Graefe's Archive for Clinical and Experimental Ophthalmology
https://doi.org/10.1007/s00417-024-06568-w

NEUROPHTHALMOLOGY

Visual recovery after oral high-dose methylprednisolone in acute inflammatory optic neuropathy

Elodie Boureaux[1] · Charlotte Laurent[1] · Thomas Rodriguez[1] · Emanuelle Le Page[2] · Frédéric Mouriaux[1,3]

Received: 20 November 2023 / Revised: 22 May 2024 / Accepted: 24 June 2024

Abstract

Purpose High doses of venous corticosteroids are currently the only validated treatment for the management of optic neuritis (ON). The objective is to assess the changes in visual function parameters after oral high-dose methylprednisolone in patients with ON.

Methods A retrospective analysis of patients with acute ON was performed. Patients received 1 g per day of oral methylprednisolone for 3 to 5 days. Visual function was measured using the ETDRS test for visual acuity, 30–2 automated visual field test, contrast sensitivity test, and color vision test before treatment, 4 days, 2 weeks, 1 month and 3 months, and 6 months following treatment. To assess anatomical changes, optical coherence tomography of the ganglion cells was performed at various timepoints.

Results Between September 2014 and September 2016, a total of 29 patients were included in the study. More than 80% of patients had recovered normal visual acuity after 3 and 6 months. This recovery of all parameters of visual function was observed as early as 4 days but occurred predominantly within 15 days after the initiation of treatment. We observed a thinning of the ganglion cell layer during the follow-up, which mainly occurs within one month. The P100 wave of visually evoked potentials was discernible in all patients at 6 months. During the 6 years of follow-up, 2 patients had experienced a relapse of ON. No serious adverse effects were observed.

Conclusion This study demonstrated a rapid recovery of all visual function parameters after oral high-dose methylprednisolone ON with no serious adverse effects.

Keywords Optic neuritis · Multiple sclerosis · Corticosteroid / Oral methylprednisolone · Optic neuritis treatment trial

Introduction

Optic neuritis (ON) is an inflammatory disease of the optic nerve mainly affecting young adults. Its annual incidence is estimated at 1 to 5 per 100 000 inhabitants per year [1]. Patients often present with a rapid, progressive decrease in visual acuity and/or an alteration in the visual field and/or a change in color vision, along with the presence of a relative afferent pupillary defect. It is often unilateral and associated with retrobulbar or periorbital pain accentuated by ocular movements. Multiple sclerosis (MS) is most often the etiology.

Since the Optic Neuritis Treatment Trial (ONTT) was published in 1992 [2], the only validated treatment in the management of ON has been the use of a bolus of corticosteroids administered intravenously (IV) at a dose of 1 g per day for 3 to 5 days. The ONTT study suggests that oral corticosteroids, at the usual dose of 1 mg/kg/day for 14 days, are not effective at treating acute episodes of ON and do not prevent relapse [3]. However, the study provides no evidence that oral administration is less efficacious than IV administration at the same dose. Indeed, very few studies have reported on the use of oral high-dose corticosteroids in

Key messages: What is known:
- High-dose intravenous corticosteroids were established as the standard of treatment for acute optic neuritis
- Oral prednisone (dose 1mg/kg/d) alone did not improve the outcome and was associated with an increased rate of recurrences of optic neuritis

What is new:
- High doses of oral corticosteroids demonstrated a rapid recovery of all visual function parameters with no serious adverse effects
- High doses of oral corticosteroids do not increase the rate of recurrences of optic neuritis

Extended author information available on the last page of the article

Published online: 31 July 2024

ON [4–7]. Interestingly, Sellebjerg et al. demonstrated, in a placebo-controlled study including 60 patients, an acceleration in visual recovery after treatment with oral high-dose corticosteroids (500 mg/day for 5 days followed by a tapering over 10 days), in ON [4]. Moreover, the COPOUSEP study, published in 2015, investigated the efficacy and tolerance of high doses of oral corticosteroids in MS attacks with ON compared to IV, and confirmed that oral corticosteroids at a dose of 1 g per day for 3 days were as effective as IV in treating bouts of MS. Moreover, the tolerance was similar and without increased risk of relapse in the following 6 months of follow-up [8].

