



CSF AND BLOOD ANALYSIS IN PATIENTS OF OPTIC NEURITIS

Ophthalmology

Dr. Shalini Mohan	M.S. Ophthalmology, DNB,MNAMS, Professor Dept. Of Ophthalmology G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India.
Dr. Deepa Kamble*	Junior Resident Dept of Ophthalmology, GSVM medical college, Kanpur, Uttar Pradesh, India *Corresponding Author
Dr. Perwez Khan	M.S. Ophthalmology, Professor & Head, Dept. Of Ophthalmology,G.S.V.M. Medical College. Kanpur, uttarpradesh, India.
Dr. Parul Singh	DOMS, DNB, Ophthalmology, Associate professor Dept of Ophthalmology ,G.S.V.M. Medical College , kanpur, uttarpradesh, India
Dr. Lubna Khan	M.D., Pathology, Professor Dept Of Pathology,G.S.V.M. Medical College,Kanpur, Uttar Pradesh, India
Dr. Manish Singh	MS, DNB, Neurosurgery, Professor & Head Dept. Of Neurosurgery,G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India
Dr. Surbhi Agarwal	MS, Ophthalmology, Assistant Professor Dept. Of Ophthalmology,G.S.V.M. Medical College,Kanpur, Uttar Pradesh, India
Dr. Namrata Patel	MS, Ophthalmology, Assistant Professor Dept. Of Ophthalmology,G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India

ABSTRACT

Purpose: The research was done to study the CSF fluid (appearance, CSF protein ,CSF glucose, cells, IL-6 levels) and blood analysis(TLC, neutrophils, platelet count, ESR and IL-6 levels) in patients of optic neuritis and to compare the CSF fluid and blood analysis between normal values and in patients diagnosed with optic neuritis. **Material And Methods:** This is proposed to be a hospital based cross sectional interventional study .Patients were examined for visual acuity, best corrected visual acuity (BCVA), Colour Vision, Intraocular pressure ,fundus examination, random blood sugar, CSF fluid and blood analysis. **Results:** In this study 50 patients of optic neuritis were included ,maximum number of patients (44%) belong to age group of 21 to 30 years mean age being 33.64.60%(30 out of 50) of patients of optic neuritis are females and males are of 40% (20 out of 50).The logmar BCVA improved subsequently from pre-treatment vision of 1.24 to 0.30 of post 3 days of treatment respectively.Thus there is significant ($p < 0.001$) increase in LOGMAR BCVA. In blood analysis we found that there is increase in TLC in 20% of patients. Serum IL-6 levels were elevated in all 50 patients with the mean of 34.47 and SD +19.03, $p < 0.0140$. In CSF analysis CSF glucose was increased in 30% of the patients (15 out of 50) with the mean of 76.28 and SD +19.25. CSF protein was increased in 30% of the patients (15 out of 50) with the mean of 41.46 and SD +11.62. CSF IL-6 levels were significantly increased in all the patients of optic neuritis with the mean value of 45.10 and SD + 23.26 , $p < 0.00012$. **Conclusion:** We found that IL-6 levels were elevated in both CSF and serum sample of all 50 patients of optic neuritis.60% (30 out of 50) of patients CSF IL-6 levels were more elevated than serum IL-6 levels. In those patients whose CSF IL-6 levels were raised more than serum IL-6 level had optic disc edema.we noticed that in 30 patients who had CSF IL-6 levels elevated more than serum IL-6 levels had poor visual outcome compared to the visual outcome in patients with higher value of serum IL-6 levels than CSF IL-6 levels. We can conclude that measuring IL-6 levels in CSF and serum can help us to prognosticate the disease and also to decide the duration of the treatment.

KEYWORDS

Optic neuritis, CSF IL-6, Serum IL-6 ,Disc edema.

