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THE IMPORTANCE OF CORTICOSTEROID THERAPY IN TREATMENT OF ACUTE ANTERIOR ISCHEMIC OPTIC NEUROPATHY

Saša Novak, Dragan Veselinović

Ophthalmology Clinic, Clinical Center, Niš, Serbia and Montenegro

Summary. *Anterior ischemic optic neuropathy is an acute ischemic disease of vascular origin whose treatment demands urgent application of an appropriate therapy.*
The research included 56 patients with an acute form of anterior ischemic optic neuropathy with 50 of them classified as idiopathic types while 6 had the arteritic form of the disease.
In this paper, we analyze the therapeutic significance and the effect of general corticosteroid therapy, with initial therapeutic doses of 120 mg of prednizolon.
Based on the changes in the visual acuity and visual field of the eyes affected by this disease, we determined a significant improvement in patients with with the idiopathic form of the disease who had undergone a timely cortico therapy, compared to those patients who had not ($p<0.01$). Apart from the application of cortico therapy, the time of initiation of the therapy, as well as the degree of ischemia of the affected part of optic nerve, were also significant factors of visual acuity recovery.
In nine cases of eyes with the arteritic form of the disease, a satisfactory improvement of vision was not achieved, regardless of the application of general corticosteroid therapy ($p>0.05$)
This paper discusses possible mechanisms of the beneficial effects of general corticosteroid therapy and the importance of an early therapeutic action and possible prevention of the disease of the other eye.

Key words: *Anterior ischemic optic neuropathy (AINO), corticosteroid therapy*

Background

Anterior ischemic optic neuropathy (AINO) represents a distinct clinical entity, caused by ischemic lesions in the anterior part of the optic nerve (1,2,3). The basis of pathogenesis of this disease can be found in the pronounced decline of perfusion pressure at the level of short ciliary arteries, which are of great importance for the vascularization of anterior parts of optic nerve (1,4,5).

On the basis of the extensive experiences of the authors who dealt with etiology of this disease it is divided into the idiopathic form, caused by systemic vascular diseases (hypertension, diabetes, arteriosclerosis etc.) and the arteritic form, caused by arteritis temporalis (2,5).

There is a large number of often-controversial opinions on the success and need of an urgent therapy for these patients. The opinion that this disease is untreatable and that no therapy has any effect, so that both ophthalmologist and patient must come to terms with that fact, is now mostly a thing of the past, although it still persists in some communities (2,6,7).

While in patients with the idiopathic form of the disease one can expect a significant improvement in visual acuity, in proportion to the degree of ischemic lesions and timely initiation of therapy, in case of the arteritic form, corticosteroid therapy usually does not have a great significance in the treatment of the affected eye, but can contribute to the prevention of the diseases on the other eye (8).

This paper analyzes the results of the treatment of anterior ischemic optic neuropathy patients with the application of the systemic corticosteroid therapy attempting to find, along with the interpretation of pathogenesis of the optical nerve ischemic damage, the explanation of the mechanism of its beneficial effect.

Materials and methods

We thoroughly examined 56 patients with acute anterior ischemic optic neuropathy. 50 of them were classified as idiopathic types, while 6 had arteritic form of the disease. The diagnosis of arteritis temporalis was made based on the clinical picture of the disease and the high values of the sedimentation, and in two cases there was biopsy of temporal artery.

In all the patients we performed a detailed ophthalmological examination, (visual acuity, ophthalmoscopic examination, Golgmsn's perimeter fluorescein angiography, visual evoked potentials and electroretinogram, color sight) and based on it, we made the diagnosis of anterior ischemic optic neuropathy.

Out of 56 eyes with idiopathic form of the disease we employed the general corticosteroid therapy with

Table 1. Age structure of AION patients

Disease form	50-55	(years)	56-60	(years)	61-65	(years)	66-67	(years)	71-75	(years)	76-80	(years)
	N	%	N	%	N	%	N	%	N	%	N	%
Idiopathic form	2	3.6	24	42.8	16	28.6	6	10.7	–	–	2	3.6
Arteric form					1	1.8	1	1.8	2	3.6	2	3.6
Total	2	3.6	24	42.8	17	30.4	7	12.5	2	3.6	4	7.2

initial doses of 120 mg of methylprednizolon in 29 cases. Other 27 eyes were treated without application of general corticosteroid therapy, mostly because of contraindications (diabetes, gastric diseases). All the patients received antiagregation and polyvitamin therapy at the same. The therapeutic effect of the application of general corticosteroid therapy was analyzed through changes in visual acuity and the research of visual fields in the beginning and at the end of the treatment. To determine the statistical significance of the results obtained in the group of patients subjected to corticosteroid therapy and in the group without this therapy, we used Chi-squared test.

