**Pharmacophore**

ISSN-2229-5402

Journal home page: http://www.pharmacophorejournal.com

# REVIEW ON OPTIC NEURITIS CLINICAL FEATURES, DIAGNOSIS, AND MANAGEMENT APPROACH

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**ARTICLE INFO**

**Received:**
10 Aug 2021
**Received** in revised form:
30 Nov 2021
**Accepted:**
04 Dec 2021
**Available online:**
28 Dec 2021

***Keywords:*** Optic neuritis, Clinical features, Management, Diagnosis

**ABSTRACT**

Optic neuritis (ON) is a sight-threatening condition characterized by inflammation of the optic nerves. The condition can be classified into typical-ON and atypical-ON. The majority of cases are typical and are the result of acute demyelination as part of multiple sclerosis. While the atypical form represents only a small portion and is caused by different underlying pathologies such as neuromyelitis Optica spectrum disorders (NMOSD), infections, and other systemic diseases. We aimed to review the literature looking into optic neurites, with their clinical features and management in particular typical optic neuritis. PubMed database was used for articles selection, papers were obtained and reviewed. Optic neuritis can manifest in many different ways, but the most common presentation is a sudden onset of unilateral retro-orbital pain with varying degrees of visual loss. The course of the disease is progressive reaching its peak in 2 weeks period with subsequent gradual improvement. majority of patients regain their base visual acuity within a year. Management of typical-ON can be broken down into two aspects acute and long-term. Acute management is aimed at decreasing the severity and duration of symptoms but doesn't change the final disease outcome. Corticosteroids are the initial drug of choice in the acute setting with other modalities being reserved for resistant cases, these alternative options include plasmapheresis, Immunoadsorption, IVIG, and possibly erythropoietin. After acute recovery patients may start long-term therapy with DMDs to decrease the chance of developing MS and prevent future relapses.



**To Cite This Article:** Al-Kalaif ZS, Alzayer HG, Al-Suwat HA, Almalki MA, Almarashi BK, Alasmari TAY, et al. Review on Optic Neuritis Clinical Features, Diagnosis, and Management Approach. Pharmacophore. 2021;12(6):23-7. https://doi.org/10.51847/7goyuqOb90

## Introduction

Optic neuritis (ON) is a sight-threatening condition characterized by inflammation of the optic nerves [1, 2]. The condition is fairly common as lifetime prevalence is 6 / 10,000 and the mean age of onset is 36 years. ON has a higher tendency to affect females as they represent up to 70% of patients, with Caucasian descendants having a higher incidence than other races [3, 4]. Majority of cases are caused by acute demyelination, as part of multiple sclerosis and is referred to as typical-ON.

Other less frequent etiologies include infections which are a major cause in the pediatric population [5]. Also, neuromyelitis Optica spectrum disorders (NMOSD) which is a rare but series condition. Additionally, systemic diseases in particular granulomatous or connective tissue diseases such as lupus and sarcoidosis. If optic neuritis occurs in the context of any of these conditions then it is classified as atypical-ON [6].

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Despite both types having a very similar presentation, but their approach to management is different. Therefore, early recognition of the underlying pathology can have a tremendous impact on a patient's future sight.

**Materials and Methods**

PubMed database was used for articles selection, and the following keys were used in the mesh ((optic neuritis) AND (clinical features)) OR (management). In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics; optic neuritis; clinical features; management. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

*Review*

*Clinical Features*

The most frequently encountered presentation is a sudden onset of unilateral pain and disturbed vision which is experienced up to 95% and 92% of cases respectively [7]. When asking patients to describe their symptoms they commonly express it as blurring, haziness, or darkening of vision. The pain is usually retro-orbital and worsens with the use of extraocular muscles. These symptoms usually develop acutely or in a subacute fashion over a few hours to a couple of days, with a progressive course reaching its maximum intensity within 1-2 weeks that's when it begins to wear off. around 80% of patients start to improve by the 3$^{rd}$ week [8].

