



# Demyelinating and Autoimmune Optic Neuritis: Approach and Management

María Isabel Silva Sánchez<sup>1\*</sup>, Paula Andrea Fernández Uribe<sup>2</sup>, Juan Pablo Gualdrón Moncada<sup>3</sup>, Génesis Giztel Carvajal Rodríguez<sup>4</sup>, Daniela Arrieta Acuña<sup>5</sup>, Raül Causil Vega<sup>6</sup>, Andres Felipe Jojoa Jojoa<sup>7</sup> and Natalia Peñaloza Barrios<sup>8</sup>

<sup>1</sup>University Teaching Physician, Universidad El Bosque, Colombia; <https://orcid.org/0000-0002-7608-8817>

<sup>2</sup>General physician, Universidad Libre, Cali, Colombia; <https://orcid.org/0000-0003-4078-2011>

<sup>3</sup>Pediatric Resident, Corporación Universitaria Remington, Colombia; <https://orcid.org/0000-0002-2187-4407>

<sup>4</sup>General physician, Universidad Católica de Honduras, Honduras; <https://orcid.org/0000-0002-7580-8843>

<sup>5</sup>General physician, Universidad del Norte, Colombia

<sup>6</sup>General physician, Universidad del Sinú, Montería, Colombia; <https://orcid.org/0000-0001-7701-9701>

<sup>7</sup>General physician, -Universidad Cooperativa de Colombia sede Pasto, Colombia; <https://orcid.org/0000-0002-9498-1801>

<sup>8</sup>General physician, Universidad del Sinú, Cartagena, Colombia

## ABSTRACT

**Background:** A healthy optic nerve is a crucial conduit for impulses generated within the layers of the retina to leave the eye. To date, the mechanism of action of optic neuritis is not entirely clear, as are the therapeutic approaches, especially in the pediatric population. To date it is estimated that the annual incidence of optic neuritis is estimated between 0.56 and 5.1 cases per 100,000 people.

**Methodology:** A systematic review was carried out through various databases from January 2015 to September 2022; The search and selection of articles were carried out in indexed journals in English.

**Results:** The first clinical manifestation that we can find in a patient with optic neuritis is a pain when moving the eyes, with subsequent worsening of vision. Only 0.4% of patients develop symptoms in both eyes simultaneously. Intravenous methylprednisolone at 1000 mg/day has been found to lead to more rapid recovery of vision. IV immunoglobulin and plasma exchange are used in patients refractory to initial treatment. Erythropoietin has demonstrated neuroprotective properties.

**Conclusion:** This review offers updated and detailed information that helps the health professional in clinical practice, to identify the main clinical symptoms and thus prevent and treat said pathology promptly.

**KEYWORDS:** Neuritis; Optic; Demyelinating; Autoimmune; Cross reaction

**ABBREVIATIONS:** IVIg: IV Immunoglobulin; AQP4: Aquaporin 4; NMO: Neuromyelitis Optica; MOG: Myelin Oligodendrocyte Glycoprotein; IVMP: Intravenous Methylprednisolone; IVE: Intravenous Erythropoietin

### Quick Response Code:



**Address for correspondence:** María Isabel Silva Sánchez, University Teaching Physician, Universidad El Bosque, Colombia; <https://orcid.org/0000-0002-7608-8817>

**Received:** December 06, 2022

**Published:** January 24, 2023

**How to cite this article:** María Isabel SS, Paula Andrea FU, Juan Pablo GM, Génesis GCR, Daniela AA, et. al. Demyelinating and Autoimmune Optic Neuritis: Approach and Management. 2023- 5(1) OAJBS.ID.000534. DOI: [10.38125/OAJBS.000534](https://doi.org/10.38125/OAJBS.000534)

## INTRODUCTION

A healthy optic nerve is a crucial conduit for impulses generated within the layers of the retina to leave the eye. Electrical signals are initiated by photoreceptors in response to incident light, modified by retinal bipolar cells, and transmitted *via* optic nerves to the lateral geniculate bodies [1]. These signals can be compromised when there is damage or some type of alteration in the nerve fiber layers or the optic nerve. Optic neuritis is considered a variety of conditions that can affect the proper functioning of the optic nerve. Many causes can compromise it, causing neuropathies, among these, we find infections, traumas, vascular insufficiency, metastasis, toxins, or nutritional deficiency [2].

