A meta-analysis of methylprednisolone in recovery from multiple sclerosis exacerbations


Authors' objectives
To assess methylprednisolone (MP) at different doses, and in comparison with other steroid products, in the treatment of multiple sclerosis exacerbations.

Searching
MEDLINE was searched from 1981 to 1998, and EMBASE from 1980 to 1998, combining 'Multiple Sclerosis' (as an index term) with 'Methylprednisolone' (either as an index term or in 'authors, title or abstract'). The references of identified articles and recent review articles were also examined. No restrictions on publication language were specified.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) where treatment was initiated within 8 weeks of relapse onset, and EDSS data had been collected within the first 4 weeks after treatment and at similarly spaced intervals thereafter, were included.

Specific interventions included in the review
MP in high doses (HD) of at least 500 mg/day for a minimum of 3 days, and low doses (LD) of at most 48 mg/day (equivalent to 60 mg prednisolone). These were compared with other glucocorticosteroid products (administered at similar dosage rates to those of MP), placebo, or no treatment.

Participants included in the review
Patients with multiple sclerosis were included.

Outcomes assessed in the review
Change in Kurtzke Expanded Disability Status Score (EDSS) were assessed.

How were decisions on the relevance of primary studies made?
Two authors independently selected the papers for inclusion using a structured evaluation process. Any disagreements were resolved by consensus.

Assessment of study quality
Full article reviews were only conducted for studies with a randomised controlled design. No other formal assessment of validity was performed. Two authors independently reviewed the papers for acceptable study design, and any disagreements were resolved by consensus.

Data extraction
Two authors independently performed the data extraction using a structured evaluation process. Any disagreements were resolved by consensus.

Data were extracted for the categories of study identification, type of comparison, treatments and dose, dose of active treatment, and EDSS assessment. Original data were requested from the authors of the included studies.

Methods of synthesis
How were the studies combined?
Effects sizes (ES), the differences between the means of EDSS scores, were calculated using both fixed-effect and
random-effects models. Their 95% confidence intervals (CIs) were also calculated.

**How were differences between studies investigated?**
The chi-squared statistic was used to test for homogeneity of treatment differences across studies. Further sensitivity analyses were not performed due to the small number of studies in the subgroups.

**Results of the review**
Nine RCTs were included in the review, although only 6 provided the original data for extraction. Six RCTs with 241 participants were included in the analysis: 110 in the HD MP group and 131 in either the LD MP, other glucocorticosteroids, or placebo group.

**HD MP versus placebo.**
Using a fixed-effect analysis in 3 studies, there was a statistically-significant benefit in favour of HD MP versus placebo at days 5 to 7 and at day 15, 21 or 28. The ES was -0.76 (standard deviation, SD 0.14; 95% CI: -1.02, -0.50, P<0.001; homogeneity, P=0.18) at days 5 to 7, and -0.85 (SD=0.21; 95% CI: -1.26, -0.45, P<0.001; homogeneity, P=0.054) at day 15, 21 or 28.

**HD MP versus LD MP.**
In 2 studies, there was no statistically-significant benefit in favour of HD MP versus LD MP at either days 5 to 7, or at day 15 or 28. The ES was 0.12 (SD=0.23; 95% CI: -0.19, +0.42, P=0.44; homogeneity, P=0.84) at days 5 to 7, and 0.08 (SD 0.23; 95% CI: -0.38, +0.54, P=0.74; homogeneity, P=0.86) at day 15 or 28.

Meta-analysis could not be performed for HD MP and other glucocorticosteroids due to a lack of raw data. However, one study suggested that HD MP (administered intravenously for 3 days) and adrenocorticotropic hormone (for 14 days) were both efficient and had a similar impact on the rate of recovery and final outcome of multiple sclerosis exacerbations.

**Authors’ conclusions**
The authors state that the results of the review supported the data obtained from the individual RCTs. These indicated that HD MP, of at least 500 mg/day for 5 days, administered either orally or intravenously, can accelerate the recovery from multiple sclerosis relapses.

**CRD commentary**
The authors stated the research question and the inclusion and exclusion criteria. The literature search was reasonably thorough, although it is possible that additional relevant studies may have been missed. There were no tests for publication bias.

The quality of the included studies was not formally assessed, although the authors assessed study design and excluded those studies that did not meet that criterion. The authors reported how the articles were selected, and who performed the selection, data extraction, and the study design assessment.

The extracted data were reported in tables and discussed in the text. The studies were statistically combined and heterogeneity was assessed. Only 6 studies were available for the meta-analysis and these were not all included in a single analysis. Two meta-analyses were performed, one with 2 studies and the other with 3 studies. The results of MP versus other glucocorticosteroids were only discussed in a narrative summary.

The authors’ conclusions appear to follow from the results presented.

**Implications of the review for practice and research**
Practice: The authors state that up to 500 mg/day of MP, administered either intravenously or orally for 5 days, can
accelerate the recovery from multiple sclerosis relapses.

Research: The authors recommend that carefully designed studies should be conducted to determine the optimum benefit in relation to dosage, the correct time for initiating therapy, and eventually, the most appropriate type of glucocorticosteroid. The new studies will also have to be designed to include patients on additional disease-modifying therapy, which can also influence the recovery process and/or the response to glucocorticosteroids.

Bibliographic details

PubMedID
10962547

Indexing Status
Subject indexing assigned by NLM

MeSH
Disability Evaluation; Dose-Response Relationship, Drug; Humans; Methylprednisolone /administration & dosage /therapeutic use; Multiple Sclerosis /drug therapy /physiopathology; Neuroprotective Agents /administration & dosage /therapeutic use; Placebos

AccessionNumber
1200001681

Date bibliographic record published
31/03/2002

Date abstract record published
31/03/2002

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.