Corticosteroids for Optic Neuritis Treatment
Preferred Practice Pattern® (PPP) Clinical Questions are evidence-based statements that guide clinicians in providing optimal patient care. PPP Clinical Questions answer specific questions in the “Patient, Intervention, Comparison, Outcome” (PICO) format.

PPP Clinical Questions are developed by the Academy’s H. Dunbar Hoskins Jr., M.D. Center for Quality Eye Care without any external financial support. Authors and reviewers of PPP Clinical Questions are volunteers and do not receive any financial compensation for their contributions to the documents.
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Preferred Practice Pattern Clinical Questions should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network (SIGN)\(^1\) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE)\(^2\) group are used. All studies used to form a recommendation for care are graded for strength of evidence individually. To rate individual studies, a scale based on SIGN\(^1\) is used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.\(^3\)

### SIGN\(^1\) Study Rating Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>I++</td>
<td>High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>I+</td>
<td>Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>I-</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>II++</td>
<td>High-quality systematic reviews of case-control or cohort studies, or high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
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<tr>
<td>II+</td>
<td>Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>II-</td>
<td>Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
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<tr>
<td>III</td>
<td>Nonanalytic studies (e.g., case reports, case series)</td>
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### GRADE\(^2\) Quality Ratings

<table>
<thead>
<tr>
<th>Quality</th>
<th>Description</th>
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<tr>
<td>Good quality</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect</td>
</tr>
<tr>
<td>Moderate quality</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate</td>
</tr>
<tr>
<td>Insufficient quality</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain</td>
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### GRADE\(^2\) Key Recommendations for Care

<table>
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<tr>
<th>Recommendation Type</th>
<th>Description</th>
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<tr>
<td>Strong recommendation</td>
<td>Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not</td>
</tr>
<tr>
<td>Discretionary recommendation</td>
<td>Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced</td>
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PPP Clinical Question

TOPIC

Corticosteroids in the treatment of optic neuritis

CLINICAL QUESTION

What is the evidence that corticosteroids are more or less effective treatments than placebo or “no treatment” conditions for patients with acute optic neuritis?

LITERATURE SEARCH

The literature search for the Cochrane Review was last updated in February 2012. To present this Clinical Question, an additional literature search was undertaken in April 2013.

Literature search details

SYSTEMATIC REVIEW


Recommendations for Care

SUMMARY

Optic neuritis is an inflammatory demyelination of the optic nerve, occurring more commonly in women than in men. Multiple sclerosis (MS) is almost always the suspected cause. Optic neuritis is typically characterized by a sudden vision loss over several hours or days. However, 95% of patients experience an improvement in visual acuity (VA) to 20/40 or better at 12 months.

While the VA symptoms associated with optic neuritis should never be treated in isolation, this review focuses predominantly on the effectiveness of oral or intravenous (IV) corticosteroid treatment to address these symptoms. Because corticosteroids are commonly used, in part, to treat optic neuritis, and their effectiveness in the treatment of optic neuritis has historically (i.e., since the 1950s) remained in question, the Cochrane Collaboration conducted a review focused exclusively on the treatment of acute optic neuritis and the outcome of VA recovery, with corticosteroids. The AAO emphasizes, however, that it is the role of the attending ophthalmologist to treat the entire person, and not just the limited symptoms discussed in this review.
The Cochrane Review authors systematically reviewed the evidence for the use of corticosteroid therapy in any form or dosage with the intention to treat or reduce the symptoms of acute optic neuritis, compared with placebo or no treatment conditions. Studies included in their review were randomized controlled trials (RCTs) where 1) study participants had acute optic neuritis; 2) the proportion of patients achieving normal VA, normal contrast sensitivity, or normal visual field at six months or more were reported; and 3) secondary outcomes, defined as immediate response (rate of recovery) for the same visual outcomes, were measured one month after treatment.

The authors of the Cochrane Review identified six RCTs meeting these criteria. A total of 750 patients were included in these trials. However, 457 patients constituted one large RCT (the Optic Neuritis Treatment Trial [ONTT]),4 and the remaining trials were small (i.e., less than 70 total patients). These studies varied considerably in terms of the corticosteroid regimens studied and patient populations sampled. For instance, different studies required various durations of symptoms for inclusion and one trial did not exclude patients with corticosteroid treatment histories.

