Efficacy and tolerance of systemic steroids in sciatica: a systematic review and meta-analysis

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Abstract

Objectives. The efficacy of pharmacological interventions in sciatica is limited and the use of systemic steroids is still controversial. We aimed at evaluating the efficacy and tolerance of systemic steroids in sciatica.

Methods. A systematic literature search was performed in the Medline, Embase and Cochrane databases until February 2010. Randomized placebo-controlled trials evaluating the efficacy and the tolerance of systemic steroids in sciatica were included. Efficacy and tolerance were assessed using the relative risk (RR) and 95% CI with the inverse variance method (RR > 1 means that the event is more likely to occur in the steroid group). We explored the heterogeneity between the studies using subgroup analysis.

Results. Seven studies (383 patients) were included. The difference in the rate of responders between both groups was not statistically significant (RR = 1.22, 95% CI 0.96, 1.56). The rate of adverse events was 13.3% for the patients in the steroid group and 6.6% for the placebo group (RR = 2.01, 95% CI 1.06, 3.80). The number needed to harm was 20 (95% CI 10, ∞). Twenty (15.3%) patients in the steroid group and seven (5.7%) patients in the placebo group underwent surgery. A trend towards a higher requirement for spinal surgery was observed in the steroid group (RR = 1.14, 95% CI 0.74, 1.75). The methodological quality slightly influenced the results. We did not find any publication bias.

Conclusion. Steroid efficacy is not superior to the placebo in sciatica, but it has more side effects. The tolerance : efficacy ratio indicates against the use of systemic steroids in sciatica.

Key words: Sciatica, Herniated disc, Steroids.

Introduction

The annual incidence of sciatica is ~0.5% in the adult population in Western countries [1], with an important impact on health resources [2]. Spinal disorders are considered one of the most important causes of disability and work absenteeism and as one of the most expensive disease categories regarding hospital care [3].

The most common cause of sciatica is an intervertebral disc herniation, which results in both nerve root compression and the release of pro-inflammatory molecules such as IL-1β, IL-6, TNF-α, nitric oxide and prostaglandin E2 [4]. Since the nucleus is an immune-privileged site because it is both an avascular area that displays a biochemical phenotype with Fas causing infiltrating T-lymphocyte apoptosis, disc extrusion results in Th1 lymphocyte activation and macrophage infiltration via INF-γ secretion. Recent studies also showed the importance of Th17 lymphocyte in this process [5]. Although NSAIDs are the first-line drug strategy, steroids are an alternative strategy that can be used systematically or locally. The use of epidural administration in sciatica is still controversial [6, 7]. Green et al. [8] reported favourable results on pain relief by systemic steroids in an uncontrolled trial of 100 patients treated by an i.m. tapering dose of dexamethasone.

Previous systematic literature reviews have suggested at limited interest of systemic steroids in sciatica [9]. During the past few years, several trials were carried out...
to compare the efficacy of steroids and placebo in sciatica with conflicting results. Therefore, we performed a systematic literature review in order to obtain a numerical conclusion necessary for an objective evaluation of systemic steroid efficacy and tolerance in sciatica.

Methods

This meta-analysis was conducted according to the Cochrane Collaboration guidelines [10].

Search strategy

An extensive search of PubMed and Embase databases and the Cochrane Central Register of randomized controlled trials (until 19 February 2010) was independently performed by two reviewers (C.R. and A.B.). The following key words were used to screen the PubMed and Cochrane databases (‘Intervertebral Disc Displacement’[Mesh] OR ‘Sciatica’[Mesh] OR ‘Low Back Pain’[Mesh] AND (‘Steroids’[Mesh] OR ‘Glucocorticoids’[Mesh] OR ‘Methylprednisolone’[Mesh]). The limit ‘clinical trial’ was applied. Key words for searches in the Embase database were: ‘ischialgia’/exp OR ‘discogenic pain’/exp AND ‘corticosteroid’/exp AND [controlled clinical trial]/lim AND [embase]/lim with ‘controlled clinical trial’/lim as the limit. This search was completed by a hand search of references from relevant articles, review papers and abstracts presented at the ACR annual scientific meetings, the European League against Rheumatism (EULAR) annual congress and the French Society of Rheumatology (SFR) scientific meetings from 2007 until 2010.

