Clinical Neuroscience & Neurological Research International Journal
ISSN: 2689-6001

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Research Article *Volume 5 Issue 1*

From Radiance to Shadow: A Journey Through Visions Fading Light-Exploring VEP, OCT, Fundoscopy, and Automated Perimeter in the Twilight of Demyelinating Disorders

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Received Date: August 21, 2024; **Published Date:** October 03, 2024

Abstract

Background of the Study: Optic neuritis is inflammation of the optic nerve. If it is associated with a swollen disc, it is called pappilitis or anterior optic neuritis. If the disc is normal, it is called pappilitis or anterior optic neuritis. There are numerous other causes of optic neuritis apart from demyelination. Excluding the other causes the study was proceeded.

Keywords: Optic Neuritis; Demyelination; Funduscopy; Prognosis; Neuroretinitis; Papilloedema; Retina; Optic Nerve; Optic Disc

Abbreviations

OCT: Optical Coherence Tomography; AP: Arterial Pressure; VEP: Visual Evoked Potentials; NMO: Neuromyelitis Optica; RNFL: Retinal Nerve Fiber Layer; mfVEPs: Multifocal Visual Evoked Potentials; CS: Contrast Sensitivity; OCT: Optical Coherence Tomography.

Rationale of the Study

The correlation of OCT, AP, VEP and funduscopy in optic neuritis with clinical disability are that these tests are potential markers of the disease burden in optic neuritis and NMO spectrum disorder**.** It is a core clinical criteria in NMO spectrum disorder. Optic neuritis is also due to post vaccination and post viral.

The treatment and prognosis of optic neuritis varies significantly, hence it is crucial that the clinician initiate appropriate investigations which includes all these VEP, Fundoscopy, Optical coherence tomography and automated perimetry. When the intra-ocular optic nerve and peripappillary retina is involved, the term neuroretinitis is used. Optic perineuritis or peri-optic neuritis is involvement of the optic nerve sheath alone without involvement of optic nerve.

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peripappillary retina is involved, the term neuroretinitis is used. Optic perineuritis or peri-optic neuritis is involvement of the optic nerve sheath alone without involvement of optic nerve.

Aim and Objective of the Study

Aim

To correlate the sensitivity of optical coherence tomography, visual evoked potentials, fundoscopy and automated perimetry to detect visual path abnormalities in demyelinating disorders to identify very early cases of optic neuritis.

Usually, Acute optic neuritis is followed by recovery of visual function, this study was done to determine whether there was any evidence of ongoing neural reorganization.

In this study, the relationship was noted between structural i.e., retinal nerve fiber layer [RNFL] thickness) and functional aspect of multifocal visual evoked potentials [mfVEPs]) which is the measure of the integrity of the visual pathway in the postacute stage of ON, Inclusion and exclusion criteria:
Age gp- above 12 years
Gender: both male and female
Both acute and recurrent optic neuritis
neuromyelitis optica

Exclusion Criteria

Congenital, Traumatic, Post Infective Causes

Materials and Methods

15 Patients with Optic Neuritis

This case control study, ethical committee approval obtained after getting written informed consent from cases and controls, they were enrolled in the study. This was conducted in the department of neurology with the assistance from ophthalmology department. Diagnosis of optic neuritis based on the h/o subacute onset of visual loss ,RAPD when unilateral, serologic studies for AQP4-IgG,MOG-IgG,CSF studies for MS panel and test to r/o other possible causes -VDRL,anti HIV,RA factor,anti Ro/La ,thyroid function test were done and results were noted.