Results

In our series of 56 subjects, the age ranged from 51 to 80 with average age structure of 68 years. The average age of the patients with idiopathic form of the disease was 60.13 years with the greatest number of subject between 56 and 65 years. Patients from the group of arteritic type of AION were averagely older (72.4 years) (Table 1).

In this series of 56 patients, there were 36 males and 20 females (Table 2).

Table 2. Sex structure of AION patients

AION type	N	Male		Female	
		N	%	N	%
Idiopathic form	50	34	68	16	32
Arteric type	6	2	33.3	4	66.7
Total	56	36	64.3	20	35.7

Visual acuity at the time of admission ranged from amaurosis to normal acuity. The next table shows visual acuity of the patients with idiopathic type of the disease at the beginning and at the end of the treatment (Table 3).

Table 3. Visual acuity before and after treatment in eyes with idiopathic AION type

Vizus	Before treatment		After treatment	
	N	%	N'	%
Amaurosis	3	5.3	3	5.3
Finger count	4	7.1	3	5.3
1/60 - 3/60	9	16.1	11	19.6
4/60 - 0.10	10	17.8	12	21.4
0.20 - 0.30	11	19.6	3	5.3
0.40 - 0.50	8	14.3	8	14.3
0.60 - 0.70	5	8.9	7	12.5
0.80 - 1.0	6	10.7	9	16.1

The previous table shows that the greatest number of patients from idiopathic AION type had visual acuity from 4/60 to 0.50. At the end of the treatment, in 11 (19.6%) of eyes, visual acuity remained unchanged, in 25 (44.6%) there was an improvement in visual acuity, and in 20 (35.7%) there was a reduction in visual acuity in spite of applied therapy.

Table 1 shows the influence of general corticosteroid therapy on changes in eyesight acuteness in eyes with the idiopathic form of the disease.

Table 4. Influence of general cortico therapy on changes in visual acuity in eyes with idiopathic form of AINO

Visual acuity	Therapy				χ^2
	without urbazon		with urbazon		
	N	%	N	%	
Unchanged	7	12.5	4	7.2	p>0.05
Improved	7	12.5	18	32.1	p<0.01
Deteriorated	13	23.2	7	12.5	p>0.05
Total	27	48.2	29	51.8	

It is evident that in the group where general cortico therapy had been applied there was a significantly higher number of eyes showing improvement in visual acuity 18 (32.1%), compared to the group without this therapy 7 (12.5%). This difference in the number of eyes with improved visual acuity has a great statistical significance ($p<0.01$). The number of eyes which demonstrated deterioration of visual acuity was higher in the group which was not treated with systemic corticotherapy, but compared to the other group the difference was not statistically significant ($p>0.05$).

We examined visual field in all patients, at least twice during the hospitalization and also later during the follow-up. In seven eyes with severe reduction of visual acuity check has not been performed. The characteristics of visual field in patients with idiopathic form of the disease are shown in the next table.

Table 5. Changes in visual field in patients with AION

Change characteristics	N	%
Concentrated narrowing of visual field > 30	14	28.6
Lower altitudinal hemianopsia	15	30.6
Visual isle	5	10.2
Visual field segment defects	3	6.1
Concentric narrowing < 30	12	24.5

Since one of the parameters for following the changes caused by therapy was the analysis of visual field changes, especially in patients with greater reduction of visual acuity, the following table shows these results.

Table 6. Influence of general cortico therapy on changes in visual field in eyes with idiopathic form of AINO

Visual field	Therapy				χ^2
	without urbazon		with urbazon		
	N	%	N	%	
Improved	8	16.3	20	40.9	p<0.01
Deteriorated	13	26.5	8	16.3	p>0.05
Total	21	42.8	28	57.2	

We analyzed 49 visual fields in patients with idiopathic form of the disease and noticed improvement in 28 eyes (57.2%) while deterioration was observed in 21 cases (42.8%). In seven cases, due to severely reduced or absent visual acuity, it was not possible to determine the visual field.