Selection

Inclusion criteria were: (i) randomized controlled trial; (ii) evaluating efficacy and/or tolerance; and (iii) adult patients with sciatica. Exclusion criteria were: (i) uncontrolled trial; and (ii) post-surgery evaluation of treatment with systemic steroids.

Quality assessment

Two reviewers (C.R. and M.D.) independently assessed the methodological quality of each study included in the meta-analysis using both the Jadad scale [11] and the Delphi list [12], ranging from 0 to 5 and 0 to 9 (a higher score for a higher methodological quality), respectively. A high-quality trial was defined by a score of 6 in the Delphi list. Both reviewers also independently assessed the clinical relevance using the Cochrane Collaboration Back Review Group [13]. A clinically relevant study was defined by a positive answer for the first, second and third items. When disagreements between both reviewers occurred, a third reviewer (A.B.) was consulted.

Data extraction

Two reviewers (C.R. and A.B.) selected the articles and collected the data using a predetermined form that included study design (randomization procedure, blinding and assessment endpoints), patient characteristics (number, age, gender, disease duration and treatment parameters), When disagreements between both reviewers occurred, a third reviewer (M.D.) was consulted. Authors of included articles were contacted in order to provide unpublished collected data.

Outcomes

The following outcomes were extracted from the publications by two independent reviewers (C.R. and A.B.).

- Efficacy: number of responders at 7 (±4) days, pain visual analogue scale (VAS) within 1 month, number of patients who underwent spine surgery, number of patients who did not resume full-time work after 1 month, use of analgesics, narcotics and NSAIDs, disability on either the Roland–Morris scale [14] or the Oswestry questionnaire [15]. When pooling the data, we considered disabled patients with an affirmative response to any of the items on the Roland–Morris disability scale.
- Tolerance: number of completers, number and type of adverse events.

When the outcome measures were recorded in a trial, but not provided in the article, the authors were contacted in order to obtain these missing data. When disagreements between both reviewers occurred, a third reviewer (M.D.) was consulted.

Statistical analysis

Heterogeneity was tested using the I² statistic [16]: I² > 50% indicated significant heterogeneity. The efficacy and tolerance of systemic steroids were compared with placebo in each study by calculating relative risk (RR) and 95% CI for binary outcomes (RR > 1 means that the event is more likely to occur in the steroid group than in the control group); the weighted mean difference (WMD) and 95% CI were calculated for continuous outcomes. Individual RRs and WMDs were pooled using the inverse variance method with a random effect model [17]. When a statistical difference was found between systemic steroids and placebo tolerance, the results were also expressed as the number needed to harm (one divided by the absolute risk reduction) [18], i.e. the number of patients who would have to be treated by systemic steroids in order to detect an additional adverse event. The CIs for the numbers needed to harm were obtained by inverting the values for the 95% CIs for absolute risk reduction. Inter-reviewer reproducibility was considered good for a kappa coefficient > 0.6 and excellent for a kappa coefficient > 0.8 [19]. The meta-analyses were performed using Review Manager 5 (RevMan Version 5.0, Copenhagen, Denmark) and additional statistics with StatsDirect (StatsDirect statistical software, Cheshire, UK).

Sensitivity analysis and heterogeneity assessment

We conducted a sensitivity analysis in order to evaluate the robustness of the meta-analysis by examining the influence of an individual study on the overall RR by removing each study individually from the meta-analysis. Subgroup analysis was performed to explore
heterogeneity. We combined the studies into two sub-
groups according to the trial design (published before or
after 2000), the methodological quality (Delphi superior
or inferior to 6 points), the treatment parameters (i.m.
or non-i.m. administration; single or multiple doses;
dexamethasone or non-dexamethasone steroids) and
concurrent treatment (including NSAIDs or not). We then
evaluated the influence of each subgroup on heterogen-
eity by forest plot analysis and the chi-square test [20].