The first objective of our study was to assess the changes in visual function parameters in patients with ON treated with oral high-dose corticosteroids. The secondary objective was to assess the number of relapses at 6 years of follow-up.

Materials and methods

Our study is a retrospective, descriptive single-center study that was conducted in our ophthalmology department. The study was approved by the ethics committee of the Rennes university hospital (approval number 20.54). Between September 2014 and 2016 we identified 39 patients who satisfied the following criteria: patients with "idiopathic ON (ION)" OR "ON occurring with MS", OR "neuromyelitis optica spectrum disorder (NMO-SD)", WITH "loss of visual acuity" AND WITH a "relative afferent pupillary defect", AND WITH "oral high-dose methylprednisolone" AND WITH "baseline brain and orbital MRI". Within these 39 patients, 10 patients were excluded (25%) for the following reasons: previous ON in the affected eye (N = 5), neurosyphilis (N = 1), onset of symptoms > 15 days (N = 2), age > 46 years (N = 2).

The therapeutic protocol of our study was identical to that of the COPOUSEP study [8]. The patients received 10 tablets of methylprednisolone equaling 100 mg per day for 3 days. The first treatment day took place at the hospital to allow a clinician to monitor and assess tolerance to the medication. The second and third days of treatment took place at the patient's home. Two supplementary days of treatment could be prescribed if there was insufficient visual recovery after medical evaluation. The pretherapeutic reporting, etiology, and associated measurements were identical to those used in the COPOUSEP study.

Following the routine procedures used in our ophthalmology department, clinical and paraclinical ophthalmologic re-evaluations were offered 4 days after corticosteroid treatment. Visual acuity was measured at day 4 for all patients. For those patients who received two supplementary doses of methylprednisolone, a second visual acuity test was performed at day 6. This second visual acuity test (day 6) was retained for statistical analysis.". Further visits were scheduled between 14 and 16 days, 3 months, and 6 months after ON diagnosis. An ophthalmology visit at 1 month was sometimes scheduled if it was considered necessary. Visual acuity was measured using the grading method according to Early Treatment of Diabetic Retinopathy study (ETDRS). Acuity was considered normal if it was above 84 letters. Color vision was assessed with a graded Lanthony Desaturated D-15 Color Vision Test, from Farnsworth-Munsell (Paris, France). The test was considered normal if there were no mistakes, if they started in a counterclockwise direction, or if there were fewer than 3 reversals of contiguous dots or a mistake connecting marker 7 to 15 with a normal end result. Contrast sensitivity (CS) was tested in static mode (MonPack3, Metrovision, Perenchies, France). We defined a mean CS corresponding to the mean of the sensitivities (expressed in dB) of 6 test frequencies. The visual field was tested by automated static perimetry using a strategy of 30–2 SITA-STANDARD (Carl Zeiss Meditec, Oberkochen, Germany). The indice used in the study was the overall mean deviation (MD) expressed in decibels (dB). Optical coherence tomography (OCT) was performed on optic nerves of average thickness and the macular ganglion cell layer (GCL) (Cirrus HD-OCT 4000–4742 500 Carl Zeiss Meditec, Oberkochen, Germany). Visual evoked potentials (VEP) were performed to analyze the P100 (MonPack3, Metrovision, Pérenchies, France). The mean P100 wave latency between the two lobes, was obtained during stimulation by checkerboard patterns and expressed in ms. Fifteen data points for each side were included in the analysis of the results of VEP.

Improvement in visual function was assessed by changes in visual acuity, CS, color vision, latencies of the P100 wave, and the thickness of the macular GCL on OCT. The secondary outcomes were tolerance to treatment and relapse of ION within the six months following treatment initiation. A clinician checked for possible adverse events linked to the treatment or recurrence of optic neuritis during each consultation. All patients were contacted in 2022 (6 years of minimum follow-up) to check for any relapses.

