Acta Scientific Neurology (ISSN: 2582-1121)

Volume 6 Issue 10 October 2023

Research Article

Steroids for Optic Neuritis. Comparison between IV Steroids and Oral Steroids: Systematic Review and Meta-Analysis

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Received: September 04, 2023

Published: September 26, 2023

Abstract

Introduction: Optic neuritis is defined as an inflammation of the optic nerve. It usually manifests with abrupt painful loss of vision. The recovery of the vision loss is almost never complete. Women are usually more commonly affected than men. Optic neuritis is most commonly due to autoimmune etiology and is closely linked to multiple sclerosis however, other etiologies including infectious do exist. Few trials evaluated the effectiveness of corticosteroids for the treatment of optic neuritis and rarely those trials compared between oral and intravenous corticosteroids use.

Search Methods: We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2023), MEDLINE (January 1950 to July 2023, EMBASE (January 1980 to July 2023), PubMed (January 1946 to July 2023), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). No date or language restrictions in the electronic searches for trials were there. The electronic databases were last searched in July 2023.

Selection criteria: We followed the PRISMA statement guidelines during the preparation of this systematic review. We included randomized controlled trials (RCTs) that evaluated intravenous corticosteroids in patients with acute optic neuritis in comparison to oral corticosteroids.

Main results: We included two RCTs with a total of 750 participants. Each trial was conducted in a different country: United States and Canada. The two trials included have low risk of bias. Both of those trials included information about the efficacy of IV steroids and oral steroids in improving visual acuity which allowed for comparison and further analysis. In the meta-analyses to assess visual acuity, the risk ratio (RR) was 0.98 (95% confidence interval (CI) 0.93 to 1.02) at six months.

Authors' conclusions: There is no conclusive evidence of difference in benefit in terms of recovery to normal visual acuity after six months of treatment with either intravenous or oral corticosteroids at the doses evaluated in trials included in this review.

Keywords: Steroids; Methylprednisolone; Prednisone; Optic Neuritis; Multiple Sclerosis

Introduction

Acute demyelinating optic neuritis (ON) is the most common cause of painful monocular visual loss, with an annual incidence in the United States of 6.4 per 100 000 persons [1,2]. In a study that was done in Olmsted county in Minnesota, USA, the prevalence rate of optic neuritis was found to be 115 per 100,000 [3]. Women are usually more affected compared to men. Optic neuritis has a similar pathogenesis to multiple sclerosis and ON might be the first manifestation of multiple sclerosis (MS) [4,5]. Corticosteroids have been used traditionally to treat acute demyelinating events including optic neuritis [6]. We have found that few clinical trials studied the effect of corticosteroids for the treatment of optic neuritis. Rarely, clinical trials studied the difference between intravenous (IV) corticosteroids therapy in comparison to oral (PO) corticosteroids therapy for the treatment of optic neuritis. The objective of our systematic review is to evaluate the current evidence about the treatment of optic neuritis with corticosteroids and to evaluate if IV corticosteroids were superior to bioequivalent doses of oral corticosteroids for the treatment of optic neuritis by evaluating the recovery of optic nerve function.

Methods

We followed the PRISMA statement guidelines during the preparation of this review.

- **Types of studies:** This review included only randomized controlled trials (RCTs).
- **Types of participants:** We included trials in which the participants had acute optic neuritis. We did not consider participants diagnosed with MS relapse in general or patients presenting with ON due to neuromyelitis optica due to the different treatment regimen and prognosis for this condition. There were no age limitations.
- **Types of interventions:** We included trials in which systemic corticosteroid therapy was administered and included a comparison between oral and intravenous corticosteroids use. We did not limit inclusion of trials in this review based on the duration of treatment or the length of follow-up.
- **Outcome measures:** Improvement in the visual acuity.
- **Search methods for identification of studies:** We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2023), MEDLINE (January 1950 to July 2023, EMBASE (January 1980 to July 2023), PubMed (January 1946 to July 2023), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). No date or language restrictions in the electronic searches for trials were there. The electronic databases were last searched in July 2023.
- **Selection of Studies:** Two authors applied the selection criteria. Eligibility
- **screening was performed in two steps:** The first step was to screen abstracts for eligibility and in the second step, full-text articles of eligible abstracts were retrieved and screened for eligibility to this study.
- **Data Extraction:** Two authors extracted the data independently using an online data extraction form. The extracted data includes the following: 1) characters of study design, 2) characters of study population, 3) risk of bias domains, 4) study outcomes.
- **Assessment of Risk of Bias in Included Studies:** Two authors independently assessed the quality of each included study in accordance with the Cochrane handbook of systematic reviews of interventions 5.1.0 (updated March 2011). Refer to figure 2.
- **Measures of Treatment Effect:** Visual acuity after 6 months of treatment. Other primary outcomes were included however due to not being similar among trials, comparison was not possible.