On examination, visual acuity is reduced in most cases from mild reduction to light perception. Also associated with difficulty in color plate recognition. Relative afferent pupillary defect is demonstrated in almost all cases of unilateral optic neuritis. When such defect is not present, either co-existing optic neuropathy in opposite eye, some previous optic neuritis or the visual loss may be due to other optic neuropathies. Slit -Lamp Examination in eyes with demyelinating optic neuritis is almost always normal. But a very mild anterior or posterior uveitis can be observed. Sheathing of retinal vessels can occur especially in patients with MS. When the cellular reaction is extensive, etiologies other than demyelination to be considered like sarcoidosis, syphilis, lyme's disease. Based on the inclusion criteria patients were selected and they underwent ophthalmologic evaluation including visual acuity which was measured by a Snellen 20-foot wall chart. to determine whether there was any evidence of ongoing neural reorganization. Contrast sensitivity (CS) was measured by a Pelli-Robson chart at 1 meter (Metropia Ltd., Cambridge, UK). Best vision was obtained with prescription glasses and Funduscopic examination , VEP, Automated perimetry for assessment of visual field and OCT.15 persons were selected and they underwent oct, AP, VEP and funduscopy and they served as controls.colour vision was assessed

Fundoscopy

About 1/3rd of the patients with typical demyelinating optic neuritis has some degree of visible optic disc swelling. The disc edema may be mild or very severe that mimics the choked disc seen in patients with papilloedema. The degree of the disc swelling does not co-relate with the severity of either visual acuity or visual field loss. Disc or peripapillary hemorrhages and segmental disc sweeling are more common in eye with acute optic neuritis than with anterior ischaemic optic neuropathy. After 4 to 6 weeks, the optic disc may appear pale even if the visual acuity or other parameters of vision are improved. The pallor may be diffuse or sectoral, most often in the temporal region.

Automated Perimetry

dle type defects in 52% patients (may be altitudinal, arcuate or nasal step were present Visual field loss – mild to severe, diffuse or focal, involve central or peripheral field. Herecomes need of our AP.Indeed any type of visual field defect can occur in ON. In the ONTT where 415 patients had baseline visual acuity of hand movements are better revealed. Automated perimetry of central 300 visual field revealed diffuse field loss in 48% patients and focal nerve fibre bunin 20 % of patients, pure central or centrocecal defects in 8% and hemianopic defects in 5%).

MRI Brain and Orbit with Gadolinium Contrast

MRI Brain and Orbit with Gadolinium Contrast is done in all patients suspecting as optic neuritis. MRI revealed optic nerve enlargement, T2 hyperintensity and enhancement of the optic nerve with gadolinium contrast in many patients with optic neuritis. the importance of MRI is the

identification of signal abnormalities in white matter of the brain usually in the periventricular region consistent with the CNS demyelination.

CSF Analysis

The role of CSF analysis is important to identify infective causes of visual loss, inflammatory causes of visual loss and demyelination particularly in OCB in MS.

Optical Coherence Tomography

Even a normal appearing optic nerve may have some retinal nerve fibre layer thickening when measured by OCT. Optical coherence tomography (OCT) measures were unrelated to disability and demographic features predicting a worse prognosis in demyelination.. OCT may provide complementary information to VEP in select cases, and remains a valuable research tool for studying optic nerve disease in populations. OCT-The extent of RNFL thinning predicted visual recovery after acute ON. Average RNFL values were lower in subclinical ON. visual function may be relatively well preserved after ON until a critical threshold of axonal integrity is violated; after which, permanent vision loss is more likely to ensue. Retinal Nerve Fiber Layer Atrophy: The Impact of Recurrent Optic Neuritis. For eyes affected by two or more ON events, however, RNFL atrophy tends to be more severe. These findings indicate that recurrent inflammatory events have a cumulative impact and erode axonal integrity in the CNS. The detection of new RNFL atrophy after ON can be more challenging in patients with prior ON as compared to patients experiencing their first ON event. Robust inter-eye differences in RNFL thickness may be observed for a CIS patient presenting with unilateral ON, because the anterior visual pathway has presumably been unscathed by prior inflammation (Figure 1).

