

## Correlation of Optic Neuritis with Multiple Sclerosis and Evaluating the Response of Optic Neuritis Treatment of Hospitalized Patients with Ophthalmologic Complaints in Imam and Motahari Hospitals of Urmia, Northwest Iran

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**Abstract:** The aim of this study was to determine the frequency rate of optic neuritis among patients with ocular symptoms, hospitalized at Imam and Motahari Hospitals and evaluating the causes and factors contributing to this disease and the extent of treatment response. It usually occurs as acute or subacute. Although there is no definitive cause in most of the time and considered as idiopathic, but in some cases, especially between young females, Optic Neuritis could be a sign for beginning of multiple sclerosis. We enrolled all cases that hospitalized as optic neuritis in Imam and Motahari Hospital in a retrospective cross-sectional study. Data about the Visual Acuity in the 1st, 3rd and 10th days of hospitalization and also the results of Visual Evoked Potential (VEP) and MRI were collected and analyzed in SPSS software version 16. Thirty two cases enrolled in the study with minimum age of 9 and maximum age of 57 years old (mean age = 32 years). 66% were female. Eleven cases (34.4%) has Hand Motion (HM) visual acuity, 12.5% has 0.5 m Finger Count (FC), 21.9% has 1 m FC, 9.4% has 2 m FC, 6.2% has 3 m FC, and finally 1 cases (3.1%) has each degrees of visual acuity as following 4, 5 and 6 m FC, 1, 2 and 3/10, respectively. Ten days after treatment, 6 cases has 8/10, 18 cases (50%) has 9/10, and 10 cases has complete visual acuity. Only in 11 cases (33%), MRI has a kind of evidence compatible with optic neuritis. VEP in 87% of cases were suggestive for optic neuritis. Lower rate of abnormal MRI results in this study could reveals early imaging with MRI. MRI after first week and through 6 months after ON could show the plaques more. VEP has more sensitivity and MRI has more specificity in diagnosing Optic Neuritis.

**Key words:** Iran, MRI, multiple sclerosis, optic neuritis, urmia, visual evoked potential

### INTRODUCTION

The optic neuritis is a rather common disease. The incidence is one to five cases per ten thousand patients. The incidence is higher among the individuals with ages of 20-49 years old, women, whites and the residents in the regions with higher attitudes (Blair and Sharma, 2003; Hickman *et al.*, 2002; Arnason *et al.*, 1974). The unilateral visual loss progressively aggravated during several days, which is along with a typical eye pain, is called optic neuritis. The degree of visual loss widely varies among the patients. Some reported only had a slight change in their vision, although the others may have severe vision loss in their involved eye. The pain of eye is very common and the results of Optic Neuritis Treatment Trial (ONTT) showed visual loss in 92% of the patients, which is aggravated by eye moving (Beck and Trobe, 1991; Arnold, 2005). This pain only lasts for some days (Hickman *et al.*, 2002; Biousse, 2005). The visual

loss during several days to a maximum of two weeks. Almost patients spontaneously recover the vision 2-3 weeks after the beginning of the symptoms, with a maximum improving time of 4-6 weeks (Beck and Trobe, 1997a). The final vision depends on the intensity of visual loss, but almost patients recover well their vision. In ONTT, 79% of patients recover a vision of 20/20 or better after six months and 95% of them recover a vision of 20/40 or better after one year (Beck and Trobe, 1997b). The efficacy of visual field is also recovered again (Fang *et al.*, 1999; El Otmani *et al.*, 2005).

The other common symptoms include diplopia, scotoma, and luminous sparkles. Decreased vision of colors, contrast sensitivity, visual field and RAPD may be detected by examination in the involved eye. The optic disc may be edematous. In ONTT 35% of cases had disc edema (papillitis) and the rest had normal discs (retrobulbar neuritis) (Beck and Trobe, 1991). Other signs have been reported in the literature, including uveitis, pars

planitis (peripheral vitreitis with exude covering the surface of peripheral retina), flame-like hemorrhage of disc, retinal periphlebitis (Hickman *et al.*, 2002; Beck and Trobe, 1991). The diagnosis of optic neuritis is based on clinical findings (Hickman *et al.*, 2002; Fazel, 2001; Hwang *et al.*, 2007). Acute optic neuritis in younger individuals is usually characterized by diplopia, eyeball pain and decreased visual acuity. This condition often occurs in the acute and sometimes peracute forms. Although in almost patients it is of an idiopathic origin, in a large number of patients, especially in young women optic neuritis is a sign of Multiple Sclerosis (MS) or a heralding sign of onset of this condition. Approximately, 50% of patients will contract MS in the future. This percentage is higher in young women (Khandaghi *et al.*, 2006; Mohammad Rabei and Abolhassani, 2001). The rate of accompanying the MS with optic neuritis is widely ranged from 13 to 85%, based on the literature reports (Riordan-Eva and Hoyt, 2004).