To date the mechanism of action is not entirely clear, but different hypotheses have been raised, such as the autoimmune reaction damaging the myelin sheath that encompasses the neurons within the optic nerve. It has been documented that patients diagnosed with autoimmune diseases are more likely to develop optic neuritis, with a causal relationship between HLA DRB1, HLA-B27 and optic neuritis [3]. One of the causes that is having great importance is cross-reaction, through molecular mimicry either between different microorganisms or natural proteins and proteins or autoantigens belonging to optic neuritis. Neuromyelitis Optica (NMO) is associated with antibodies against aquaporin 4 (AQP4). It is hypothesized that AQP4 antibodies may be triggered by exposure to environmental proteins. Human AQP4 with plant and bacterial proteins were found to have significantly similar structures and sequences. High similarity to a known epitope for NMO-IgG, AQP4, was observed for maize ZmTIP4-1. Demonstrating cross-reactivity to plant tissue [4,5].

To date it is estimated that the annual incidence of optic neuritis is estimated between 0.56 and 5.1 cases per 100,000 people. The main risk factors that have been reported are Caucasian race, female sex, and age plays an important factor, predominantly between 20 and 40 years of age. Although optic neuritis is very infrequently identified in children, its appearance is not suggestive of developing multiple sclerosis in adulthood. Regarding the climate, it is believed that in temperate climates its incidence can increase. Optic neuritis is thought to be the initial inflammatory event in 15-20% of multiple sclerosis patients, and half of the multiple sclerosis patients will ultimately have had at least one attack of optic neuritis in the previous 15 years. Oligoclonal bands within the cerebrospinal fluid are pathognomonic for multiple sclerosis [6].

Optic neuritis-related vision loss in patients with neuromyelitis optica spectrum disorders and myelin oligodendrocyte glycoprotein IgG is usually more severe and results in larger scotomas. Since both disorders affect the optic nerve, chiasm, and optic pathways, bilateral vision loss is common. The damage often extends longitudinally into the spinal cord in both conditions [7]. Given that this pathology is of great importance due to its still wide incidence and with effects that compromise the quality of life of the patient, it is necessary to carry out this study, in order to provide updated and detailed information that helps in practice. clinic to health professionals.

## MATERIALS AND METHODS

In this study we carried out a systematic review, the databases used were PubMed, Scielo and ScienceDirect. Articles in English were collected from the years 2015 to 2022. The terms were used as keywords: Neuritis; Optics; Demyelinating; autoimmune; Cross reaction. In this review, 156 original and review publications

related to the subject studied were identified. Only 24 articles met the inclusion requirements, articles that were in a range of no less than the year 2015, that were full-text articles and that reported on optic neuritis, its therapeutic approach, as well as its possible mechanism of action.

## RESULTS

### Optic Neuritis

Most patients who develop optic neuritis typically present primarily with impaired visual acuity, either acute or severe, with no clear diagnostic findings on ocular examination. It is very common to find it in young, otherwise healthy individuals [8]. This pathology is considered an autoimmune disease, due to the presence of an autoimmune reaction directed against the optic nerve. This may be associated with other autoimmune diseases, especially multiple sclerosis [9]. It is increasingly being used in clinical trials as a model for multiple sclerosis relapses, because visual function is relatively easy to measure and, in particular, because changes in the retinal nerve fiber layer can be visualized in detail with tomography. optical coherence [10]. The incidence of optic neuritis in central Europe is 5 cases per 100,000 people per year. The mean age of onset is 36 years. It is rare in people younger than 18 or older than 50. Approximately more than 70% of patients are women. According to a current study, optic neuritis accounts for 43% of cases of clinically isolated neurological syndromes that are considered potential precursors of multiple sclerosis [11].