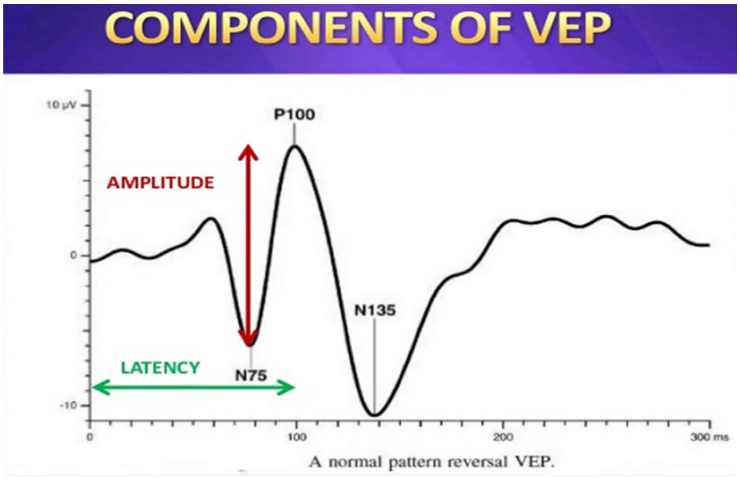

Figure 1: A Normal Pattern Reversal VEP.

VEP

VECP or VER or VEP is an electrical signal generated by the occipital visual cortex in response to stimulation of the retina by either light flashes or patterned stimuli .The response to many alterations is recorded and averaged. The use of the checkerboard stimuli is preferable when the eye is optically correctable because the occipital cortex is sensitive to sharp edges and contrast, whereas it is relatively insensitive to diffuse light. Because VECP represents the end point of the visual pathway, it can indicate an abnormality .The VEP is charecterised by 2 negative and two positive peaks,whose amplitudes and implicit times depend on the check size ,contrast and alternation frequencies of the stimulus. Although absolute amplitude of the VEP can be measured ,using them as clinical distinction is difficult because of variability among normal responses. The temporal (delay in peak appearance)aspect of the VEP is less variable and more reliable as a clinical measure. Visual evoked potentials (VEP) remains the preferred test for detecting clinical and subclinical optic neuritis.

Numerous studies have shown that a high percentage of patients with multiple sclerosis exhibit VEP abnormalities, most commonly a prolongation of P100 latency. As in conventional NCSs, conditions producing demyelination elicit an increase in response latency, whereas axonal loss produces a reduction in response amplitude.

VEPs are used to evaluate pathologic conditions affecting the visual pathways. VEPs are generated primarily in the visual cortex and may be affected by abnormalities anywhere along the visual pathway from the cornea to the occipital cortex. Because the anterior visual pathway from the cornea to

the retina may be evaluated directly by ophthalmologic examination, the VEP is used mainly to assess the optic pathway posterior to the retina.

The most common stimulus used to elicit the VEP is a reversing checkerboard pattern, typically transmitted through a video monitor and producing checks that alternate from black to white and vice versa. This is referred to as a pattern-reversal VEP.

Visual evoked potential (VEP) P100 latencies (normal mean 98.95 msec; upper limit, also defined by 2 SD, was 112.9 msec) were read blinded. If the waveform was unobtainable because of poor vision, the value of 170 msec was used, representing the most prolonged obtainable waveform for this machine. The nadir VA during the acute phase of the ON was determined from chart review when available.

Clinical Presentations

The symptoms of optic neuritis are loss of central vision and pain in and around affected eye. Diminished visual acuity is noted in more than 90% of the patients. Visual loss is typically abrupt, occurring over hours to days. If it occurs over a prolonged period of time , you should consider alternate diagnosis. Occasionally , the patient complaints of partial visual loss either superior or inferior. It is mono-ocular in most cases , particularly in children . but both eyes can be simultaneously affected. Furthermore in patients with improvement in visual function to “normal” may complain of movement induced photopsias or transient loss of vision with overheating or exercise (Uhthoff symptom). Uhthoff symptom is most common in patients with other evidence of MS, but it is also experienced after isolated optic neuritis by patients with chronic or subclinical optic neuritis, and occasionally by patients with optic neuropathies from other causes. Two major hypotheses regarding Uhthoff phenomenon symptoms are thatElevation of boday temperature interferes directly with axon conduction Exercise or rise in body temperature changes the metabolic enviroinemt of the axon that in turninterferes with conduction Subjectively, patients with recovered optic neuritis frequently complain that their vision in the affected eye is not right or that colors are washed out.

