Comparison of oral and pulse steroid therapy in nonarteritic anterior ischemic optic neuropathy

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ABSTRACT

Purpose: To compare oral and pulse steroid therapies in terms of visual functional improvement in patients with non-arteritic anterior ischemic optic neuropathy (NAION).

Materials and Methods: Twenty-six eyes of 25 NAION cases who were refered to Balikesir University Department of Ophthalmology between April 2019 and July 2021 were studied retrospectively. Visual functional outcomes were evaluated between patients treated with pulse steroid (group 1, n=14) and oral steroid (group 2, n=11) and followed for at least 3 months. The two groups were compared in terms of age, gender, duration of symptoms, systemic diseases, initial and final best corrected visual acuity (BCVA).

Results: In Group 1, median of initial BCVA was 0.15 (0.008-0.8) and median of final BCVA was 0.4 (0.008-1.0) (p=0.011). In Group 2, median of initial BCVA was 0.3 (0.04-1.0) and median of final BCVA was 0.5 (0.02-1.0) (p=0.028). There was no difference between two groups in terms of initial and final BCVA (p=0.281, p=0.721, respectively). BCVA increased in 73.3%(n=11) of the eyes in group 1 and 54.5%(n=6) in group 2 (p=0.659). There was no difference between two groups in terms of visual acuity gain (p=0.494).

Conclusions: Our results suggest that pulse steroid therapy had no superiority over oral steroid therapy in terms of visual gain in NAION patients.

Keywords: Nonarteritic anterior ischemic optic neuropathy, Steroids, Visual acuity.

INTRODUCTION

Non-arteritic ischemic optic neuropathy (NAION) is an acute or subacute optic neuropathy thought to develop as a result of transient hypoperfusion or nonperfusion of the vessels in the optic nerve head, leading to optic disc edema.[1] It is the most common type of ischemic optic neuropathies, and causes unilateral painless permanent vision loss, especially in hypertensive patients over the age of 50.[2] Although etiopathogenesis of the NAION is not fully understood, nocturnal arterial hypotension in a vulnerable optic nerve head is an important risk factor.[1] Small optic disc, the absent or small cupping and relative crowding of the axons at the nerve head (disc-at-risk) are the most important known ocular risk factors.[3,4] The incidence of fellow eye was reported as 14.7 % in 5 years in Ischemic Optic Neuropathy Decompression Trial (IONDT).[5]

Despite numerous agents and procedures have been proposed for the treatment of NAION, there is no high-quality evidence to support any of these treatment regimens. Studies have failed to show significant functional advantages of topical brimonidine,[6] intravitreal injection of anti-vascular endothelial growth factors (VEGFs) and optic nerve decompression surgery.[7-11] Although there are few studies on neuroprotective agents (vincamine, granulocyte-colony stimulating factor (G-CSF), citicoline, RPh201, QPI-1007, etc.), none of them can provide enough evidence for clinical practice.[12-17] In the largest non-randomized study, the use of high-dose systemic corticosteroids has been shown to be significantly effective in terms of final visual functions.[18] Corticosteroids reduce capillary permeability and provide faster resolution of optic nerve head edema, and it has been reported that treating with steroids, especially in the acute phase (within 2 weeks)

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is effective in improving final visual acuity and visual field parameters. From this point of view, visual functions can improve more significantly with rapid resolution of optic disc edema if the treatment begins with pulse steroid treatment. Some animal studies in NAION support pulse steroid therapy and a few studies compared pulse steroid therapy with controls.[19-22] To the best of our knowledge, there is no previous study comparing pulse and oral steroid for the treatment of NAION. In this study, we aimed to compare oral and pulse corticosteroid treatments in terms of visual improvement in patients with acute NAION.

MATERIALS AND METHODS

This study follows the tenets of the Declaration of Helsinki and was approved by institutional Ethical Review Board(n: 2022/22). The data of 26 eyes of 25 NAION patients who were refered to our University Hospital Ophthalmology Department between April 2019 and July 2021 were reviewed, retrospectively. The criteria for the diagnosis of NAION were: (1) painless, sudden visual loss with a relative afferent pupillary defect and without other ocular, systemic, orbital or neurological diseases that may cause the visual symptoms of the patient; (2) optic disc edema at the time of presentation; (3) visual field anomalies compatible with optic neuropathy; (4) optic atrophy following resolution of optic disc edema.

Exclusion criteria for the study were: (1) Any ocular (glaucoma etc.), neurologic, or systemic disease that could affect visual field test and visual acuity; (2) elevated erythrocyte sedimentation rate and serum C-reactive protein clinically compatible with arteritic anterior ischemic optic neuropathy; (3) a history of previous ocular surgery other than uneventful cataract surgery; (4) any previous treatment history for NAION; (5) a follow-up period of less than 3 months.