### OPTIC NEURITIS CLINIC

The first clinical manifestation that we can find in a patient with optic neuritis is a pain when moving the eyes, with subsequent worsening of vision. Only 0.4% of patients develop symptoms in both eyes simultaneously [12]. Most patients can accurately identify the day of the occurrence of symptoms. Unlike patients who present loss of vision or alteration of visual acuity associated with optic nerve tumors. In Figure 1 we can show an illustration of what a person who develops optic neuritis would look like. Patients report seeing things that are dark, unclear, and with low contrast, colors appear dirty, and pale. If the disease is not treated promptly, visual acuity could deteriorate, reaching its maximum point of deterioration in approximately one or two weeks with subsequent improvement in acuity [13]. The pain and worsening vision are so bothersome that almost no one wants to see if it improves spontaneously; patients tend to find their way to an ophthalmologist very early in the course of the disease. Pain when moving the eyes is absent in 8% of patients whose inflammatory focus is located in the intracranial portion of the optic nerve and, therefore, proximal to its mobile portion [14].

### VISUAL ACUITY TEST

In unilateral optic neuritis, the reaction to direct pupillary light and the accompanying consensual reaction from the opposite pupil are weaker with illumination from the affected eye than with illumination from the unaffected eye [15]. This finding, known as a relative afferent pupillary defect, is best seen with the aid of the swinging-lantern test. Pain on eye movement should be elicited with appropriate movements if the patient does not spontaneously report that she has it. Any unusual sensation is diagnostically relevant because eye movements are normally not felt at all. In Figure 2, we can see an example of this test, this figure was taken from the study carried out by [16]. Since it clearly shows the reactivity of the pupils in a healthy person and a person with optic neuritis.

The pupils react faster, and to a greater extent, with illumination from the healthy right eye, compared to the affected left eye. The presence of central scotomas and cecal centers is frequently found in patients suffering from this disease. At the level of the optic disc,

we can find mild edema, although it tends to be confused with a normal optic disc. In Figure 3, we can see the symptoms and signs that together could be considered pathognomonic of optic neuritis [17,18].



Figure 1: A vision of a person who develops optic neuritis.

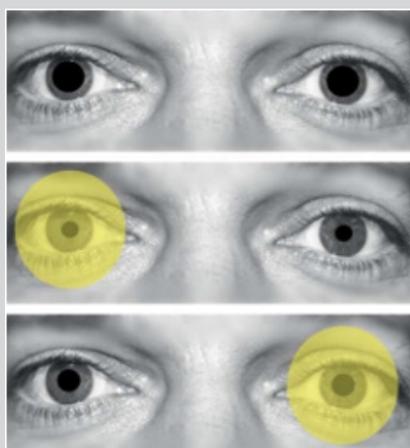


Figure 2: Oscillating flashlight test in a patient with left optic neuritis.

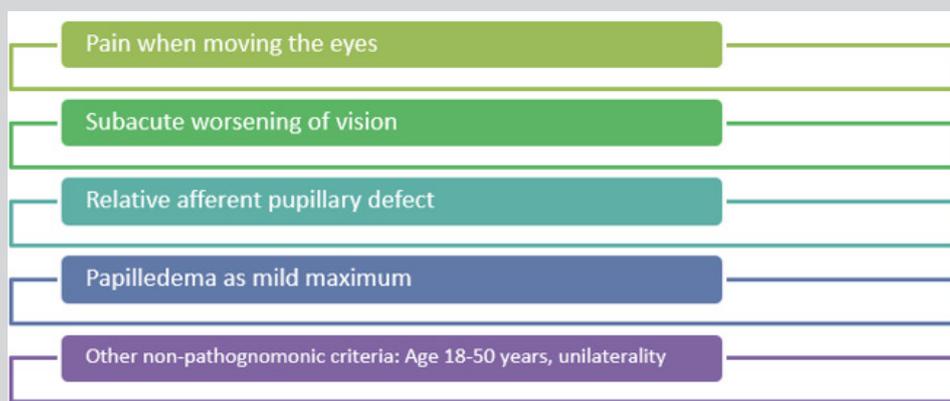


Figure 3: Pathognomonic symptoms and signs of optic neuritis.