Thsese symptoms have been correlatd with persistently reduced contrast sensitivity that can be identified using low contrast sloan letters. In patiens with prior optic neuritis OCT is used to assess the morphological changes, retinal thickness, NFL thickness, retinal volume and other parameters.

Optical coherence tomography (OCT) uses infrared light reflected from retinal subsurfaces to measure the retinal nerve fiber layer (RNFL) thickness via optical interferometry [1-3]. Optic nerve axonal count and RNFL thickness have been correlated by histopathology [4]. Optic neuritis (ON) has been an established etiology of optic nerve injury that contributes to a reduced RNFL after 6 months [5]. Optic atrophy and RNFL thinning have been noted in many patients with multiple sclerosis (MS) [6]. Flashes of light may also be used to produce VEPs, but they result in greater variability in response and are less sensitive to abnormalities in the pathway than pattern-reversal testing is [7-9]. Flash-elicited VEPs are used primarily when an individual cannot cooperate with pattern-reversal testing and gross determination of visual pathway integrity is required (e.g., in infants or comatose patients and during general anesthesia). A flash stimulus is also used to produce the electroretinogram, a specialized type of VEP that reflects the function of the retina and distal portion of the optic nerve. OCT has been established as a sensitive technique for detecting optic nerve injury within a population. It may serve as an objective measure of axonal injury after ON, and may reflect subclinical disease or progressive axonal attrition in the clinically unaffected eye [9,10]. The degree of RNFL thinning correlates with decreases in visual function, overall disability, and brain atrophy [10].

The main objective of this study was to explore the utility of OCT in clinical practice, as it might be used for the individual patient. We hypothesized that OCT would provide objective confirmation after a clinical episode of ON and could reveal subclinical optic nerve involvement for confirmation of CNS dissemination. RNFL thickness may provide useful information about the disease process and function of the optic nerve as it relates to visual outcome categories, recurrent episodes, the severity of vision loss during the acute phase of ON, and the use of IV glucocorticoids. A thinned RNFL might reflect the severity of disease affecting the entire CNS as assessed by overall disability and demographic factors associated with prognosis assessed by overall disability and demographic factors associated with prognosis.

Assessed by overall disability and demographic factors associated with prognosis. OCT measurements of fast RNFL thickness were obtained by a trained technician on a Zeiss Stratus OCT III with version 4.0 software, using a signal strength of ≥5. In eyes with poor visual function, OCT was obtained by external fixation of the “good eye” as the technician ensured scan quality. Normal RNLF thickness for adults is 100.1 ± 11.6 μm (n = 328). The RNFL thickness cutoff was based on published reference values, which comprise the built-in Zeiss Stratus OCT database, using 2 SD below the normal mean, stratified by age. Thus, average RNFL thickness cutoffs for defining abnormal were 84.3 μm for ages 18–29 years, 83.9 μm for 30–39 years, 75.5 μm for 40–49 years, 74.0 μm for 50–59 years, and 75.3 μm for 60–65 years. The established reference for the temporal RNFL

quadrant thickness is 69.0 ± 12.7 µm,18 and a cutoff of 44 µm was defined as abnormal.

Clinical Features

Regarding pain in eye, it is mild in 90% cases. And in 10%, it may be severe. Pain may proceed or occur concurrently with visual loss and usually exacerbated by eye movement. This peculiar pain helps to differentiate the acute optic neuritis from anterior ischaemic optic neuropathy and leber's optic neuropathy where there is painless visual loss. Regarding symptoms, 30% of patients have positive visual phenomena called photopsia which are spontaneous flashing of black squares, flashes of light or showers of sparks which may be precipitated by eye movement or certain sounds (Figures 2-4).