All cases underwent detailed ophthalmologic evaluation including: best-corrected visual acuity (BCVA) with Snellen chart, color vision test with Ishihara pseudoisochromatic plates, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement, stereoscopic indirect ophthalmoscopy, Humphrey 30-2 automated visual field test (Carl Zeiss Meditec Inc, Dublin, CA, USA). Systemic diseases and drug use of the patients were also questioned.

Patients without any contraindications for the steroid treatment were divided into two groups. Group 1 (pulse steroid group, 14 patients) was given intravenous pulse 1 gr methylprednisolone per day for 3 days, followed by 1mg/kg/day oral prednisolone for 11 days. It was gradually discontinued by decreasing 10mg every 5 days until it reached 60mg/day, and then 5mg every 5 days. In group 2 (oral steroid group, 11 patients), 80 mg/day oral steroid treatment was started for the first 2 weeks, 70 mg/day for the next 5 days, 60 mg/kg for the next 5 days, then gradually decreasing by 5 mg every 5 days. The two groups were compared in terms of age, gender, duration of complaints, presence of systemic disease, initial and final BCVA, mean deviation (MD). A subgroup analysis was performed based on initial BCVA. Visual acuity outcomes of pulse and oral steroid therapies were compared seperately in eyes with initial BCVA ≤0.1 and and those with initial BCVA >0.1. All patients were informed about the treatment, and a diet restricted from sugar and salt was recommended.

Statistical analyses were carried out with using SPSS software, version 25.0 (SPPS Inc.,Chicago, IL, USA). Quantitative data were expressed as mean and standard deviation or median and range, as appropriate. Student's t-test, Mann Whitney U test and X^2 test were applied. A P value less than 0.05 was taken as statistically significant.

RESULTS

The comparison of demographic and clinical data of the patients in two treatment groups is given in Table 1. A patient in group 1 had bilateral NAION, sequentially. There was no statistically difference between group 1 and group 2 in terms of age, gender, hypertension, diabetes mellitus, duration of complaints and erythrocyte sedimentation rate and C-reactive protein levels ($p<0.05$). Although some patients have high erythrocyte sedimentation rate and C-reactive protein levels, the clinical findings were compatible with NAION. No significant side effects due to the treatment was observed in any of the patients. As expected, initial and final BCVAs improved significantly in both treatment groups ($p_1= 0.011$, $p_2= 0.028$). There was no difference in visual acuity gain and initial and final MD between the groups ($p_1=0.494$,$p_2=0,700$ and $p_3=0.747$) (Figure 1). BCVA increased in 73.3%(n=11) of the eyes in group 1 and 54.5%(n=6) in group 2 (p=0.659). The mean initial color visions were 3.00±3.18 and 5.00±3.29 plates and the mean final color visions were 5.33±4.25 and 7.00±3.55 plates correct out of 12 in group 1 and 2, respectively ($p_1=0.132$, $p_2=0.301$).

Of 12 eyes with an initial visual acuity of ≤0.1, 7 had pulsed and 5 had oral steroid therapy. The median of final BCVA of those who were administered pulse steroid was 0.1 (0.008-1.0), and the median of final BCVA of those

Table 1: *Demographic and Clinical Data of Patients in two groups.*

Parameter	Group 1	Group 2	P Value
Age (yrs), mean±SD[a]	60.3±10.2	61.7±12.4	*0.746*
Gender (M/F)[b]	5:9	3:8	*0.741*
HT[c] (n,%)	6(42.8%)	3 (27.3%)	*0.500*
Diabetes (n,%)	6 (42.8%)	4 (36.4%)	*0.599*
Erythrocyte sedimentation rate (sc), median(min-max)	24 (11-49)	17 (7-68)	*0.080*
CRP[d] (mg/L), median(min-max)	3.3 (3.0-15.0)	3.1 (1.7-17.0)	*0.370*
Duration of complaints (days), median(min-max)	7 (1-30)	7 (1-60)	*0.919*
İnitial VA[e], median(min-max)	0.150 (0.008-0.800)	0.300 (0.040-1.000)	*0.281*
Final VA[e], median(min-max)	0.400 (0.008-1.000)	0.500 (0.020-1.000)	*0.721*
Follow-up time (month), median(min-max)	4 (4-26)	4 (4-8)	*0.574*
İnitial MD[f], mean±SD	-12.00 ± 6.01	-14.59 ± 9.75	*0.700*
Final MD[f], mean±SD	-20.79 ± 12.15	-14.70 ± 6.50	*0.747*

[a]:Standard deviation, [b]:Male/female, [c]:Hypertension, [d]:C-reactive protein, [e]:Visual acuity, [f]:Mean deviation.