Publication bias
Publication bias was assessed using funnel plot analysis,
Begg’s test and Egger’s test.

Results

Trial flow
The review process is summarized in Fig. 1. Four hundred
and six abstracts were retrieved by database searching.
Of these, 37 full-text articles were analysed and 7 articles
were finally included [21–27]. The inter-reviewer reliability
was good for abstract selection ($\kappa = 0.76$, agreement 97%)
and full-text article selection ($\kappa = 0.72$, agreement 86%).

Study characteristics
The study characteristics are summarized in Table 1.
Seven studies comprising 383 patients (188 patients
in the systemic steroid group and 195 patients in the
placebo group) were included in this meta-analysis.
The mean age varied from 37.0 to 49.0 years, while the
mean disease duration ranged from 1 week to 36 months.
Female rate ranged from 32.0 to 54.0% of the population.
The mean (s.d.) of the methodological scores on the Jadad
scale and the Delphi list were 3.2 (1.5) and 5.7 (1.5), re-
spectively. The mean (s.d.) of the clinical pertinence score
was 7.5 (1.0). The inter-reviewer reliability for methodo-
logical and clinical relevance assessments was moderate
($\kappa = 0.49$, agreement 83%).

Intervention parameters
The intervention characteristics are summarized in
Table 1. Steroids were given intramuscularly in five stud-
ies, intravenously in one study and orally in another
study. Treatment consisted of dexamethasone in four stud-
ies, methylprednisolone in two studies and prednisolone
in one study. Steroid treatment duration ranged from a
single day to 10 days.

Efficacy of systemic steroids in sciatica
Four studies, including 212 patients, reported the number
of responders. The rate of responder was 57.7% (60 out of
104 patients) in the systemic steroids group and 50.0%
(54 out of 108 patients) in the placebo group. The differ-
ence between the systemic steroids and the placebo was

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Fig. 1 Literature search flow chart.

![Flow chart](https://www.hematology.oxfordjournals.org/1605)
<table>
<thead>
<tr>
<th>Studies</th>
<th>Jadad score</th>
<th>Delphi list</th>
<th>Clinical relevance</th>
<th>Disease duration</th>
<th>Additional treatments</th>
<th>Steroids</th>
<th>Intervention group</th>
<th>Placebo group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedman et al. [26]</td>
<td>5/5</td>
<td>7/9</td>
<td>9/11</td>
<td>1 week</td>
<td>NSAIDs, analgesics</td>
<td></td>
<td></td>
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<tr>
<td>Finckh et al. [27]</td>
<td>4/5</td>
<td>7/9</td>
<td>7/11</td>
<td>&lt;6 week</td>
<td>NSAIDs, analgesics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haimovic et al. [25]</td>
<td>3/5</td>
<td>5/9</td>
<td>8/11</td>
<td>NR</td>
<td>Bed rest, analgesics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hedeboe et al. [24]</td>
<td>1/5</td>
<td>3/9</td>
<td>8/11</td>
<td>&lt;8 week</td>
<td>NSAIDs, physiotherapy</td>
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<tr>
<td>Hofferberth et al. [23]</td>
<td>3/5</td>
<td>6/9</td>
<td>8/11</td>
<td>36 months</td>
<td>Analgesics</td>
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<tr>
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<td>6/9</td>
<td>7/11</td>
<td>&gt;6 week</td>
<td>Analgesics</td>
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<tr>
<td>Porsman et al. [21]</td>
<td>3/5</td>
<td>6/9</td>
<td>8/11</td>
<td>&gt;6 week</td>
<td>Analgesics</td>
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NR = not reported.
not statistically significant (RR = 1.22, 95% CI 0.96, 1.56, P = 0.11; I² = 0%; Fig. 2A).

The data on pain VAS modification were available in three studies including a total of 85 patients in the steroid group and 86 in the placebo group. Both groups displayed a similar variation of VAS leg pain (WMD = -0.16, 95% CI -0.87, 0.55, P = 0.67, I² = 13%; Fig. 2B).

