Glucocorticoids in systemic sclerosis: weighing up the benefits and risks – a systematic review
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CRD summary
The review concluded that evidence of a beneficial effect of glucocorticoids in patients with systemic sclerosis was limited. Despite some concerns about the review process, the limited quality of the included studies and the inability to distinguish the effects of glucocorticoids alone, the authors’ conclusion seems reasonable.

Authors’ objectives
To evaluate the efficacy and safety of glucocorticoids in patients with systemic sclerosis.

Searching
PubMed, EMBASE, and The Cochrane Library were searched up to October 2012 for English language articles. Search terms were reported. Reference lists of included studies were screened.

Study selection
Eligible for inclusion were any studies of local or systemic glucocorticoids as monotherapy or co-medication for a specified indication in adult patients with systemic sclerosis (diagnosed according to American College of Rheumatology and/or Leroy criteria).

The included studies focused on glucocorticoids to treat interstitial lung disease, diffuse cutaneous disease, myopathy, painful hands, to prevent serum sickness, and to deal with other indications (reported in the paper). Various clinical outcomes were reported, as well as scleroderma renal crisis and other adverse events. In most studies, glucocorticoids (dexamethasone, prednisone, prednisolone, methylprednisolone) were used as co-medication with other immunosuppressive drugs (reported in the paper). Doses were classed as low, medium, high, and pulse therapy (defined in the paper).

Two reviewers were involved in the study selection process. Disagreements were resolved by discussion with all authors.

Assessment of study quality
Study quality was assessed by Jadad criteria (for experimental studies) and by the Newcastle-Ottawa scale (for observational studies).

The authors did not state how many reviewers assessed study quality.

Data extraction
Data were extracted on changes between pre-treatment and post-treatment values for the outcomes of interest.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
A narrative synthesis was presented.

Results of the review
Forty-four studies (comprising randomised controlled trials/RCTs, controlled trials and observational studies) were included in the review, together with 93 case reports. The overall quality of trials seemed low; quality of observational studies appeared reasonable. Follow-up ranged from six to 72 months, where reported.

Interstitial lung disease (three RCTs; two controlled trials; 18 observational studies; 478 patients): Results of three observational studies using glucocorticoids as monotherapy were mixed. A high quality RCT showed a trend towards stabilisation of lung function following combination therapy compared with placebo, although the difference was not
statistically significant. Other results of co-medication were mixed. Adverse events were reported; those that could be partially attributed to glucocorticoids were infections, mood disturbances, dyspepsia, cushingoid appearance, transient shortness of breath, and cataract. There was one case of scleroderma renal crisis.

**Diffuse cutaneous disease** (two RCTs; eight observational studies; 238 patients): Glucocorticoids as monotherapy was studied in one low-quality RCT, which showed a small benefit (decrease of total skin score from baseline) in the treatment group, compared with placebo; monotherapy resulted in an improvement of skin disease in one observational study. The remaining observational studies showed positive effects of combination therapy involving glucocorticoids. Adverse events possibly related to glucocorticoids were infections, gastrointestinal complaints, vertigo, and hypertension. Scleroderma renal crisis was reported in 10 cases.

**Prevention of serum sickness** (one controlled trial; five observational studies; 80 patients): It was not possible to evaluate the efficacy of glucocorticoids, but ten cases of scleroderma renal crisis were reported.

Other results were reported in the paper.

**Authors' conclusions**
Evidence of a beneficial effect of glucocorticoids in systemic sclerosis was limited.

**CRD commentary**
The review question was clear. Inclusion criteria were specified for all aspects, apart from outcomes. Literature searching included relevant databases. There was no apparent search for unpublished studies and the restriction to papers in English may mean that relevant studies were missed. The selection of studies included measures to minimise error and bias; the transparency of the remainder of the review process was unclear.

Study details were presented, but patient characteristics were lacking, which meant that the generalisability of the findings was unclear. Quality assessment of included studies was carried out, and the results of this were woven into the review findings. The authors' conclusion reflected the limited evidence presented.

Despite some concerns about the review process, the limited quality of the included studies and the inability to distinguish the effects of glucocorticoids alone, the authors' conclusion seems reasonable.

**Implications of the review for practice and research**
**Practice:** The authors stated that awareness for the risk of scleroderma renal crisis should be maintained, particularly in patients with diffuse disease who were treated additionally with potentially nephrotoxic drugs.

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

**Funding**
Not stated.

**Bibliographic details**

**PubMedID**
23910618

**Original Paper URL**
http://www.clinexprheumatol.org/pubmed/find-piia.asp?pii=23910618

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Evidence-Based Medicine; Glucocorticoids /administration & dosage /adverse effects; Humans; Risk Assessment;
Scleroderma, Systemic /drug therapy

**AccessionNumber**
12013048071

**Date bibliographic record published**
16/09/2013

**Date abstract record published**
28/10/2013

**Record Status**
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.