Without treatment 2 or 3 weeks after onset of disease, vision improves and sometimes during few days, it reaches normal rate. Ten years after onset of optic neuritis, patients with zero, one, two and more than two brain lesion at T2 sequence in MRI have 22, 52 and 56%, respectively risk of optic neuritis occurrence, respectively (Brass *et al.*, 2008). CMV, infection with herpes zoster, syphilis, tuberculosis and *Cryptococcus* infection are other reasons of optic neuritis. One or two weeks after viral infection or vaccination especially in children, an optic neuritis (almost with simultaneous bilateral involvement) may be occur, that its pathogenesis is similar to idiopathic demyelination optic neuritis. Involvement of optic nerve in acute idiopathic polyneuropathy seems like Guillian-Barré syndrome. In lupus, probably the involvement of optic nerve in of immunological cause or due to occlusion of small vessels. The involvement of optic nerve is prevalent in sarcoidosis and needs a treatment with high dose of steroids. Systematic *lupus erythematosus* through autoantibodies and immune complexes causes fiber damage as micro vacuities circulated in different body organs. The most common injury to eye is occlusive inflammation of retinal artery and optic nerve involvement that has variable and often poor prognosis and in 55% of the cases, it causes visual loss that in 50% of them vision falls to less than 20/200th (Rood Peyma and Ahmadi, 1992; Papais-Alvarenga *et al.*, 2008).

Adjacent inflammatory disease like intraocular inflammatory, orbital disease (orbital cellulitis and vasculitis), sinus disease, intracranial disease: meningitis and encephalitis with involvement of optic nerve may cause optic neuritis (Riordan-Eva and Hoyt, 2004). Treatment with chloramphenicol and etambutol may also result in optic neuritis (Wingerchuk and Alireza, 2007). The recurrence rate of optic neuritis in either eye is 28% (Beck and Trobe, 1997a; Plant, 2008).

Therapy with intravenous methylprednisolone accelerates early recovery of vision but its results during six months in long term outcomes of vision have been similar to placebo. Therefore, at this stage using prednisolone depends on patient's quality of life (Blair and Sharma, 2003; Woung *et al.*, 2007). Considering above, in this study we intended to determine the frequency rate of optic neuritis among patients with ocular symptoms, hospitalized at Imam and Motahari Hospitals and evaluating the causes and factors contributing to this disease and the extent of treatment response.

## MATERIALS AND METHODS

Descriptive-sectional and retrospective study conducted on the records of patients hospitalized at Imam and Motahari hospitals of Urmia, northwestern Iran, during Sept. 2006 and Des. 2007 with optic neuritis symptoms. Records with incomplete information removed. In this study, 45 patients with optic neuritis, confirmed by diagnosis, participated but because of incomplete information or patients not referring for pursuing and completing documents, 13 cases removed from study. So analyzes performed on 32 remaining cases. Examined data contained age, sex, involved eye (right or left), neuritis cause (underlying disease like multiple sclerosis, Giant cell arthritis, idiopathic), treatment received and patient's response to treatment. A check list was prepared by plan's researchers that completed by referring to patients records. Through the recorded phone numbers contact made with the patients participated in plan and asked them to refer to eye clinic at certain date and also asked them to bring their nerve bars and MRI for analyzing. Collected data entered into statistical software and through descriptive statics (frequency, percentage, mean and standard deviation) analyzed statistically. Questionnaires completed as anonymous and individual's information would be protected by the plan's researchers.

## RESULTS

In this study, 45 patients with optic neuritis, confirmed by diagnosis, participated but because of incomplete information or patients not referring for pursuing and completing documents, 13 cases removed from study. The minimum and maximum ages of patients with optic neuritis were 9 and 57, respectively; with an average of 31.97, mean = 31, mode = 44, standard deviation = 11.423, variance=130.483 and range = 48, respectively. Dividing ages into the age intervals of ten-years, the resulted groups included: one case (3.1%) in 1-10 year old age group; four cases (12.5%) in 11-20 year old age group; 11 cases (34.4%) in 21-30 year old age group; 7 cases (21.9%) in 31-40 year old age group; 8