Statistical analyses were performed using SAS, v.9,4 (SAS Institute software (Cary, NC, USA). Quantitative variables were described as follows: n, mean ± standard deviation. The groups were compared using a parametric Student's t-test after being checked for normal distribution of values. Correlations between 2 quantitative variables were calculated using Pearson's coefficient of correlation. To compare CS between the affected eye and the healthy eye at different spatial frequencies, a mixed model was used to take into account repeated values (several spatial frequencies) as well as patient-dependent data (diseased and healthy eyes). For all analyses, significance was set at $p < 0.05$.

Results

Thirty-nine patients with acute ON were treated with high dose oral corticoids between September 2014 and September 2016 and followed in our unit. Among them, 29 patients fulfilled inclusion criteria and were included in the study with a mean of 5.9 ± 3.8 days after the onset of symptoms. The mean age was 30.8 ± 8.1 years and 15 patients were female. Four patients were known to have MS when ON was diagnosed and thus did not benefit from an additional MRI exam during the acute phase. No patients were known to have NMO-SD. One patient received Fingolimod during the period of inclusion. Another patient received Diméthyle fumarate in 2017 whereas two another patient received Interferon bêta-1a from 2009 to 2010 (before the inclusion). 18 patients underwent treatment with an oral corticoid consisting of 3 g of methylprednisolone (1 g per day for 3 days) and 11 with a treatment of 5 g of methylprednisolone (1 g per day for 5 days). None of the patients experienced adverse events due to the treatment requiring interruption of treatment, readjustment of the treatment, or hospitalization. All the patients were seen at four days (D4) (3.9 ± 0.9 days), while 26 patients were seen at D15 (15.9 ± 2.9 days), 15 patients at D30 (32.8 ± 64 days), 25 patients at D90 (100.7 ± 16.4 days), and 17 patients at D180 (195.6 ± 16.5 days).

Best-corrected visual acuity

Upon inclusion in the study, the mean best-corrected visual acuity of the 29 patients was 43.7 ± 29.1 (ETDRS scale). Moreover, the best-corrected visual acuity was 35 letters or less for 11 (38%) patients. At D5 ± 1 (depending of the number of boluses, see material and methods), 4 patients did not perceive any improvement in visual acuity after boluses of oral methylprednisolone. The lack of improvement in visual acuity in these patients may be due to their relatively high baseline scores (60–85 letters). Moreover, improvement did occur between at D15 in 3 of these patients, while the 4th did not follow up. Interestingly, only 2 patients of the 26 tested had a visual acuity measurement of less than 75 letters at D15. However, in these 2 patients, the mean increase in visual acuity was high compared to baseline, with 31 and 45 letters more than the visual acuity at D0. Among the 11 patients who received 5 boluses of oral methylprednisolone, the mean increase in visual acuity was already noted after the third bolus. It was, on average, a gain of 20.5 ± 19.8 letters compared to D0. In total, 31.0% patients had normal visual acuity (≥ 84 letters) at D5 ± 1 days 50.0% at D15, 60.0% at D30, 80% at D90, and 82.4% at D180 (Fig. 1). All patients had a visual acuity measurement above 75 letters at D180 with a mean of 85.4 ± 3. As illustrated by the curves, recovery of visual acuity predominantly occurred within the first 15 days. The clinical improvement after this period is less remarkable.

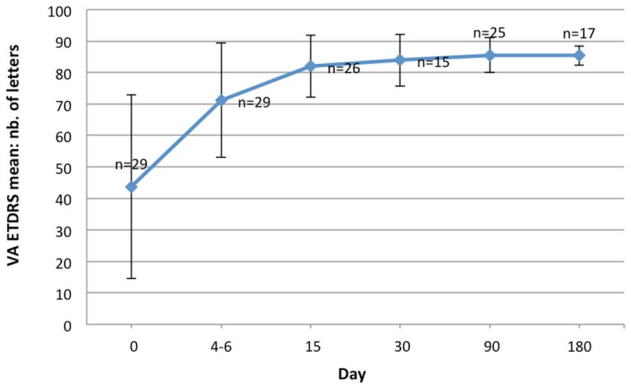

Fig. 1 Changes in best-corrected visual acuity after high doses of oral corticosteroids in patients with optic neuritis