Visual impairment can vary greatly from one case to another, as some may have a fully preserved visual acuity of 20/20, while on other hand few unfortunate patients may not even be able to perceive light. This heterogenicity also applies in regards to the visual field, as visual defects can occur at any region but central scotomas are the most frequent. Alterations in color perception are a common complaint specifically for red and green colors, as many patients will report a decrease in perceived color saturation or feeling as if colors are fainter [4].

A couple of unique phenomena have been linked to ON. The first is the Pulfrich phenomenon, which refers to the perception of a three-dimensional movement from an object moving in a two-dimensional pathway, this could be elicited by swinging a pendulum back and forth in front of the patient and he will describe it as moving in circles, Its postulated that it arises as a result of delayed signal processing by the retina. But such phenomena are not unique only for ON and therefore not specific [9-11]. The second is the Uhthoff phenomenon which denotes a sudden aggravation of symptoms during periods of elevated body temperature, which could be the result of strenuous physical exercise or hot showers. Unlike the former Uhthoff phenomenon is highly specific for optic neuritis, but it lacks sensitivity as it is found merely in around 50%. Both phenomena usually only start to appear when other symptoms begin to diminish [3, 12].

On examination, the physician should assess the visual field, acuity, color perception in addition to performing the afferent pupillary reflex looking for any deficit. As patients will commonly have a delayed response in the affected eye, but if response was equal on both sides this could be due to bilateral ON or the possibility of another diagnosis. funduscopic examination is normal in around 3 out of 4 patients due to the inflammation being retrobulbar [7]. While the rest could suffer from Papillitis (inflammation of the optic disc). In these patients, you might identify an edematous disk with blurred margins [13].

Fortunately, the majority of patients will return to their baseline visual acuity within a year, but patients may exhibit chronic changes, most notably optic disc atrophy. The degree of atrophy is variable but the temporal aspect is more likely to be affected. Another common long-term sequel is Photopsias (the perception of seeing flickering or flashes of light) [5, 14, 15].

The aforementioned symptoms and signs are the classical presentation of typical-ON, and despite having a lot of similarities and overlap with atypical-ON. The latter can present with some differentiating features. chiefly, bilateral affection, absence of pain, progressive deterioration extending past 3 weeks, severe reduction of visual acuity, bilateral disease or equal afferent pupillary reflex, early atrophic changes of the optic disc, and lastly, presence of hemorrhagic changes or signs of uveitis on examination [8, 10]. Identification of such clues should alert the physician to the possibility of atypical-ON, as failure to do so might lead to dire consequences on the patient's eyesight.

Diagnosis of ON is a clinical diagnosis based on the patient's presentation in addition to typical findings on ophthalmic examination. With the role of investigation being confined to either attaining supportive evidence or excluding underlying pathology in atypical presentation. These tests include but are not limited to MRI, lumper puncture, visual evoked testing, and Optical coherence tomography. But we won't go through details in this paper as it is beyond our scope [15].

*Management*

Management of typical optic neuritis can be broken into two main domains, the first being acute treatment of the episode. In addition to long-term therapy to prevent MS development and minimize the risk of relapse.

As for atypical-optic neuritis, the management approach is aimed at treating the underlying pathology, which differs greatly from one etiology to the other. Henceforth trying to include such a vast topic in this paper won't give it justice.