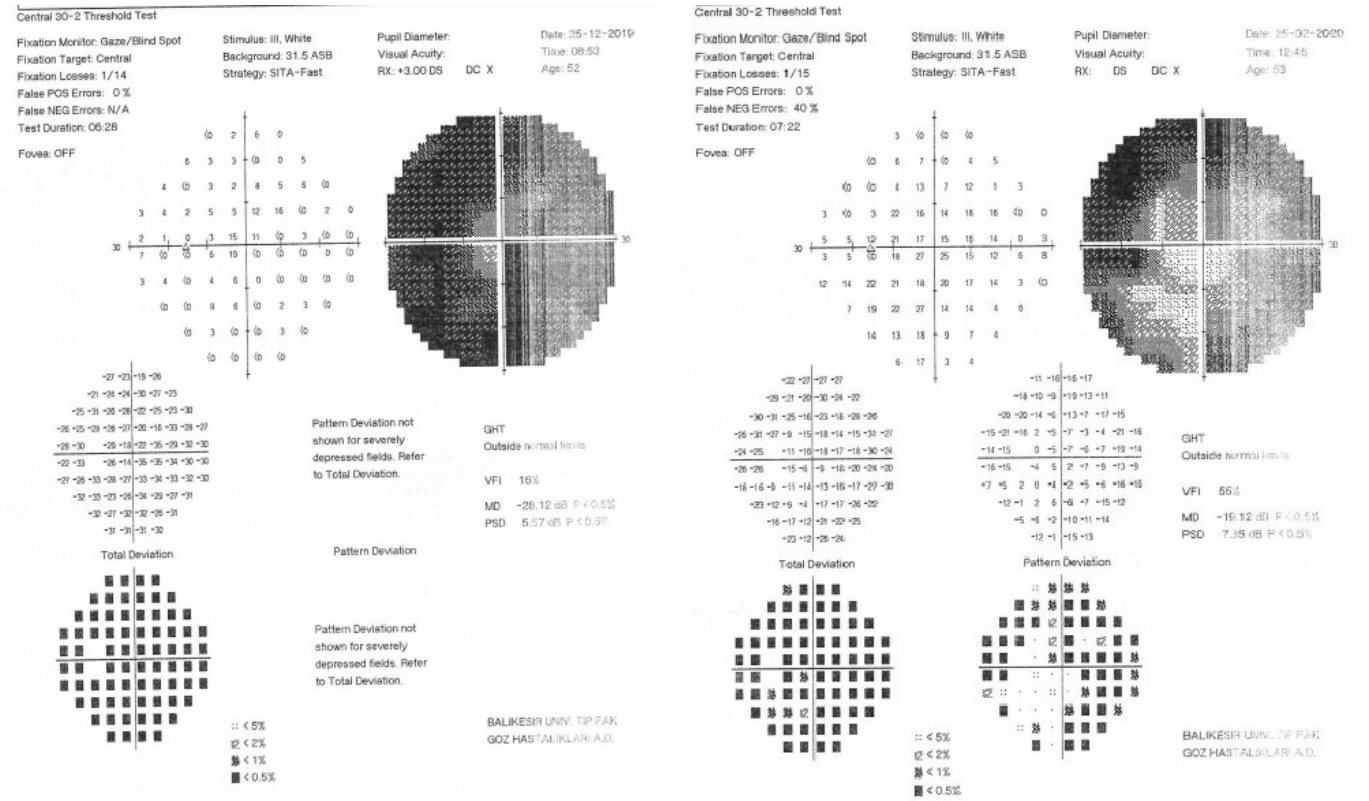

Figure 1: *Examples of pre-(a) and post-treatment(b) visual fields of a patient with NAION in group 2.*

who were administered oral steroid was 0.2 (0.02-0.8) (p=1.00). Compared to baseline, the median of the visual gain was 0.084 (0.0-0.9) in eyes received pulse steroid and 0.1 ((-0.02)-0.75) in eyes treated with oral steroids (p=0.530). Pulse steroid treatment was administered in 8 of 14 eyes with a baseline BCVA of >0.1, and oral steroid treatment was administered in 6 eyes. The median of final BCVA was 0.65 (0.15-1.00) in those who were given pulse steroid and 0.8 (0.4-1.00) in those who were given oral steroid (p=0.282). The median of visual gain from baseline was 0.175 ((-.0.10)-0.60) in pulse steroid treated and 0.05 (0.0-0.50) in oral steroid treated eyes. (p=0.852) (Table 2).