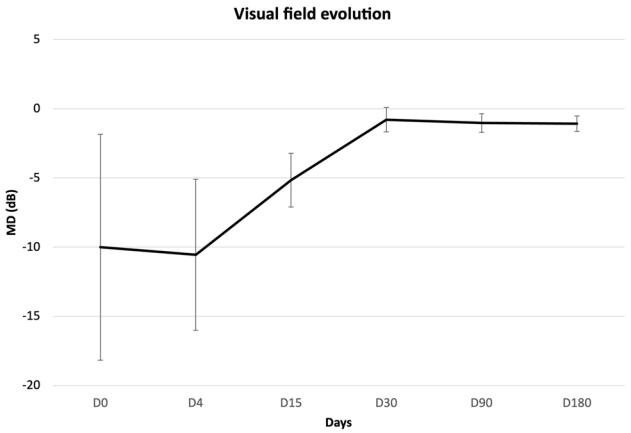

Fig. 2 Changes in visual field after high doses of oral corticosteroids in patients with optic neuritis. MD: Mean deviation or mean defect

Visual field

All patients had alterations of their visual field upon inclusion in the study. As with visual acuity, improvements in the automated 30–2 visual field (AVF) test mostly occurred within the first 15 days. Interestingly the mean MD was -1.12 ± 1.08 at D180. The results of the AVF 30.2 are shown in Fig. 2.

Contrast sensitivity

All patients had altered CS at D0 with a mean sensitivity of 6 test frequencies of 8.93 ± 4.95 dB. Improvement

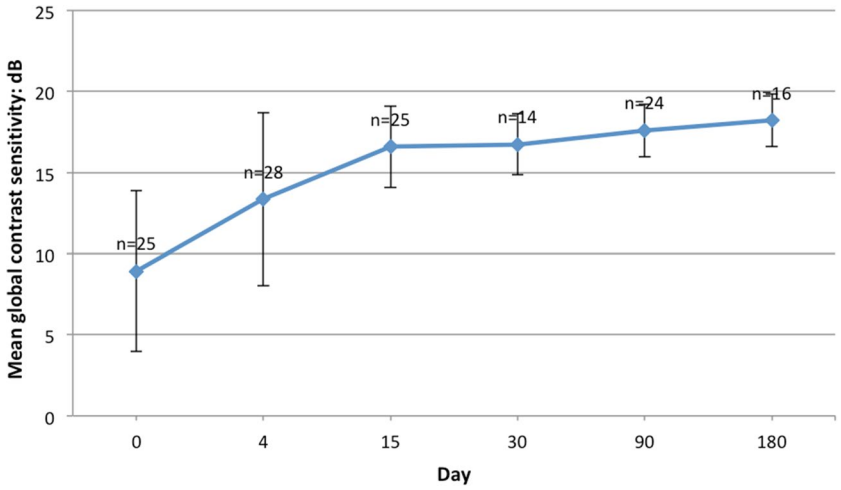

Fig. 3 Changes in global contrast sensitivity (in decibels) after high doses of oral corticosteroids in patients with optic neuritis

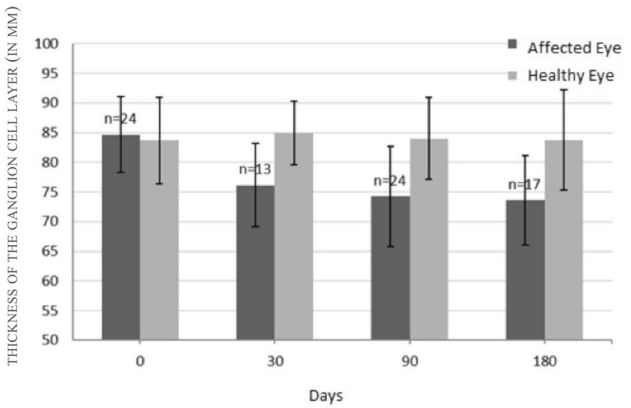

Fig. 4 Changes in GCL (Ganglion Cell Layer) thickness after high doses of oral corticosteroids in patients with optic neuritis