### MANAGEMENT OF OPTIC NEURITIS

Intravenous methylprednisolone 1000 mg/day has been shown to lead to more rapid recovery of vision, but the result regarding visual acuity, fields, contrast and color perception was no better than with prednisone. oral alone or, indeed, with a placebo [19].

Neurological and ophthalmological guidelines establish that optic neuritis should be treated with methylprednisolone at a dose of 500-1000 mg/day for 3-5 days, followed by 11 days of oral prednisolone at 1 mg/kg for faster recovery, but without improvement of the final result concerning visual acuity. During steroid treatment, a proton pump inhibitor is also given to prevent peptic ulcers. Osteoporosis

prophylaxis, by contrast, is not necessary because steroids are only given for a short time. Complete blood count, serum glucose, and electrolyte levels are checked before the first intravenous dose of methylprednisolone and on the third and (sometimes) fifth day of treatment.

IV immunoglobulin (IVIg) and plasma exchange have been evaluated in patients with optic neuritis refractory to high-dose corticosteroid therapy. IVIG (2 g/kg) did not improve contrast sensitivity or visual function in patients with acute optic neuritis [20]. But plasma exchange has resulted in better visual outcomes in patients with corticosteroid-refractory optic neuritis. Although the frequency of responders varied, the majority of patients with optic neuritis treated with plasmapheresis improved their visual function.

### Management for Demyelinating Optic Neuritis

Erythropoietin, best recognized as a regulator of erythropoiesis, has shown potential neuroprotective properties in animal models of brain injury, including those of ischemia, trauma, epilepsy, and optic neuropathy. A rat model using myelin oligodendrocyte glycoprotein (MOG) immunization showed functional and histopathological improvement of retinal ganglion cells and optic nerves when erythropoietin treatment was combined with high-dose methylprednisolone. The use of erythropoietin in humans with optic neuropathy has been reported in multiple studies from Iran. Conditions treated included traumatic optic neuropathy, anterior ischemic optic neuropathy, multiple sclerosis, and methanol optic neuropathy [21].

It evaluated the addition of intravenous recombinant human erythropoietin (IVE) to intravenous methylprednisolone (IVMP) in patients with retrobulbar optic neuritis. Thirty-five patients were treated with IVMP alone and twenty-seven with the combination of IVMP and IVE (20,000 international units). Both groups were treated with intravenous agents for 3 days and then received 11 days of oral prednisolone at 1 mg/kg. The primary outcome measure was the change in best-corrected visual acuity, which was assessed up to 120 days. The use of erythropoietin appears to be safe, which is encouraging [22].

### DISCUSSION

Optic neuritis is still a disease that requires extensive study, mainly to clarify its mechanism of action, and provide adequate care. To date, one of the mechanisms that is having great importance is that of autoimmunity caused by cross-reactivity, either between different environmental epitopes or microorganisms. One of the criteria for this to happen is that the two epitopes can share the same sequence or that they present similarity in their structure, as well as that this autoimmunity is reproducible in other sample organisms. Humanity had one of the pandemics that had a great impact on the population recently, it is one caused by COVID-19, therefore, the association that optic neuritis and SARS.COV-2 can have has been studied. The study carried out by [23] reports a clinical case of a patient who developed optic neuritis after SARS-COV-2. The most common neurological symptoms of COVID-19 are headache, anosmia, and dysgeusia. In this study, they propose a possible cause for the development of optic neuritis, which is molecular mimicry causing cross-reactivity.