Six studies, including 150 patients in the systemic steroid group and 142 patients in the placebo group, reported the number of patients who underwent spine surgery during the trial. Thirty (20.0%) patients in the systemic steroid group and 20 (14.1%) patients in the placebo group underwent surgery (RR = 1.14, 95% CI 0.74, 1.75, P = 0.55, I² = 0%; Fig. 3). Two studies (111 patients) evaluated the number of patients who returned to work. The proportion of patients who returned to their baseline work hours ranged from 8 to 60% after 1 month without any significant difference, according to the treatment allocation (RR = 0.90, 95% CI 0.43, 1.87, P = 0.78, I² = 0%).

The data concerning the influence of systemic steroids on NSAIDs and narcotics consumption were available in two studies (89 patients). No statistically significant difference was shown between both groups (RR = 0.82, 95% CI 0.57, 1.20, P = 0.32, I² = 0% and RR = 0.59, 95% CI 0.25, 1.42, P = 0.24, I² = 0%, respectively). Another study showed no statistical difference between both groups in the overall use of analgesics.

Three studies (170 patients) evaluated patient disability. Two studies recorded the Roland–Morris disability scale whilst one study recorded the Oswestry questionnaire. The difference in the number of patients with an affirmative response to any of the items on the Roland–Morris disability scale was not statistically different between the steroid and control groups (RR = 0.76, 95% CI 0.21, 2.75, P = 0.68), with a substantial heterogeneity between both studies (I² = 90%; P = 0.002). One study recorded the Oswestry questionnaire, without any statistical differences between the steroid and placebo groups. No significant impact of steroids on the quality of life Health Survey Scoring Demonstration (SF-12) was observed in the single study evaluating this outcome measure.

Tolerance of systemic steroids in sciatica

Data concerning the number of completers were available in five studies, including 119 patients in the systemic steroid group and 113 patients in the placebo group. Nine (7.6%) patients withdrew in the systemic steroid group, whereas three (2.7%) patients withdrew in the placebo group (RR = 0.99, 95% CI 0.92, 1.06, P = 0.72, I² = 5%).

Five studies, including 152 patients in the systemic steroid group and 167 patients in the placebo group, reported adverse events. The detail of these adverse events is described in the supplementary table available as supplementary data at Rheumatology Online. Adverse events were reported in 25 (13.3%) patients in the systemic steroid group and 12 (6.2%) patients in the placebo group (RR = 2.01, 95% CI 1.06, 3.80, P = 0.03, I² = 0%). The number needed to harm was 20 (95% CI 10, ∞) (Fig. 4).

Heterogeneity exploration and sensitivity analysis

Moderate heterogeneity was detected in the meta-analysis comparing the rate of responders. Publication date and treatment parameters (molecule, duration, administration route and co-treatments) had little impact.
on the results (Table 2). Methodological quality slightly impacted on the results. Studies with a lower methodological score were more likely to show more adverse events in the systemic steroid group. Given the low heterogeneity between the included studies in terms of mean age, disease duration and sex ratio, we did not explore the impact of these above-mentioned parameters on the results. Sensitivity analyses showed that the RR and 95% CIs were not substantially altered by removing any trial (data not shown).

**Publication bias**

Begg’s and Egger’s methods did not detect a significant publication bias (see supplementary figures available as supplementary data at Rheumatology Online). However, funnel plot analysis suggested an asymmetry in the funnel plot related to the need for spine surgery meta-analysis (see supplementary figure 3 available as supplementary data at Rheumatology Online).

**Discussion**

Our systematic review and meta-analysis provided several lines of evidence to support the avoidance of systemic steroid use in sciatica. First, we showed that systematic steroid efficacy is not superior to that of a placebo in pain relief. The rates of responders were similar in both groups. No positive impact on the return to work and analgesic consumption was shown. Secondly, steroids induced a substantial enhancement of adverse events. We were able to provide numerical data about the poor tolerance to steroids. Thirdly, a trend towards a higher requirement for surgery in the steroid group was observed. This result is in agreement with Genevay et al. [28], who hypothesized that steroids might hinder disc
herniation resorption, which would lead to a longer evolution of the disease. Finally, we did not retrieve any study to support the use of steroids in sciatica complications such as muscle weakness or cauda equina syndrome.