started within the first 4 days following treatment, and most of the recovery occurred within the first 15 days (Fig. 3). After this time, the improvement was less remarkable. At D180, the mean global CS was 18.22 ± 1.63 dB. The difference in contrast sensitivity between the two eyes was no longer significant ($p = 0.56$).

Ocular coherence tomography

The thickness of the macular GCL decreased during follow-up and predominantly occurred within the first 30 days (Fig. 4). There was no statistically significant correlation between the thinning of the GCL and visual acuity at the end of follow-up in the patients ($r = -0.02$, $p = 0.94$). Unfortunately, we were only able to measure RNFL thickness in 25% of patients at 6 months.

Visual evoked potentials

VEP was performed on all patients at D0 (100%), and on 17 patients at 6 months (58.6%). At D0, the P100 wave stimulated by a 15' checkerboard pattern was undiscernible in 14 patients (48.3%). Among the 15 remaining patients, the mean P100 wave was 120.36 ± 14.01 ms and its latency was above 125 ms in 6 patients. At 6 months, all patients had a discernable P100 wave with a 15' checkerboard pattern and the mean was 129.53 ± 17.91 ms. There was a statistically significant correlation between GCL thickness and VEP latencies at D180 ($r = -0.60$, $p = 0.01$). Not surprising we observed that the thinner the GCL, the longer the latency of the P100 wave at D180.

Development of MS and relapses after 6 years of follow-up

Of the 29 patients, 4 were known to have MS upon inclusion in the study. Cases of MS were discovered in 11 of 25 patients who were not known to have MS (44%) at the initial neurologic review. MS was discovered in 1 additional patient after the 2-year follow-up. One patient was diagnosed with a Devic's disease. 3 patients are currently followed every 2 years by MRI due to inflammatory CSF, without MRI criteria for MS. Among the 15 patients with MS, 2 experienced a new neurological MS attack with a sensitivity deficit in the 6 months following treatment, and one patient presented with a relapse of ON. At the 6-year follow-up, only 2 patients of 25 experienced a new episode of ON. Four patients did not follow up.

Discussion

In the best of our knowledge, this is the first report of rapid overall improvement in all visual function parameters in patients with ON treated with oral high-dose

steroids, predominantly occurring within the first 15 days after ON. Furthermore, at 6 months, 82.4% of the patients had normal visual acuity, 100% had normal color vision and 81.25% had a normal visual field. Interestingly, in our study, the mean MD was -1.12 ± 1.08 at D180. In comparison, after 6 months following IV methylprednisolone treatment in the ONTT study, only 60.9% of patients regained normal visual acuity, 80.1% regained a normal visual field, and 66.9% had normal color vision [2]. More recently, Morrow et al. published a randomized clinical trial studying the recovery of vision following treatment of acute optic neuritis with a high-dose IV corticosteroid or with a bioequivalent dose of an oral corticosteroid. They found that bioequivalent doses of oral corticosteroids may be used as an alternative to IV corticosteroids to treat acute optic neuritis [5]. Recently, a systematic review by Pietris et al. found that treating acute optic neuritis with oral methylprednisolone has similar efficacy and adverse effect profiles in comparison to intravenous methylprednisolone [9]. Taken together, high oral dose of methylprednisolone is an effective treatment option, but may in fact, outperform the current IV treatment protocol.