DISCUSSION

The use of steroids in the treatment of NAION was first discussed in the 1960s. Then, the case-control studies of Foulds and Hayreh, in 1970 and 1974, respectively, supported oral steroid therapy due to significant visual

Table 2: *Comparision of visual outcomes of pulse and oral steroids in eyes with BCVA ≤0,1 and with >0.1*

Parameter	Initial BCVA ≤0.1			Initial BCVA >0.1		
	Group 1	Group 2	P Value	Group 1	Group 2	P Value
Number	7	5		8	6	
Initial BCVA[a], median (min-max)	0.016 (0.008-1.0)	0.1 (0.04-0.1)	0.048	0.4 (0.15-0.8)	0.5 (0.3-1.0)	0.345
Final BCVA[a], median (min-max)	0.1 (0.008-1.0)	0.2 (0.02-0.8)	1.0	0.65 (0.15-1.0)	0.8 (0.4-1.0)	0.282
Visual gain	0.084 (0.0-0.9)	0.1 ((-0.02)-0.75)	0.530	0.175 ((-0.1)-0.6)	0.05 (0.0-0.5	0.852

[a]: Best corrected visual acuity

improvement in steroid group compared to non-steroid group.[23,24] In the largest study to date by Hayreh and Zimmerman, published in 2008, comparing 312 NAION patients who were treated with steroids within the 2 weeks of symptoms onset, and 301 patients who did not receive, steroids were found to provide significantly more improvement in visual functions than the non-steroid group.[18] Also optic disc swelling resolved more quickly in the steroid-treated group. Involving a large number of patients was the most important feature of this study. However, there were some limitations. The lack of randomization and blindness in patient selection for treatment can lead to biases. The fact that systemic diseases were more common, as hypertension which is the one of the most important systemic risk factor for NAION, was statistically significantly higher and also consisting of older patients in the control group were the important limitations of this study.

The effect of corticosteroid treatment in acute NAION is thought to occur by reducing capillary permeability and fluid leakage.[18] The faster decrease in the compression of the capilleries by reduction of edema, the more hipoxic nerve fibers can be refunctionalized by increased blood flow. Also in experimental animal studies, it is stated that steroids given especially in the acute period can reduce inflammation by decreasing the expression of proinflammatory stokins and prevent the death of retinal ganglion cells.[19,20] However, a study with a small number of patients claiming that steroid therapy was ineffective,[25] a meta-analysis also pointed out that steroids have no beneficial effect in visual outcome in NAION.[26] Multiple drug administration methods (intravitreal, oral, or intravenous) and failure to evaluate the visual field parameters were important limitations of this meta-analysis. Besides, optic nerve head perfusion may be further impaired due to short or long-term increase in intraocular pressure with intravitreal steroid applications.

Due to the conflicting results in the literature, it is not possible to argue that steroids are definitely beneficial in NAION patients. However, it should be noted that oral use had been preferred as the systemic steroid administration route in all studies in the literature. As it is known, the goal of steroid use in NAION disease is to reduce the pressure on the nerve fiber quickly by reducing the edema in the optic disc, and thus to ensure less nerve fiber loss in the long term. From this point of view, achieving a faster edema resolution with pulse steroid therapy than with oral steroid therapy may result in less nerve fiber loss. To our knowledge, there is no study comparing pulse and oral steroid therapies in the treatment of NAION and we hypothesized that resolution in optic disc edema can occur faster with pulse steroid therapy and with more retinal ganglion cell survival, the more visual gain can be provided. Although the MD in visual fields of the patients, especially in group 1, was worse after the treatment and the visual aquities of the two groups increased, our study did not reveal any statistically significant difference in terms of visual acuity or visual field improvement between oral and pulse steroid therapies. In our opinion, the worse MD values of the visual fields of the patients in group 1 may be related to the higher initial visual loss. We also evaluated the response of patients with low initial BCVA of ≤0.1 to pulse and oral therapy. There was no significant difference between eyes trated with pulse and oral steroids. Similarly, no difference in visual gain was observed between pulse and oral steroid therapy in patients with initial BCVA above 0.1. Any severe steroid-related side effects were not encountered in both patient groups. Nevertheless, since they are equal in efficacy, oral steroid therapy may be considered more appropriate at this stage, given that pulse

steroid therapy may cause more side effects related to high dosage.[27,28]

There were some limitations in this study. The first limitation is the small number of patients in both groups. This is due to the fact that some of the patients were lost in follow up or the data were recorded insufficiently for the study. No randomization was performed due to the retropective design of the study and the absence of a control group is among the limitations of the study. In addition, the begining time of the treatment was variable due to the different application times. Pre- and post-treatment retinal nerve fiber layer thicknesses could also be compared. However, they were not evaluated in this study, since reliable measurements could not be obtained due to fixation difficulties in patients.

CONCLUSION

Any difference in visual acuity gain or visual field improvement between pulse and oral steroid treatment in NAION was not detected in the current study. Randomised and prospective studies with larger number of patients must be conducted for better evaluations.

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