Previous systematic reviews found no clear evidence for differences between NSAIDs and placebos in sciatica [9, 29, 30]. Similarly, the efficacy of steroid injections has not clearly been established [6]. A positive effect on short-term pain relief is possible [31], whereas a positive effect beyond 1 month on work absenteeism and on the need for surgery is unlikely [32]. Data on the preferential route of steroid injection (epidural or transforaminal periradicular) are controversial [33]. No differences between steroid and placebo injections on long-term pain, function and the need for surgery or systemic steroids were detected. Given that TNF-α plays a central role in neuropathic pain in sciatica [34, 35], the use of TNF-α blockers was proposed for sciatica treatment. However, the size effect size of such a treatment is small [36–38].

This meta-analysis had a few limitations. Although we decided to only include randomized placebo-controlled studies, barely a few articles achieved a high methodological quality. Randomization procedures, blinding procedures and drop-out descriptions were seldom well reported, as shown by the moderate agreement between reviewers assessing these parameters. The inclusion of small studies in the meta-analysis was previously reported as a potential distortion [39]. Thanks to data pooling, we were able to show that steroid inefficacy in sciatica was not due to a lack of statistical power. Despite an extensive literature search, our meta-analysis included a limited number of studies, hampering clear conclusions concerning publication bias. Moreover, steroid dosage and route were different between the studies. However, we did not identify heterogeneity among the studies according to steroid dosage, route of administration or treatment duration. Another potential bias could have been the choice of the efficacy outcome, since responders were defined differently in each study. In some studies, the responders were defined by subjective appreciation by the physician, whereas in others an objective cut-off point of the VAS value was applied to define the responders. Given that data concerning VAS pain evaluation were in agreement with the evaluation of responder rate, it is unlikely that this potential bias strongly influenced the results.

Finally, only a few studies evaluated the impact of systemic steroids on quality of life or disability.

Several important issues were not explored by this systematic review. We could not explore the

<table>
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<th>TABLE 2 Heterogeneity exploration</th>
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<tr>
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<td>Treatment duration</td>
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<td>Single dose</td>
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<td>Administration route</td>
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<td>Non-i.m.</td>
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<tr>
<td>Molecule</td>
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<tr>
<td>Dexamethosone</td>
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<tr>
<td>Other steroids</td>
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<td>Delphi ≥ 6</td>
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<td>Subgroup difference, chi-square test</td>
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NA = Not applicable.
medico-economic impact of systemic steroids. Since sciatica has a great impact on health-care resources, the evaluation of first-line medical treatments is mandatory. Previous studies reported that disc herniation with a large spinal canal [41], extra-foraminal localization and nerve root compression [42] were associated with a positive outcome. Given that only a few studies included spine imaging, we could not examine whether these parameters influenced the results. Several authors [23, 26, 27] stated that some patients included in these trials may not have suffered from a herniated disc-related sciatica. Since sciatica is a heterogenous condition, they proposed that a single steroid bolus could be used as a test dose to select patients who might benefit the most from extended steroid therapy.

In conclusion, we showed in this meta-analysis that the efficacy of systemic steroids is not superior to that of a placebo in sciatica management. Given the methodological limits of most of the studies evaluating sciatica treatment, further studies are mandatory in order to improve sciatica management.

Rheumatology key messages

- Systemic steroid efficacy is not superior to placebo in sciatica.
- Systemic steroids are tolerated less than a placebo in sciatica.

Acknowledgements

The authors thank Ms Anais Perret for her help in writing the manuscript. The authors are very grateful to Dr RL Holve, Dr H Barkan, Dr A Finckh and Dr BW Friedman for answering our questions concerning unpublished data.

Disclosure statement: The authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at Rheumatology Online.

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