Systemic therapy with immunosuppressive agents and retinoids in hidradenitis suppurativa: a systematic review
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CRD summary
The authors concluded that based on the evidence, infliximab and adalimumab were the most effective immunosuppressive agents for hidradenitis suppurativa. Due to the limited synthesis and evidence presented in the review, the authors' conclusions are unlikely to be reliable.

Authors' objectives
To evaluate the effectiveness and of systemic immunosuppressive agents and systemic retinoids in hidradenitis suppurativa, and assess which agents were most effective for the treatment of hidradenitis suppurativa.

Searching
MEDLINE and EMBASE databases were searched with no language restriction up to May 2012 for published papers. Search terms were reported. Reference lists of included studies and relevant reviews were handsearched for additional studies.

Study selection
Papers that assessed systemic retinoids or immunosuppressive treatments for hidradenitis suppurativa localised at the typical inverse regions in adults over 18 years of age were included. The primary endpoints were the percentages of significant responders (defined as a reduction of the Sartorius score of ≥50%, improvement in quality of life of >50% or if stated by the authors), moderate responders (defined as score reductions <50% or if stated by the authors) and non-responders. Other endpoints were relapse rates and adverse events.

Drugs used for the immunosuppressive therapies were biological agents (such as adalimumab, etanercept, infliximab, ustekinumab), colchicine, ciclosporin, methotrexate, dapsone; systemic retinoids were acitretin and isotretinoin. Dosing regimens and treatment duration of all drugs varied across studies.

Two researchers independently searched for eligible studies.

Assessment of study quality
The quality of evidence was graded as either: A) systematic review or meta-analysis, randomised controlled trial with consistent findings, or all-or-none observational study; B) lower-quality clinical trial or study with limitations and inconsistent findings, cohort study or case–control study; or C) consensus guidelines, usual practice, expert opinion or case series.

The authors did not state how many reviewers were involved in quality assessment.

Data extraction
Two reviewers independently extracted outcomes data using standardised forms; discrepancies were resolved through discussion. Study authors were not contacted for missing data. Drop-outs were considered to be non-responders.

Methods of synthesis
Data were analysed by means of descriptive statistics. Number of events were added across the studies to calculate percentages.

Results of the review
A total of 87 papers were included (518 patients). Overall the quality of the studies was low (mostly grade B and C).

Biologics: Total of 44% showed a significant response to adalimumab, 35% had a moderate response and 21% did not respond to adalimumab (15 papers, 68 patients). Thirty-nine percent of patients taking etanercept showed a significant
response to treatment, 17% had a moderate improvement and 44% did not respond (nine papers, 54 patients). Fifty percent of patients had a significant response with infliximab, 39% showed a moderate response and 11% showed no response (42 papers, 147 patients). Two patients showed a significant response to ustekinumab, one patient had a moderate response and one did not respond to treatment (two papers, four patients).

**Retinoids**: Eighteen percent of the patients had a significant improvement with isotretinoin, 17% had a moderate improvement and 64% had no response with the treatment (seven papers, 174 patients). Seventy-three percent of patients treated with acitretin and etretinate had a significant improvement, 23% had a moderate response and 5% did not respond to therapy (six papers, 22 patients).

**Other treatments**: Thirty-five percent of patients treated with dapsone had a significant improvement, 21% had a moderate improvement and 44% did not respond to therapy (three papers, 34 patients). Twenty-five percent of patients treated with colchicine had a moderate response and 75% did not respond to treatment (one paper, eight patients). Fifty percent had a significant response with ciclosporin treatment and another 50% had a moderate response (three papers, four patients). None of the patients responded to treatment with methotrexate (one paper, three patients).

Further data on relapse rates and adverse events were reported in the review. The highest number of withdrawals due to adverse events occurred with infliximab and isotretinoin.

**Authors’ conclusions**
Based on the evidence, infliximab and adalimumab were the most effective immunosuppressive agents for hidradenitis suppurativa. Acitretin was also effective in hidradenitis suppurativa, but the quality of the evidence was low.

**CRD commentary**
The review question and inclusion criteria were clear. The literature search was limited to two databases and the authors did not search for unpublished studies, so there was potential for publication bias. No language restrictions were applied to the search, which reduced the risk of language bias. Appropriate methods were used to reduce the risk of reviewer error and bias for the selection of studies and extraction of data, but it was unclear whether similar methods were used for assessing the study quality.

The overall quality of the evidence was considered to be low; studies were small, and most were case series and case reports. Some patients treated with infliximab received add-on therapy which may have confounded the effect of infliximab. Reporting of participant and intervention characteristics was limited. Adding number of events across studies of different study designs did not appear appropriate.

Due to limitations in the evidence presented and the synthesis, the authors’ conclusions are unlikely to be reliable.

**Implications of the review for practice and research**
**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that randomised controlled clinical trials are needed in order to identify the most effective treatment targets and the most effective therapy for hidradenitis suppurativa.

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