Results and Discussion

Our search retrieved 20 unique citations which were screened and assessed for eligibility. Of the 20 full text article, 18 articles were excluded and two RCTs (n = 502 patients) were included in this study (See PRISMA flow diagram; figure 1). The reasons for excluding other studies were as follows: studies that were secondary analysis for the primary clinical trial and studies that were irrelevant to the primary research topic. We excluded a trial that wasn't in English. For the included studies [6,7] a summary of their design and main results is shown in table 1. The baseline characteristics of their populations are shown in table 2. The quality of the included studies was from high quality according to the Cochrane risk of bias assessment tool.

Visual acuity at 6 months was an outcome for both of the clinical trials involved and this allowed us to conduct analysis on both of

the trials. In one of the trials, poor visual acuity outcome was defined to be 20/50 or worse [6]. The first trial concluded that there is no difference between IV or oral steroids therapy for optic neuritis in terms of recovery [7]. The second trial expressed concerns about the efficacy of oral prednisone and the risk of recurrence of optic neuritis however, only 11 patients our of 156 patients had poor visual acuity outcome compared to the IV group in which 9 patients had poor outcome out of 151 patients. We have found in our meta-analysis that there was a slight difference between IV and oral steroids therapy for optic neuritis however not statistically significant (RR 0.98, CI 0.93-1.02, P = 0.30), refer to figure 3.

In order to minimize the publication bias, we performed an extensive search method, and we retrieved citations from multiple electronic databases. We could not include any unpublished study or studies that were discussing the effect on MS exacerbation in general rather than optic neuritis.

The quality of this evidence is credible as it is based on high quality studies with low risk of bias as indicated by risk of bias assessment provided by Cochrane bias assessment tool. The search methods and eligibility criteria were well defined. We followed PRISMA checklist and all steps were performed strictly following Cochrane handbook of systematic reviews for interventions.

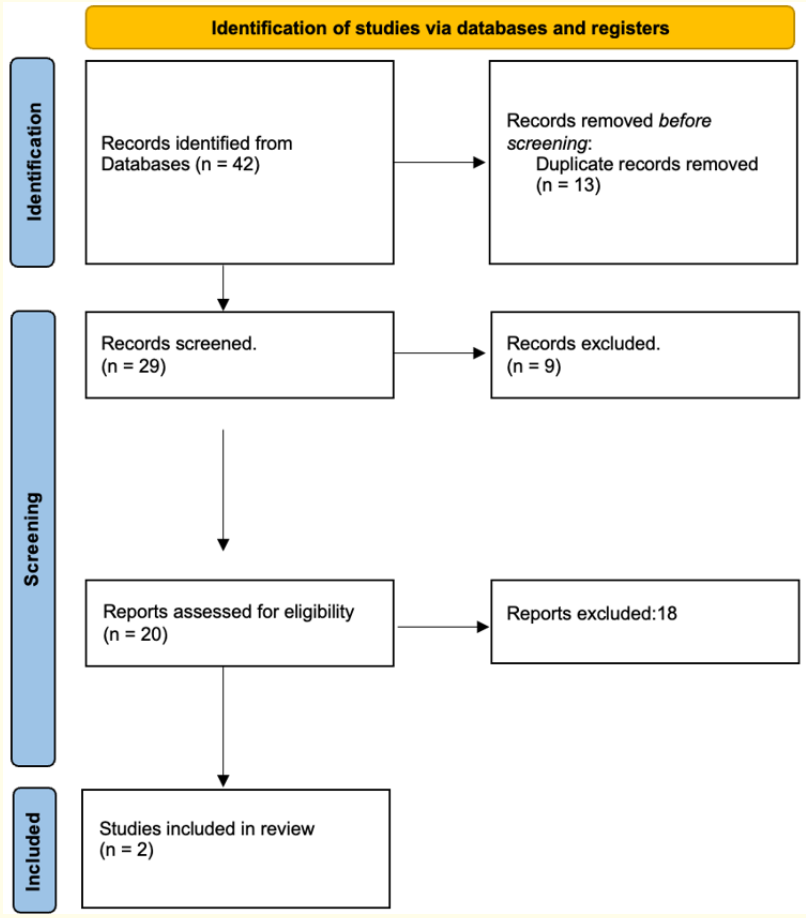

Figure 1: PRISMA flow diagram.