Regarding the change in thickness of the GCL over the 6 months of follow-up, a thinning of this layer in the eyes with ON is consistent with the results of previous studies, i.e., a ganglion cell loss [10, 11]. The thinning predominantly occurred within the first 30 days post ON, in line with the results of Kupersmith et al. [12]. Moreover, Costello et al. reported that up to 75% of patients with multiple sclerosis and acute optic neuritis develop 10–40 mm of RNFL loss within 3–6 months [13]. One of the most important findings from OCT in studies of patients with acute optic neuritis is the correlation between RNFL thickness and visual function, and longitudinally over time [14]. These findings suggest the possibility of screening potential neuroprotective or repair-promoting strategies in multiple sclerosis by their ability to prevent axonal loss measured by OCT RNFL thickness in acute optic neuritis [15].

Interestingly, we observed a statistically significant correlation between thinning of the GCL and increased latency from P100 to J180 ($r = -0.60$, $p = 0.01$). This result give strength to the serial study of acute optic neuritis showing that P100 prolongation of VEP latency predicted subsequent retinal axonal loss measured by OCT (Henderson et al., 2011). Together these results suggest that demyelinated axons are predisposed to degenerate in the setting of acute inflammation. However, one limitation of pattern VEP as an outcome measure for patients is that the VEP may be undetectable early in the course of optic neuritis, so demonstrating changes in VEP latency from baseline may be challenging. Use of multifocal VEP, which captures a significantly larger area of the visual field than pattern VEP and can provide topographic assessment of amplitude and latency, may provide a useful adjunct or alternative in the setting of acute optic neuritis [16]

On main considerable benefits for the patient treated by high doses of oral corticosteroids is the quick accessibility to treatment and the increasing comfort. Furthermore, the economic burden of the disease is greatly reduced: a Canadian study reported the cost of a 4-day IV treatment to be approximately US $580 and a 4-day course of 1250 mg of oral prednisone costs approximately US $16 [17]. In the United States, oral corticosteroids are more cost-effective because IV infusions in the United States are estimated to cost US $800 per hour [18]. More recently the COPUSEP group analyzed the cost-utility of oral methylprednisolone in the treatment of multiple sclerosis relapses: they found that oral high-dose corticoids is cost-effective [19]. Moreover, Pietris et al. (2024) found that oral methylprednisolone is more cost-effective than intravenous methylprednisolone [9].

The ONTT showed that high-dose intravenous methylprednisolone followed by oral prednisone accelerated visual recovery but did not improve the 6-month or 1-year visual outcome compared with placebo, whereas treatment with oral prednisone alone did not improve the outcome and was associated with an increased rate of recurrences of optic neuritis. [2]. Interestingly, in our study, we observed only one relapse of ON at 6 months and two relapse of ON at the 6-year follow-up (3.4% and 8% respectively). This is closed to 13% of patients in the IV methylprednisolone arm of the ONTT study at the 6-years of follow-up [20]. The functional recovery after high dose of oral corticoids can be explained in part by the pharmacokinetics of corticoids. Synthetic glucocorticoids are lipophilic drugs with the bioavailability of oral dosage forms ranging from 60 to 100%. When administered orally, with the maximum concentration typically seen within 1 to 3 h after administration for immediate release formulations and the half-life of the drug is similar for all forms of oral and IV administration. Although there are some benefits to IV administration, such as a slightly lower dose and rapid passage into the bloodstream, these benefits do not outweigh advantages of oral administration [21]. None of the patients in the present study experienced serious adverse events leading to discontinuation of the treatment or hospitalization, demonstrating oral high-dose corticoids are well tolerated., which is consistent with previous studies [8, 22–26]. However, although oral high-dose corticoids are well tolerated, they should not be administered without a confirmed diagnosis of ON by an ophthalmologist or a neurologist who considers the treatment necessary. [8]. Importantly, only 2 of 25 patients (8%) in our study had a relapse of ON within the 6 years following the initial episode.

Even though this study is the first report of rapid overall improvement in all visual function parameters in patients with ON treated with oral high-dose steroids with 6 years

of follow-up, there are some limitations of this study namely its retrospective nature and, above all, the small number of patients included, which makes statistics difficult.