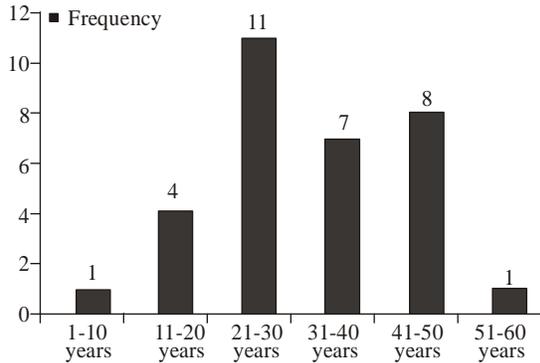


Fig. 1: The frequency of patients in different age groups

Table 1: The values of visual acuity in the first day of the admitted and referred patients with optic neuritis

Visual acuity	Frequency	Percentage (%)
NLP	0	0
LP	0	0
HM	11	34.4
0.5 m FC	4	12.5
1 m FC	7	21.9
2 m FC	3	9.4
3 m FC	2	6.2
4 m FC	1	3.1
5 m FC	1	3.1
6 m FC	1	3.1
1/10	1	3.1
2/10	1	3.1
3/10	1	3.1

NLP: no light perception; LP: light perception; FC: finger count; HM: hand motion

cases (25%) in 41-50 year old age group and one case (3.1%) included in 51-60 year old age group. 21 patients out of 32 cases (66%) were female and 11 cases (33%) were male Fig. 1.

Visual acuity of involved eye with optic neuritis were analyzed on first, third and tenth day of follow-up.

Among individuals participated at the study no one had visual acuity to the extent of NLP (no light perception) or LP (light perception). Eleven cases had a visual acuity to the extent of half a meter or FC (finger count), 7 cases (21.9%) 1 m FC, 3 cases (9.4%) 2 m FC, and 2 cases (6.2%) up to 3 m FC. Therefore, one case (3.1%) was in each of the visual acuity groups, 4, 5 and 6 m FC, 1, 2 and 3/10, respectively. No one had visual acuity better than 3/10 (Table 1).

There was no significant difference between third and first day's visual acuity. At the study of visual acuity of patients with optic neuritis, on tenth day after the onset of optic neuritis symptoms, 6 cases (18.75%) had visual acuity up to 8/10, 18 cases (50%) up to 9/10 and finally 10 cases had a full visual acuity equal to 10/10. Through the recorded phone numbers, contact made with the patients participated in study and asked them to bring

their EEG and MRI for analysis. Among patients participated at this study 21 cases (66%) had normal MRI and it means that there was no finding in MRI in favor of optic neuritis. At 11 cases (33%) important positive findings were in favor of optic neuritis. At the MRI of one of the female patients that was 21 years old although there was no finding in favor of optic neuritis but multiple sclerosis plaques were seen and she was an MS patient. For another patient that was a 50 years old woman finally after follow-up, Giant Cell Arthritis diagnosed. In analyzing EEG or Visual Evoked Potential (VEP) of referred patients, 28 cases equal to 87% had findings in favor of optic neuritis. However, in EEG of four cases, there was nothing in favor of optic neuritis.

In cross-tab of four patients that had negative VEP, a single case in his MRI had findings in favor of optic neuritis. Three others had a negative MRI results. From 28 cases with positive VEP, just 10 cases had a MRI with findings in favor of optic neuritis. From 11 persons with positive findings in their MRI in favor of optic neuritis, just one person had negative VEP.

From 21 cases with normal MRI, VEP of 18 cases had findings in favor of optic neuritis. Considering above, it can be concluded that VEP is more sensitive than MRI in diagnosing optic neuritis and MRI has higher sensitivity and specificity in diagnosing optic neuritis. However measuring the sensitivity and specificity of each of these methods requires further and more precise studies.

## DISCUSSION

Optic neuritis can be considered as a leading cause of multiple sclerosis but it is hard to predict the onset of MS by the attack of visual neuritis (McDonald and Barnes, 1992).

At this study diagnosis of acute optic neuritis was made by an ophthalmologist. The criteria of abnormal MRI and report based on the neuroradiologist according to hypotense regions in T1 and Hypertense regions in T2. Few days to few months after the onset of optic neuritis symptoms, MRI was made on the patients. The minimum and maximum age of patients with optic neuritis was 9 and 57, respectively. With an average equal of 37.97, mean = 31, mode = 44, standard deviation = 11.423, variance = 130.483 and range = 48, respectively.