The pediatric population is not exempt from the development of optic neuritis, the study carried out by Silvia, in which they carry out a systematic review, reports that children are more

likely to require hospitalization and to undergo magnetic resonance imaging of the orbits for correct diagnosis. In Table 1, we can identify the main preventive/chronic therapies proposed depending on the clinical condition [24]. Although many studies are searching for better therapeutic measures for both the pediatric and adult populations, there is still no clear consensus on effective therapies to treat this disease. A strength of the current study is the methodology implemented, regarding the literature search, and steps in the selection of relevant articles, quality assessment, and data extraction. However, this study has several limitations, which should be taken into account before concluding, among these, we find little evidence from studies, analysis of clinical trials and *in-vitro* studies that demonstrate the proposed mechanisms of action for neuritis. optics, to focus on the correct handling, so more studies, are needed to answer these questions.

**Table 1:** Preventive/chronic therapies in the pediatric population depending on their clinical condition.

| Condition  | Driving   |
|--|---|
| Neuromyelitis Optica Spectrum Disorder Treatment (NMOSD) pediatric AQP4-IgG seropositive | Predicts relapses of myelitis and optic neuritis in adults and children.  |
|  | Rapid initiation of immunosuppressive therapy: Rituximab, mycophenolate mofetil, and azathioprine   |
| Treatment of AQP4-IgG seronegative NMOSD   | Rituximab, mycophenolate mofetil, and azathioprine  |
| Treatment of the clinical phenotype of pediatric NMOSD associated with MOG-IgG           | There is no consensus regarding preventive therapy. Although it seems to be quite sensitive to corticosteroids, recommended against long-term use |

### CONCLUSION

This pathology is considered an autoimmune disease, due to the presence of an autoimmune reaction directed against the optic nerve. This may be associated with other autoimmune diseases, especially multiple sclerosis.

The first clinical manifestation that we can find in a patient with optic neuritis is a pain when moving the eyes, with subsequent worsening of vision. Only 0.4% of patients develop symptoms in both eyes simultaneously. In Figure 1,2 we can identify the clinical aspects of a patient with optic neuritis. Intravenous methylprednisolone at 1000 mg/day has been found to lead to more rapid recovery of vision. IV immunoglobulin (IVIg) and plasma exchange have been evaluated in patients with optic neuritis refractory to high-dose corticosteroid therapy. Erythropoietin, best recognized as a regulator of erythropoiesis, has shown potential neuroprotective properties in animal models of brain injury, including those of ischemia, trauma, epilepsy, and optic neuropathy.

### REFERENCES

- Soelberg K, Nilsson AC, Nielsen C, Jarius S, Reindl M, et al. (2018) Autoimmune and immunogenetic profile of patients with optic neuritis in a population-based cohort. *Mult Scler Relat Disord* 21: 97-102.
- Zhao S, Zhou H, Peng X, Zhu J, Wang W, et al. (2016) Optic neuritis with positive HLA-B27: Characteristic phenotype in the Chinese population. *J Neurol Sci* 362: 100-105.
- Shen T, You Y, Arunachalam S, Fontes A, Liu S, et al. (2019) Differing structural and functional patterns of optic nerve damage in multiple sclerosis and neuromyelitis optica spectrum disorder. *Ophthalmology* 126(3): 445-453.

