Adverse events of intravenous glucocorticoid pulse therapy in inflammatory diseases: a meta-analysis

Smits NA, Duru N, Bijlsma JW, Jacobs JW

CRD summary
The review concluded that intravenous glucocorticoid pulse therapy resulted in a high adverse event rate; cardiovascular adverse events were the most commonly reported. The review had methodological and data limitations that limit the reliability of the authors' conclusions.

Authors' objectives
To determine the adverse events associated with intravenous pulse glucocorticoids for inflammatory diseases.

Searching
PubMed, EMBASE and The Cochrane Library were searched to October 2009 for articles published in English. Full search strategies were reported. Reference lists of retrieved studies were searched.

Study selection
Full text randomised controlled trials (RCTs), prospective trials, cohort studies and observational studies of intravenous pulse glucocorticoid (≥250mg prednisone equivalent) in adults with inflammatory disease were eligible for inclusion. Studies had to report the number of adverse events caused by glucocorticoid treatment. Studies of glucocorticoid therapy in combination with more than one disease modifying antirheumatic drug were excluded. Case studies were excluded.

The included studies considered glucocorticoid (methylprednisolone or dexamethasone) versus placebo or no comparator in patients with rheumatoid arthritis, systemic sclerosis or asthma. In the placebo-controlled studies, most patients were female, mean age of patients ranged from 33.7 to 60 years and the cumulative prednisolone equivalent dose ranged from 1,250mg to 7,875mg.

Two reviewers independently performed study selection.

Assessment of study quality
Study validity was assessed using criteria of predefined adverse events, standardised adverse events scoring protocol, and missing data to give a maximum score out of three (3 represented highest quality).

The authors did not state how many reviewers assessed validity.

Data extraction
Data were extracted on adverse events and used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for comparative studies. Data were extracted on events/exposed patients for non-comparative studies.

The authors did not state how many reviewers extracted data.

Methods of synthesis
Meta-analysis was undertaken to calculate pooled odds ratios and 95% CIs. A narrative synthesis was presented.

Results of the review
Eight studies were included in the review: four placebo-controlled studies (438 participants) and four uncontrolled studies (124 participants). The quality of the placebo-controlled studies was variable: one study scored 3, two scored 2 and one scored 1. Study duration ranged from two days to 4.5 years. The number of patients per study group ranged from five to 143.

Three hundred and twenty-three patients out of 344 who received glucocorticoids reported adverse events. The adverse event rate was 35/100 patient years. Cardiovascular adverse events were noted most commonly, followed by infections.
In the placebo-controlled studies, when glucocorticoid was compared with placebo there was a non-significantly greater rate of adverse events with glucocorticoids (OR 1.83, 95% CI 0.98 to 3.40; four trials), a significantly greater risk of flushing with glucocorticoids (OR 15, 95% CI 5.3 to 40; one study), a significantly greater risk of headache with glucocorticoids (OR 6.2, 95% CI 2.3 to 16; one study), a significantly greater risk of heart rhythm disorder with glucocorticoids (OR 2.93, 95% CI 1.03 to 8.36; one study) and a significantly greater risk of lower respiratory tract with glucocorticoids (OR 5.62, 95% CI 1.18 to 26.85; one study).

In the non-controlled studies, the most frequently reported adverse effect was increased diastolic blood pressure (88%; one study), flushing (24%; one study), diabetes mellitus (20%; one study), headache (20%; one study) and angina pectoris (20%; one study).

Other results were presented in the review.

**Authors’ conclusions**
Glucocorticoid pulse therapy resulted in a high adverse event rate; cardiovascular adverse events were the most commonly reported.

**CRD commentary**
Inclusion criteria for the review were broadly defined and three relevant data sources were searched. There was potential for language bias, as only articles in English were included. Publication bias was not assessed. Attempts were made to reduce reviewer error and bias during study selection; it was unclear whether the same methods were used for data extraction and quality assessment. Quality assessment indicated that the quality of the included studies was variable; several studies also had small sample sizes. Placebo-controlled studies were combined using meta-analysis but most of the results came from adverse event data provided by single studies. Many of the adverse events reported had only a small number of patients and it was unclear whether the reported adverse events were due to glucocorticoid or the underlying disease or other medication. Statistical heterogeneity neither reported nor discussed.

The review had methodological and data limitations that limit the reliability of the authors’ conclusions.

**Implications of the review for practice and research**
**Practice:** The authors stated that a detailed cardiovascular history should be obtained for patients prior to glucocorticoids therapy. Blood glucose should be monitored.

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

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