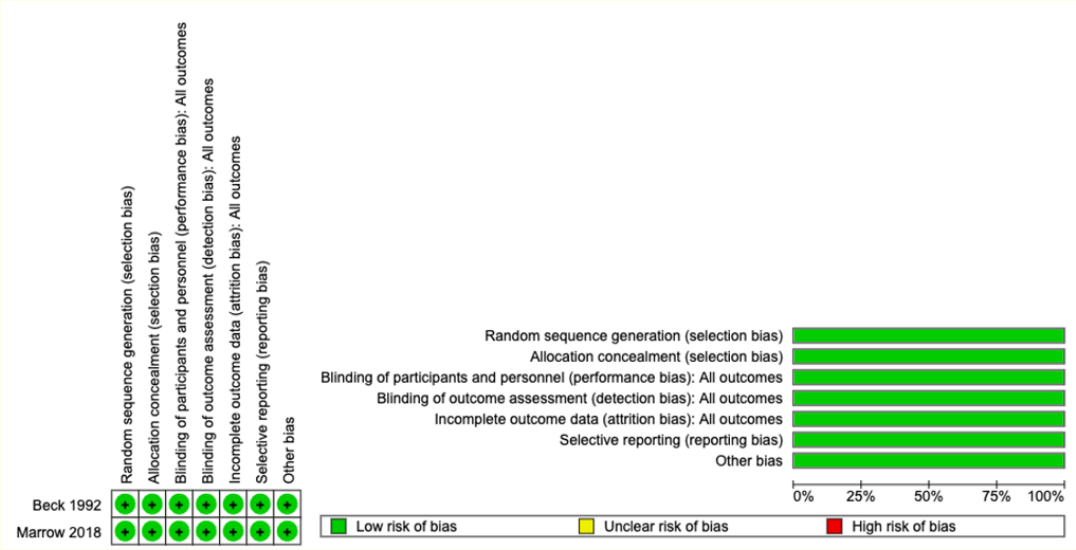

Figure 2: Summary of assessment of risk of bias.

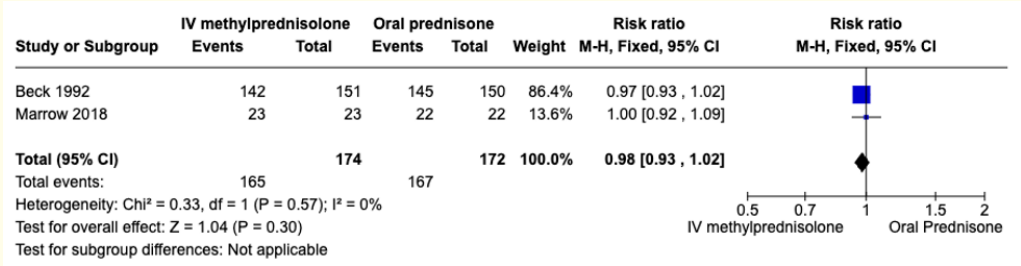

Figure 3: Forest Plot for risk ratio with CI of 95%.

Study	Location	Year	Sample size	Design	Population	Intervention	Comparator	Outcome
Morrow, 2018	Canada	2018	55	RCT single blinded	First episode of optic neuritis patients presenting within 14 days of onset of symptoms	IV methylprednisolone sodium succinate (1000-mg)	Oral prednisone (1250-mg)	1. recovery of the latency of the P100 component of the visual evoked potential at 6 months. 2.Best corrected visual acuity
Beck, 1992	USA	1992	457	RCT single blinded	First episode of optic neuritis. Patients presented within 5 days of symptoms onset.	Methylprednisolone (Solu-Medrol, 250 mg every 6 hours for 3 days) followed by oral prednisone (Deltasone, 1 mg per kilogram of body weight per day for 11 days)	Oral prednisone (1 mg per kilogram per day for 14 days) AND Placebo	Visual field and contrast sensitivity were the primary measures of outcome; visual acuity and color vision were secondary measures.

Table 1: Summary of the included studies.

Study	Group	Number of patients	Age (mean)	Sex (female%)	Race (white%)
Morrow, 2018	IV	23	33.1	60.9%	90%
	PO	22	30.1	63.6%	90.9%
Beck, 1992	IV	151	32.4	77	81
	PO	156	32.2	79	90
	Placebo	150	31.1	75	84

Table 2: Baseline characteristics for population of the included studies.

Conclusions

There is no conclusive evidence of difference in benefit in terms of recovery to normal visual acuity after six months of treatment with either intravenous or oral corticosteroids at the doses evaluated in trials included in this review.

Conflict of Interest Statement

None.

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