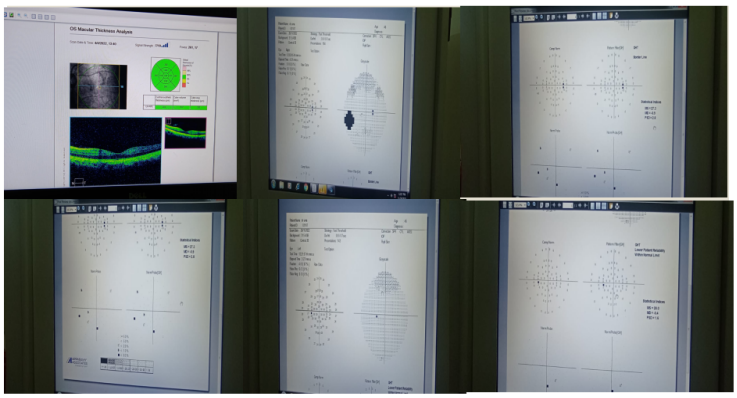

Figure 2: Muscular Thickness Analysis.

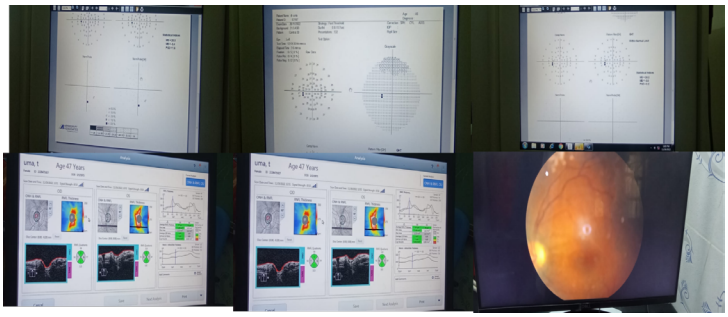

Figure 3: Analysis.

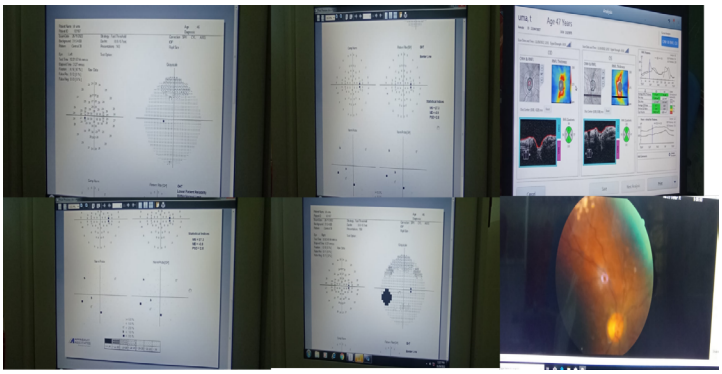

Figure 4: Frequencies.

Results

VEP is a useful tool in identifying abnormality relative to the integration of optic pathways, and aids the diagnosis of central nervous system demyelinating disorders. the sensitivity of VEP in detecting early optic abnormality as a visual function surrogate is Proven. Recent studies showed that low-contrast VEP increases sensitivity in early detection of optic demyelination.

VEP was superior in detecting optic neuritis at the earliest and also the first episode of optic neuritis .OCT There were significant but opposite changes in RNFL thickness and mfVEP amplitude. The average asymmetry of RNFL thickness between affected and fellow eyes increased from 16.5 ± 11.5 to20.1 ± 12.8 μm (P = 0.0003), indicating progressive axonal loss, whereas mfVEP amplitude asymmetry decreased from 44.2 ± 30.8 to 38.3 ± 31.1 nV (P = 0.0015), indicating ongoing recovery of the optic nerve. Optic disc edema was found in 1/3 of cases. Automated perimetry was done .RNFL thickness was correlated with visual field defects and visual acuity. Patients with normal visual fields in AP had reduced RNFL thickness (p<5%).

Discussion & Conclusion

Bilateral simultaneous acute optic neuritis is uncommon in adults although relative frequency increases when evaluating patients with MS. ONTT shows relatively high percentage of asymptomatic fellow eye defecits at baseline i.e., 14% with visual acuity abnormalities , 22% with color vision abnormalities, 74.7 % with visual field defects

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