INTRODUCTION

Optic neuritis (ON) is an acute demyelinating inflammatory disease of the optic nerve and primarily influences young females.[1,2] It is usually related to multiple sclerosis (MS) or neuromyelitis optica (NMO) or can be seen isolated.[2] It is observed after paranasal sinuses infections or viral infections.[3,4] First attack of ON occurs 70% unilaterally and 30% bilaterally of the patients in the third decade of life.[5] ON's incidence is 1–5 in 100,000 population in every year.[6]

The term optic neuritis (ON) refers to inflammation of the optic nerve due to many causes, indicated by sub-acute unilateral painful visual loss mostly in a young healthy female and by excluding glaucoma. ON is the most common optic neuropathy in persons under 50 years coming to general ophthalmic practice. It is the earliest clinical symptom in about 20% of cases of MS.[7,8,9,10,11]

ON is mainly idiopathic in nature; though, it could be related to demyelinating lesions (e.g. MS[10,12,13,14] neuromyelitis optica (NMO)[10,12,13] or other less common etiologies such as autoimmune disease (e.g. sarcoidosis[7,10,13], systemic lupus erythematosus (SLE)[10,13], infectious and parainfectious causes (e.g. syphilis[7,10,13,14], tuberculosis [10,13,15], inflammatory and post vaccination immunological responses.[10]

Clinical Features And Diagnosis

Based on the location of involvement, ON can be categorized as:

1. Retrobulbar neuritis (2/3 of cases) with normal optic disc appearance;
2. Papillitis with swollen disc
3. Perineuritis, which involves the optic nerve sheath while the optic disc may or may not be swollen;
4. Neuroretinitis with optic disc oedema and macular star exudates. Retrobulbar neuritis and papillitis are mainly associated with MS while perineuritis and neuroretinitis are more often associated with infectious or inflammatory pathologies.[7,8,10,12,16]

Systemic inflammation is detectable with many biochemical and hematological tests. However, specific tests are quite expensive and complicated. Blood analysis and CSF analysis is an effective, easy, and inexpensive method to determine systemic inflammation.[17] We aimed to demonstrate the relation between ON and Systemic inflammation markers as TLC, neutrophils, platelet count, ESR Inflammatory marker IL-6, and CSF fluid analysis which includes protein, glucose, cells , Inflammatory marker IL-6, to evaluate decrease or increase in these markers to predict the occurrence of optic neuritis.

Aims And Objective

- To study the CSF fluid analysis in patients of optic neuritis
- To study the blood analysis in patients of optic neuritis
- To compare the CSF fluid analysis and blood analysis based on age and sex between normal values and in patients diagnosed with optic neuritis.

MATERIAL AND METHODS

This is proposed to be a hospital based cross sectional interventional study which includes CSF and Blood analysis in patients of optic neuritis at Department of Ophthalmology, G.S.V.M Medical College and LLR Hospital, Kanpur, Uttar Pradesh. Patients whose age is between 20-50 years, cases diagnosed with optic neuritis, patients with no contraindications to lumbar puncture, ability to provide written consent were selected. Patients with history of any other eye disease except optic neuritis and patients in which lumbar puncture is contraindicated were excluded

METHODS

Detail history and examination was done with regards to following points of interest-

1. Visual acuity and best corrected visual acuity (BCVA) by Snellen's chart and EDRS chart.
2. Colour Vision by Ishihara chart
3. Intraocular pressure by Applanation tonometer
4. Indirect ophthalmoscope examination with 20D lens
5. Fundus image of the patient by fundus camera
6. Random Blood Sugar by glucometer
7. CSF fluid analysis (Appearance, glucose, protein, cells, IL-6 levels) by lumbar puncture
8. Blood analysis (TLC, platelets, Neutrophils, ESR, IL-6 levels) by venipuncture

Statistical Analysis

Sample size was calculated using formula:-

$$\text{Number of patients } \{n\} = \left(\frac{Z^2 \cdot \alpha \cdot (1 - \alpha/2)}{\alpha^2} \right) \cdot \Delta^2$$

Where α =significance level; β = power, probability of detecting a significant result; σ =SD of data; Δ = size of difference.

At 95% confidence interval, results were considered statistically significant when p value was <0.05. Power of the test was 80% and α error was 5%.