*Acute Management*

*Corticosteroids (CS)*

corticosteroids are considered to be the drug of choice for the short-term management of optic neuritis. This is due to their effect in shortening the duration of symptoms. In addition, to their ability to prevent the occurrence of visual loss if administered early in the course of the disease during the acute phase, in particular within 48hours from the onset of symptoms. But these effects are not significant over the long-term and do not seem to alter the outcome of the condition, as numerous data have shown that no significant difference in visual outcome was achieved if compared to placebo [4, 14, 16, 17].
They could be used either in oral (prednisolone) or intravenous (methylprednisolone) forms. Even though older studies have advised against the use of oral CS due to higher recurrence rates [10], but these findings are likely to be attributed to the low dosage used back then. As new evidence has emerged showing no significant difference in outcomes between oral and IV, which makes the oral route more favorable due to ease of administration and being cheaper [16].
Recommended daily dose of IV methylprednisolone is between (500mg and 1g) administered for 3–5 days. To achieve a bioequivalent dose by oral prednisolone, a higher dose is required typically 1250 mg daily. Despite the high dosage of these regimens, they are considered to be relatively safe due to the short duration of use. the possible adverse effects can include immunosuppression, GI disturbance, mood alteration, acute psychiatric episodes of mania or depression, avascular necrosis, and lastly elevation of glucose levels. Henceforth, simultaneous use of proton pump inhibitors is advised to alleviate GI complaints. In addition to frequent monitoring of serum glucose levels in known diabetic patients. Therefore, a conscious decision needs to be made taking into consideration the aforementioned benefits and the possible risks of adverse effects [18].

*Plasma Exchange (PE) / Immunoadsorption (IA)*
Both these methods are regarded as alternative lines of therapy in ON and are usually reserved for severe cases who are irresponsive to CS or when they can not be used. Their mechanism of action is similar, acting through the removal of antibodies and immune complexes from patients 'plasma. Therefore, they are used in both typical-ON and Atypical-ON when the underlying etiology is autoimmune such as NMO. Despite both being generally safe Immunoadsorption is more preferred due to lower rates of adverse effects, this due to it being more selective unlike PE which removes all plasma proteins, but the downside of IA is higher cost and limited availability [10, 19-21].

*Immune Globulins*
intravenous immune globulins (IVIG) are not commonly used due to the absence of concrete supporting evidence, as different studies which looked into assessing their efficacy have yielded conflicting results. And therefore, they are only used in severe cases that were irresponsive to CS, PE, and IA [22]. Another possible indication of their use is recurrent ON where it has been shown to decrease recurrence, but further research is warranted as this evidence was obtained from small retrospective studies [23].

*Erythropoietin*
erythropoietin is emerging as a potential therapy in ON, as it has displayed a positive effect on the survival of retinal ganglion cell (RCG) in rats. Which lead to it being tested in a small phase 2 clinical trial, where it demonstrated a remarkable increase in The Retinal Nerve Fiber Layer Thickness (RNFL) and visual acuity of the patient [24, 25]. But a more recent study has failed to replicate such positive outcomes and conclude that erythropoietin had no significant results [14]. The mutual finding in both of these studies was the safety of erythropoietin as none of the included patients had any series of side effects. A phase 3 Randomized, Double-blind, Placebo-controlled Trial is looking into this efficacy of erythropoietin but results are yet to be published [26].

*Long Term Management*
The aim of long-term therapy in typical-ON is to reduce the risk of developing Multiple sclerosis. This is because ON is a frequent initial presentation of multiple sclerosis found in approximately 20% of cases, additionally, the risk of developing MS within the next 15 years in these patients ranges from 25% to 75% of patients [15].

*Disease-Modifying Drugs (DMDs) Immunomodulatory Therapy*
DMDs are a group of immunomodulatory drugs in particular interferon β-1a, interferon β-1b, and glatiramer acetate, they are used as prophylactic measurements in patients with a high risk of MS. As they were proven to lower the risk of developing MS by up to 50%, in addition to delaying the onset of any future episode. Their main downside is the need for prolonged use to achieve such a result, which could reach up to 6 years of therapy to prevent one relapse [13]. There is a general lack of guidelines to help determine whom and when to commence such therapy. Therefore, its generally advised that patients will have regular follow-ups with a neurologist, to decide the optimal time of initiation of DMDs based on each patient's condition and characteristics [10].

**Conclusion**

Optic neuritis can manifest in many different ways, but the most common presentation is the sudden onset of unilateral retro-orbital pain with varying degrees of visual loss. The course of the disease is progressive reaching its peak in 2 weeks with subsequent gradual improvement. majority of patients regain their base visual acuity within a year. Management of typical-

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**Acknowledgments:** None

**Conflict of interest:** None

**Financial support:** None

**Ethics statement:** None

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