Conclusion

This study shows a rapid overall improvement in visual function parameters after early administration of oral high-dose corticosteroids for idiopathic ON or for ON occurring in MS, with few side effects. The improvement starts within the first 4 days following treatment initiation, and improvement predominantly occurs within the first 15 days for all parameters of visual function. After 6 years of follow-up, relapse of ON in our study did not occur more frequently than in the intravenous methylprednisolone arm of the ONTT study.

Acknowledgements Statistics were performed with the help of Chloé Rousseau. We also thank Andrew Mitchell for his careful rereading and his comments.

Funding No funding was received for this research.

Declarations

Ethical Approval The study was approved by the ethics committee of the Rennes university hospital (approval number 20.54).

Informed Patient consent As this is a retrospective study started before 2016 in France, the agreement of the ethics committee is required-see above but informed consent was not necessary.

Conflicts of interests No Conflicts of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

1. (1991) The Clinical Profile of Optic Neuritis: Experience of the Optic Neuritis Treatment Trial. Arch Ophthalmol 109:1673–1678. https://doi.org/10.1001/archopht.1991.01080120057025
2. Beck RW, Cleary PA, Anderson MM et al (1992) A Randomized, Controlled Trial of Corticosteroids in the Treatment of Acute Optic Neuritis. N Engl J Med 326:581–588. https://doi.org/10.1056/NEJM199202273260901
3. Beck RW, Trobe JD (1995) What We Have Learned from the Optic Neuritis Treatment Trial. Ophthalmology 102:1504–1508. https://doi.org/10.1016/S0161-6420(95)30839-1
4. Sellebjerg F, Nielsen HS, Frederiksen JL, Olesen J (1999) A randomized, controlled trial of oral high-dose methylprednisolone in acute optic neuritis. Neurology 52:1479–1484. https://doi.org/10.1212/wnl.52.7.1479
5. Morrow SA, Fraser JA, Day C et al (2018) Effect of Treating Acute Optic Neuritis With Bioequivalent Oral vs Intravenous Corticosteroids: A Randomized Clinical Trial. JAMA Neurol 75:690–696. https://doi.org/10.1001/jamaneurol.2018.0024
6. Naumovska M, Sheikh R, Bengtsson B, et al (2018) Visual outcome is similar in optic neuritis patients treated with oral and i.v. high-dose methylprednisolone: a retrospective study on 56 patients. BMC Neurol 18:. https://doi.org/10.1186/s12883-018-1165-6
7. Poujade A, Le Page E, Baudet D et al (2016) Amélioration rapide de la fonction visuelle après corticothérapie orale à forte dose chez des patients atteints de neuropathie optique inflammatoire. J Fr Ophtalmol 39:691–699. https://doi.org/10.1016/j.jfo.2016.03.008
8. Le Page E, Veillard D, Laplaud DA et al (2015) Oral versus intravenous high-dose methylprednisolone for treatment of relapses in patients with multiple sclerosis (COPOUSEP): a randomised, controlled, double-blind, non-inferiority trial. Lancet Lond Engl 386:974–981. https://doi.org/10.1016/S0140-6736(15)61137-0
9. Pietris J, Lam A, Bacchi S et al (2024) The Efficacy, Adverse Effects and Economic Implications of Oral Versus Intravenous Methylprednisolone for the Treatment of Optic Neuritis: A Systematic Review. Semin Ophthalmol 39:6–16. https://doi.org/10.1080/08820538.2023.2287100
10. Walter SD, Ishikawa H, Galetta KM et al (2012) Ganglion Cell Loss in Relation to Visual Disability in Multiple Sclerosis. Ophthalmology 119:1250–1257. https://doi.org/10.1016/j.ophtha.2011.11.032
11. Syc SB, Saidha S, Newsome SD et al (2012) Optical coherence tomography segmentation reveals ganglion cell layer pathology after optic neuritis. Brain 135:521–533. https://doi.org/10.1093/brain/awr264
12. Kupersmith MJ, Garvin MK, Wang J-K et al (2016) Retinal ganglion cell layer thinning within one month of presentation for optic neuritis. Mult Scler J 22:641–648. https://doi.org/10.1177/1352458515598020
13. Costello F, Coupland S, Hodge W et al (2006) Quantifying axonal loss after optic neuritis with optical coherence tomography. Ann Neurol 59:963–969. https://doi.org/10.1002/ana.20851
14. Talman LS, Bisker ER, Sackel DJ et al (2010) Longitudinal study of vision and retinal nerve fiber layer thickness in multiple sclerosis. Ann Neurol 67:749–760. https://doi.org/10.1002/ana.22005
15. Balcer LJ, Miller DH, Reingold SC, Cohen JA (2015) Vision and vision-related outcome measures in multiple sclerosis. Brain 138:11–27. https://doi.org/10.1093/brain/awu335
16. Klistorner A, Arvind H, Nguyen T et al (2009) Multifocal VEP and OCT in optic neuritis: a topographical study of the structure-function relationship. Doc Ophthalmol Adv Ophthalmol 118:129–137. https://doi.org/10.1007/s10633-008-9147-4
17. Robson LS, Bain C, Beck S et al (1998) Cost analysis of methylprednisolone treatment of multiple sclerosis patients. Can J Neurol Sci J Can Sci Neurol 25:222–229. https://doi.org/10.1017/s0317167100034053
18. Kister I, Corboy JR (2016) Reducing costs while enhancing quality of care in MS. Neurology 87:1617–1622. https://doi.org/10.1212/WNL.0000000000003113
19. Michel M, Le Page E, Laplaud DA et al (2022) Cost-utility of oral methylprednisolone in the treatment of multiple sclerosis relapses: Results from the COPOUSEP trial. Rev Neurol (Paris) 178:241–248. https://doi.org/10.1016/j.neurol.2021.06.009
20. Beck RW, Cleary PA, Anderson MM et al (1992) A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. N Engl J Med 326:581–588. https://doi.org/10.1056/NEJM199202273260901