RESULTS

Total of 50 patients of optic neuritis were included in this study

Table.1: Age And Sex Distribution In Patients Of Optic Neuritis

AGE	NO OF PATIENTS	%
21-30 YEARS	22	44%
31-40 YEARS	21	42%
41-50 YEARS	7	14%
SEX	NO OF PATIENTS	%
MALE	20	40%
FEMALE	30	60%
TOTAL	50	100%

Table.2: Etiology In Patients Of Optic Neuritis

DEMYELINATING	INFECTIOUS	IDIOPATHIC
4	10	36

Table. 3: Logmar Visual Acuity In Patients Of Optic Neuritis On Methyl Prednisolone

Parameter	Mean Pre treatment logmar	SD Pre treatment logmar	Mean Post 3 days	SD Post 3 days	t	p
Logmar visual acuity	1.24	0.30	0.40	0.25	30.24	<0.001

There is significant increase in LOGMAR BCVA in patients of optic neuritis given iv methyl prednisolone ($p < 0.001$).

Table. 4: Comparison Between Post Treatment Visual Acuity In Patients With Raised Csf Il-6 Levels And Serum Il-6 Levels

Logmar Visual acuity	Post treatment logmar visual acuity in patients with IL6 elevated more in CSF than serum	Post treatment logmar visual acuity in patients with IL6 elevated more in serum than CSF
Number of patients	30	20
Mean	0.59	0.26
SD	0.19	0.10

There is significant improvement in visual acuity in all the patients on the 3rd day post treatment with inj. IV methyl prednisolone. But we

found that in comparison to the patients with raised CSF IL-6 levels more than Serum IL6 levels had poor improvement in vision.

Table.5: Blood And Csf Analysis , Disc Edema In Patients Of Optic Neuritis

TLC	NO OF PATIENTS	%
4000-10000	40	80%
>10000	10	20%
CSF protein	NO OF PATIENTS	%
15-45mg/dl	35	70%
>45 mg/dl	15	30%
CSF GLUCOSE	No of patients	%
40-80 mg/dl	35	70%
>80 mg/dl	15	30%
DISC EDEMA	NO OF PATIENTS	%
PRESENT	30	60%
ABSENT	20	40%
TOTAL	50	100%

Table.6: Significant Relationship Between Blood And Csf Il-6 Levels

Group	N	Mean	+ SD	t	p	95% confidence interval
Blood	50	34.47	± 19.03	2.50	<0.0140	2.1958 to 19.00
CSF	50	45.10	+23.26			

There is significantly increase in CSF IL-6 levels in comparison to blood IL-6 levels

Table.7: Significant Relationship Within Group Of Csf Il-6 Levels

Group	N	Mean	+ SD	T	P	95% confidence interval
Disc edema present	30	50.73	± 26.31	3.33	<0.00012	5.7237 to 22.59
Disc edema absent	20	36.60	+14.54			

There is highly significant increase in CSF IL-6 levels in patients with disc edema

Table.8: Significant Relationship Within Group Of Serum Il-6 Levels

Group	N	Mean	+ SD	T	P	95% confidence interval
Disc edema present	30	27.76	± 13.24	4.597	0.0001	-23.9950 to -9
Disc edema absent	20	44.52	+22.12			

There is highly significant increase in serum IL-6 levels in patients without optic disc edema

DISCUSSION

In this study 50 patients of optic neuritis were included. CSF analysis was done which includes appearance, CSF protein, CSF glucose, cells, IL-6 levels and blood analysis which includes TLC, neutrophils, platelet count, ESR and IL-6 levels. These parameters values which we obtained from patient samples were compared with the normal values. In the study group of optic neuritis maximum patients (44%) belong to age group of 21 to 30 years mean age being 33.64.60% (30 out of 50) of patients of optic neuritis are female which correlates with Balcer LJ[20] study in which they found 55.3 % were females and males are of 40% (20 out of 50)

Out of 50 patients 4 were MS, 10 were of infectious etiology and rest 36 patients were of idiopathic etiology. These patients of optic neuritis were given inj IV methyl prednisolone. The logmar BCVA improved subsequently from pre-treatment vision of 1.24 to 0.30 of post 3 days of treatment respectively. Thus there is significant ($p < 0.001$) increase in LOGMAR BCVA. This correlates with the ONTT trial performed.[19] (Optic Neuritis Treatment Trial) 2006 – It was a multi-centered randomized trial involving 454 patients from 1988 to 2006, mainly undertaken to evaluate the efficacy of corticosteroid treatment for acute optic neuritis and to investigate the relationship between optic neuritis and MS. The patients were randomized into 3 different treatment groups: oral placebo for 14 days; intravenous methylprednisolone (250 mg, 6 hourly) for 3 days, followed by oral

prednisolone (1 mg/kg/d) for 11 days and a 3-day tapering of prednisolone thereafter; oral prednisolone (1 mg/kg/d) for 14 days, followed by a 3-day tapering. The study found that most patients experienced rapid visual recovery within 2 weeks after starting the treatment.