This finding approximately is consistent with other studies. The patients in the study of Navikas *et al.* (1996) were at the age ranged 12-53 and Jacob *et al.* mentioned age range of 12-61 (Navikas *et al.* 1996; Jacobs *et al.*, 1991). Among patients, the most common age group was group 21-30 that formed 34.4% of the whole patients.

At this study, 66% of patients with optic neuritis were female, which is consistent with other studies.

Most common starter symptom of disease in our patients was loss of vision. Visual acuity of involved eye with optic neuritis analyzed on first, third and tenth day after refer.

Among individuals participated at the study, 11 cases (34.41%) had a visual acuity to the extent of Hand Motion (HM). Four cases (12.5%) had a visual acuity to the extent of half a meter or FC (Finger Count). 7 cases (21.9%) 1 meter FC and 3 cases (9.4%) 2 meter FC. Therefore, a single case (3.7%) was in each of the visual acuity groups 4, 5 and Gm FC, 1.10, 2.10 and 3.10, respectively. No one had visual acuity better than 3.10. Now the best treatment method is to use corticosteroid pulse with high dose in a short time (Beck *et al.*, 1993).

Considering the needed time for pulse therapy, patients with optic neuritis were hospitalized for 3-4 days in the ward of ophthalmology of Imam Hospital. Then, they were admitted in the ward of neurology of the same hospital for 5-6 days. In the follow-up as outpatient, 6 cases (18.751) had a vision to the extent of 8/10, 18 cases (50%) to the extent of 9/10 and finally 10 cases had a full vision up to 10/10. That was a remarkable improvement, which can be seen in patient's vision. The same situation also occurred in the study of (Soltanzadeh and Javadian, 1997). Their study, which was conducted based on the higher risk of MS in optic neuritis with abnormal MRI by following patients, this fact was proved that if in optic neuritis MRI is abnormal, the risk of MS will be higher.

From patients participated in the study, 21 cases (66%) had normal MRI that it means there was nothing in favor of optic neuritis in their MRI. In MRI of 11 cases (33%), there was important finding in favor of optic neuritis. In MRI of one of the female patients that was 21 years old though there was no finding in favor of optic neuritis but multiple sclerosis plaques were seen and she was a MS patient.

At this study because of not following up of patients in a long time after optic neuritis diagnosis, the rate of MS diagnosis among patients with optic neuritis was very low in comparison with previous studies. Therefore, the results of this study do not deny the higher probability of multiple sclerosis in patients with optic neuritis. In the study of Soltanzadeh and Javadian (1997) of 20 cases that were followed for 1-8 months 15 persons (75%) had abnormal MRI. A similar study by Soltanzadeh and Javadian (1997). Reported abnormality of MRI in such cases about 49% that it was during fifth day to fourth month (on average 43 day) from the onset of visual impairment Beck *et al.* (1993), in analyzing 418 patients, mentioned abnormality rate of MRI up to 60%, despite the absence of any MS clinical symptoms (Beck *et al.*, 1993). Miller *et al.* reported MS plaques through analyzing 53 patients involved with optic neuritis that MRI performed on them 7-40 days after the onset of symptoms (Morrissey *et al.*, 1993).

From 15 persons with abnormal MRI in the study of Soltanzadeh and Javadian (1997) 11 cases (73%) had shown MS clinical symptoms in the next follow-up. In our study, patients examined in an 8-year range, therefore, high rate of MS patients with optic neuritis can be attributed to long term following toward present study. Lower frequency of abnormal MRI in some statistics is early MRI reflective after optic neuritis and it seems if MRI is performed after first weeks and before sixth month, the plaques will be more likely detected (Brodsky and Beck, 1994). Visual Evoked Potential (VEP) is useful diagnostic method in nervous system disease specially multiple sclerosis and optic neuritis (Ramroodi *et al.*, 2004). This method is noninvasive for evaluation of nerve signal transmission through the optic nerve (Khandaghi *et al.*, 2006).

Evaluation of EEG or VEP of referred patients was 87% in 28 cases, average delay of the wave called P100 was abnormal and in favor of optic neuritis. Whereas, in four cases of nerve bars there were nothing in favor of optic neuritis. In the study of Khandaghi *et al.* (2006) in Tabriz, the sensitivity of VEP or Visual Evoked Potential obtained in optic nerve lesions detected as nearly 80%.

## CONCLUSION

Regarding the results, lower rate of abnormal MRI results in this study could reveals early imaging with MRI. MRI after first week and through 6 months after ON could show the plaques more. VEP has more sensitivity and MRI has more specificity in diagnosing Optic Neuritis. As a conclusion, we recommend other long-term studies for precise evaluation of the optic neuritis in patients with MS disease.

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