The objective of this review was to assess the effectiveness of corticosteroids for acute optic neuritis. There is conclusive evidence that high-dose corticosteroids—either oral or IV corticosteroids—produce a more rapid recovery of vision in the short-term, but do not provide a long-term visual benefit. There is also a delay in the onset of subsequent demyelination, and a decrease in the rate of subsequent demyelination events,5 in those with higher risk MRI findings for 2-3 years with high dose corticosteroids as compared to those not treated with high dose corticosteroids.

(Study Rating Scale I+, Moderate Quality, Discretionary Recommendation)

DISCUSSION

**Oral Corticosteroids vs. Placebo**

None of the trials found evidence of a statistically significant benefit of oral corticosteroid treatment (generally low-dose prednisolone), compared to placebo, as measured by the proportion of patients achieving normal VA, normal contrast sensitivity, or normal visual field at one month, six months, or one year. Trials evaluating the oral corticosteroids used varying dosages of the medication. The ONTT found that there was no difference between the proportion of patients achieving normal VA and contrast sensitivity at one year in comparison to the placebo group (Risk Ratio (RR): 0.93; 95% Confidence Interval (CI): 0.86–1.00), the VA between the three groups was similar. (There was an oral prednisone group, an intravenous methylprednisone group, and a placebo group.) Also, oral corticosteroid therapy at a specific dose of 1 mg/kg prednisone was associated with an increase in rate of new episodes of optic neuritis as suggested by the analyses reported in the ONTT.

**Intravenous Corticosteroids vs. Placebo**

None of the trials found evidence of a statistically significant benefit of IV corticosteroids (dexamethasone or methylprednisolone (>3,000 mg total dose)), compared to placebo, as measured by the proportion of patients achieving normal VA at one month, six months, or one year. No trials found evidence of a benefit as measured by the proportion of patients achieving normal contrast sensitivity at one month or six months. One small RCT6 found that IV corticosteroids were associated with a significantly higher proportion of patients achieving normal contrast sensitivity at one year (RR: 1.33; 95% CI: 1.02–1.72). However, this association was both of marginal significance and not replicated in the ONTT. In fact, the ONTT found no benefit for contrast sensitivity using corticosteroids at one year (RR: 0.99; 95% CI: 0.93–1.06). A life-table analysis reported in the ONTT found that the rate of return of vision to normal was faster with IV
corticosteroids compared with placebo (P=0.09 for VA, 0.02 for contrast sensitivity, and 0.00001 for visual field), yet this outcome was not sustained over time.

None of the trials found a benefit as measured by the proportion of patients achieving a normal visual field by six months or one year. The ONTT found evidence of a benefit using this measure at one month (RR: 1.36; 95% CI 1.05–1.75), but the effect was not maintained over time. At six months, the RR associated with corticosteroids was 1.07 (95% CI: 0.95–1.21), and at one year, the RR was 1.00 (95% CI: 0.85–1.18).

CONCLUSION

A systematic review of one large RCT and five smaller RCTs found that high-dose IV corticosteroids produce a more rapid recovery of vision among patients with acute optic neuritis in the short-term, but do not provide a long-term visual benefit overall. Although high-dose IV corticosteroid treatment does lead to a more rapid recovery of vision, there were no consistent improvements as measured by patient recovery to normal VA, normal contrast sensitivity, or normal visual field. High dose corticosteroid treatment does, however, delay the onset of subsequent demyelination events for 2-3 years for patients with MS. Comparisons among the trials are limited by heterogeneity across the patients sampled, the corticosteroid regimens studied, and small treatment effects.

From a clinician’s perspective, treatment with high-dose IV corticosteroids followed by oral corticosteroids may be appropriate, in terms of helping patients achieve faster recovery to normal vision; no treatment for these symptoms may also be an appropriate course of action. We emphasize that patients with acute optic neuritis are often afflicted with MS or other underlying conditions. Appropriate care for these patients must not focus solely on the visual symptoms in exclusion of potential neurological implications. Neural damage occurs with the great majority of patients even though VA returns to normal. Going forward there is a clear need for future research for improved pharmacologic therapy.

References