But we found that in patients whom CSF IL6 levels were more raised than serum IL6 levels had poor improvement in vision with mean logmar visual acuity of 0.59, SD: 0.19 than that of patients in which serum IL6 was more raised than CSF IL6 with mean logmar visual acuity of 0.26, SD :0.10. On comparing pupillary reaction from pretreatment to post treatment 3rd day. There is no significant improvement as pupillary reaction was 8% pretreatment which is been increased to 10% on post 3 days of treatment. On comparing color vision in patients of optic neuritis from pre treatment day 1 to post treatment day 3 there is no improvement in color vision in 3 days of post treatment.

On comparing the blood analysis (TLC, Neutrophil, ESR, IL-6) of the patients value against normal values. We found that there is increase in TLC in 20% of patients and in 80% of the patients TLC remained within normal limit.

Neutrophil were within normal limit with the mean of 2.92 and SD + 1.39. ESR was within normal limit with the mean of 7.32 and SD +1.54. Platelet count was within normal limit with the mean of 2.47 and SD +0.75. Serum IL-6 levels were elevated in all 50 patients with the mean of 34.47 and SD +19.03, $p < 0.0140$. Which correlates with M Deckert Schulte[18] study in which they found there was significant increase in serum IL-6 levels with $P < 0.01$ in patients of optic Neuritis.

On comparing CSF analysis (appearance, CSF glucose, CSF protein, Cells, IL-6) of patients value with the normal values. CSF appearance was normal in all the patients. CSF glucose was increased in 30% of the patients (15 out of 50) with the mean of 76.28 and SD +19.25. CSF protein was increased in 30% of the patients (15 out of 50) with the mean of 41.46 and SD +11.62. Cells were within normal limit with the mean of 1.52 and SD +1.29.

CSF IL-6 levels were significantly increased in all the patients of optic neuritis with the mean value of 45.10 and SD + 23.26, $p < 0.00012$. There is highly significant increase in CSF IL-6 levels in all the patients of optic neuritis which correlates with M Deckert Schulte[18] study in which they found there was significant increase in CSF IL-6 levels with $p < 0.01$ in patients of optic Neuritis. We found that there is significantly increase in CSF IL-6 levels in comparison to blood IL-6 levels with the mean value of 45.10 and SD + 23.06, $p < 0.00012$ for CSF IL-6 levels and mean of 34.47 SD + 19.03, $p < 0.0001$ for serum IL-6 levels.

Out of 50 patients of optic neuritis 60% (30 out of 50) of patients had optic disc edema with the mean value of 50.70 and SD + 26.31, $p < 0.00012$. and 40% (20 out of 50) of patients did not have optic disc edema with the mean value of 36.60 and SD + 14.54, $p (0.0001)$. We found that in 60% of the patients whose CSF IL-6 levels were more elevated than serum IL-6 levels. These patients had optic disc edema.

CONCLUSION

- We conducted this cross sectional study on 50 patients of optic neuritis. We found that IL-6 levels were elevated in both CSF and serum sample of all 50 patients of optic Neuritis.
- We found that in 60% (30 out of 50) of patients CSF IL-6 levels were more elevated than serum IL-6 levels.
- In those patients whose CSF IL-6 levels were raised more than serum IL-6 level had optic disc edema.
- In this study all the 50 patients of optic neuritis had improvement in vision on 3rd day of post treatment with injection IV methyl prednisolone. But we noticed that in 30 patients who had CSF IL-6 levels elevated more than serum IL-6 levels had poor visual outcome compared to the visual outcome in patients with higher value of serum IL-6 levels than CSF IL-6 levels.
- We can conclude that measuring IL-6 levels in CSF and serum can help us to prognosticate the disease and also to decide the duration of the treatment.

Limitation of the study

- Sample size is small

- Duration of the study is less
- It does not represent the actual population since patients were collected from those who visit the Ophthalmology OPD and not from the community.

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