (such as safety profiles and quality of life measures) were not reported. Despite this limitation, the authors’ conclusion that TNF inhibitors were superior to T-cell agents and systemic non-biologics seems reasonable.

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

Practice: The authors stated that adalimumab and infliximab were superior to conventional systemic therapies and etanercept based on PASI response criteria, but suggested that decision makers may wish to consider other factors such as adverse event rates, quality of life issues and economic cost as well.

Research: None stated.

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