21. Czock D, Keller F, Rasche FM, Häussler U (2005) Pharmacokinetics and pharmacodynamics of systemically administered glucocorticoids. Clin Pharmacokinet 44:61–98. https://doi.org/10.2165/00003088-200544010-00003
22. Morrow SA, Stoian CA, Dmitrovic J et al (2004) The bioavailability of IV methylprednisolone and oral prednisone in multiple sclerosis. Neurology 63:1079–1080
23. Sellebjerg F, Nielsen HS, Frederiksen JL, Olesen J (1999) A randomized, controlled trial of oral high-dose methylprednisolone in acute optic neuritis. Neurology 52:1479–1484
24. Sellebjerg F, Frederiksen JL, Nielsen PM, Olesen J (1998) Double-blind, randomized, placebo-controlled study of oral, high-dose methylprednisolone in attacks of MS. Neurology 51:529–534
25. Martinelli V, Rocca MA, Annovazzi P et al (2009) A short-term randomized MRI study of high-dose oral vs intravenous methylprednisolone in MS. Neurology 73:1842–1848. https://doi.org/10.1212/WNL.0b013e3181c3fd5b
26. Barnes D, Hughes RA, Morris RW et al (1997) Randomised trial of oral and intravenous methylprednisolone in acute relapses of multiple sclerosis. Lancet Lond Engl 349:902–906

Authors and Affiliations

Elodie Boureaux[1] · Charlotte Laurent[1] · Thomas Rodriguez[1] · Emanuelle Le Page[2] · Frédéric Mouriaux[1,3]

✉ Frédéric Mouriaux
frederic.mouriaux@chu-rennes.fr

[1] Ophthalmology Department, CHU Rennes, Université Rennes 1, Rennes, France

[2] Neurology Department, CRC-SEP Rennes, University Hospital Pontchaillou, CIC1414 INSERM35033 Rennes, France

[3] CUO-Recherche, Centre de Recherche du CHU de Québec – Université Laval, Axe Médecine Régénératrice, Hôpital du Saint-Sacrement, Québec, Canada