4. Jurynczyk M, Messina S, Woodhall MR, Raza N, Everett R, et al. (2017) Clinical presentation and prognosis in MOG-antibody disease: a UK study. *Brain* 140(12): 3128-3138.
5. Beck RW, Cleary PA, Backlund JC (2020) The course of visual recovery after optic neuritis: experience of the optic neuritis treatment trial. *Ophthalmology* 127(4S): S174-S181.
6. Longbrake EE, Lancia S, Tutlam N, Trinkaus K, Naismith RT (2016) Quantitative visual tests after poorly recovered optic neuritis due to multiple sclerosis. *Mult Scler Relat Disord* 10: 198-203.
7. Ryu WY, Kim JS (2017) Optic perineuritis simultaneously associated with active pulmonary tuberculosis without intraocular tuberculosis. *Int J Ophthalmol* 10(9): 1477-1478.
8. Kahloun R, Abroug N, Ksiai I (2015) Infectious optic neuropathies: a clinical update. *Eye Brain* 7: 59-81.
9. Northey LC, Skalicky SE, Gurbaxani A, McCluskey PJ (2015) Syphilitic uveitis and optic neuritis in Sydney, Australia. *Br J Ophthalmol* 99(9): 1215-1219.
10. Abdelhakim A, Rasool N (2018) Neuroretinitis: a review. *Curr Opin Ophthalmol* 29(6): 514-519.
11. Kubaisi B, Abu Samra K, Foster CS (2016) Granulomatosis with polyangiitis (Wegener's disease): an updated review of ocular disease manifestations. *Intractable Rare Dis Res* 5(2): 61-69.
12. Bridel C, Courvoisier DS, Vuilleumier N, Lalive PH (2015) Cerebrospinal fluid angiotensin-converting enzyme for diagnosis of neurosarcoidosis. *J Neuroimmunol* 285: 1-3.
13. Gordon L, Dinkin M (2019) Paraneoplastic syndromes in neuro-ophthalmology. *Continuum (Minneapolis)* 25(5): 1401-1421.
14. Igarashi N, Sawamura H, Kaburaki T, Aihara M (2017) Anti-collapsing response-mediating protein-5 antibody-positive paraneoplastic perioptic neuritis without typical neurological symptoms. *Neuroophthalmology* 41(1): 24-29.
15. Asgari N, Jarius S, Laustrup H (2018) Aquaporin-4-autoimmunity in patients with systemic lupus erythematosus: a predominantly population-based study. *Mult Scler* 24(3): 331-339.
16. Chen JJ, Aksamit AJ, McKeon A (2015) Optic disc edema in glial fibrillary acidic protein autoantibody-positive meningoencephalitis. *J Neuroophthalmol* 38(3): 276-281.
17. Kleiter I, Gahlen A, Borisow N (2016) Neuromyelitis optica: evaluation of 871 attacks and 1,153 treatment courses. *Ann Neurol* 79(2): 206-216.
18. Bonnan M, Valentino R, Debeugny S (2018) Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. *J Neurol Neurosurg Psychiatry* 89(4): 346-351.
19. Aungsumart S, Apiwattanakul M (2017) Clinical outcomes and predictive factors related to good outcomes in plasma exchange in severe attack of NMOSD and long extensive transverse myelitis: case series and review of the literature. *Mult Scler Relat Disord* 13: 93-97.
20. Pakravan M, Esfandiari H, Hassanpour K, Razavi S, Pakravan P (2017) The effect of combined systemic erythropoietin and steroid on non-arteritic anterior ischemic optic neuropathy: A prospective study. *Current Eye Research* 42(7): 1079-1084.
21. Pakravan M, Esfandiari H, Sanjari N, Ghahari E (2016) Erythropoietin as an adjunctive treatment for methanol-induced toxic optic neuropathy. *The American Journal of Drug and Alcohol Abuse* 42(6): 633-639.
22. Pakdel F, Sanjari MS, Naderi A, Pirmarzashti N, Haghighi A, et al. (2018) Erythropoietin in Treatment of Methanol Optic Neuropathy. *Journal of Neuro-Ophthalmology* 38(2): 167-171.
23. Rodriguez M, Romero R, Alvarado C, Gonzalez M, Garcia A, et al. (2021) Optic neuritis following SARS-CoV-2 infection. *J Neurovirol* 27(2): 359-363.
24. Tenenbaum S (2020) Pediatric NMOSD: A review and position statement on approach to work-up and diagnosis. *Front Pediatr* 8: 339.