As in the previous analysis we received a statistically significant difference in improved visual fields, compared to the group without cortico therapy (p<0.01). Visual field deterioration was most commonly observed in patients who were not subjected to systemic corticosteroid therapy, but this difference, compared to the other group of patients, was not statistically confirmed (p.0.05).

Previous analyses did not include 6 patients (9 eyes), with arteritic form of the disease, most of all because their small number did not allow statistical analysis**.** In two eyes with arteritic type of AION, the visual acuity was amaurosis, while for one eye it was waving one hand in front of the eye, while four eyes had visual acuity of 1/60 to 0.10. At the admission, two eyes had visual acuity of 0.4-0.5. At the end of the treatment visual acuity was improved in 2 eyes, it worsened in 5 while it remained unchanged in 2 cases.

All the patients from this group received general corticosteroid therapy with initial doses of 120 mg of prednizolon (Table 7).

Table 7. Influence of general cortico therapy on changes in visual acuity in eyes with arteritic form of AINO with use of general corticosteroid therapy

Visual acuity	N	%
Unchanged	2	22.2
Improved	2	22.2
Deteriorated	5	55.6
Total	9	100.0

Six patients and 9 eyes from this group were too small a number for statistical processing because two of the patients were not followed up after the hospitalization, so definitive state of their visual acuity remained unknown.

All the patients from this group received general corticotherapy with initial pronizon doses of 120 mg with complete additional therapy received by other patients with idiopathic form of the disease. In spite of the therapy 5 eyes demonstrated vision deterioration, two cases demonstrated improvement while two cases remained unchanged.

Discussion and conclusions

The issue of successful therapy of anterior ischemic optical neuropathy is very complex and in this paper we tried to point out the significance of pharmacotherapeutic action of the systemic corticosteroid therapy as one of the main therapeutic techniques applied for this disease.

Our results show that in the group with idiopathic form of the disease there was a statistically significant improvement of visual acuity and the visual field in patients with the idiopathic form of the disease, treated with initial prednizolon doses of 120 mg. A statistical analysis lead us to the conclusion that the general corticosteroid therapy in patients with anterior ischemic optical neuropathy has a significant effect for the improvement of vision. Most of the authors dealing with problem of therapy for idiopathic form of AINO reached the same conclusions (2,7,9,10,15).

Earling et Al. (11) in retrospective study of 40 eyes affected by idiopathic form of AINO concluded that corticosteroids given in adequate doses during the initial phase of the disease have a favorable therapeutic effect in a significant number of patients. Hayreh.S. (3) in the study of 115 eyes registered visual acuity or field of vision improvement in 77.6% of eyes treated by corticosteroids while this improvement in the group without corticosteroids was only 36.4%.

Bastiansen (7) suggests that AINO therapy must begin with high doses of corticosteroids regardless whether it is the case of idiopathic of arteritic form of the disease. Ilić and Milenkivić (6) do not achieve visual acuity improvement in a single case out of 15 patients with AINO observed reduction of visual acuity (below 0.1) in spite of intensive therapy. Unfavorable experience in therapy of AINO with systemic corticosteroids was also recorded by Boghner and Gaser (1). According to retrospective study of 37 patients of non-arteritic type they concluded that corticosteroids are not important for the therapy.

The latest experiences point to the efficiency of systemic steroid therapy with explanation that the cases of therapy failure are usually the cases of untimely application of the therapy or the cases of great decline of visual acuity caused by severe ischemia (9,10,13,14). Most authors believe that their beneficial therapeutic effect is based on edema reduction, which is the reason why for a long time now, they are used by neurologists in cerebral edema and cerebral apoplexy cases (13,16). It is known that corticosteroids influence the stabilization of cellular and liposome membranes thereby enabling their protective role at endothelia capillary level (13). At the same time, corticosteroids take part in stabilization of ionic pump, mitochondria stabilization and prevention of autolytic processes in axon cell, which mostly manifests as anti-edematous effect. One other important characteristic of corticosteroids is the inhibition of thrombocyte aggregation, inhibition of chaotic thrombocyte activation and protection of prostaglandin metabolism.

In recent years, much more has been learnt about steroid action during the inflammation process. Now we know that corticosteroids perform their anti-inflammatory action by means of inhibition of Phospholipase A2, which is necessary for arachidonic acids, which are very important in inflammation reaction chain (17,20). In this way, corticosteroids inhibit the creation of important inflammation mediators, prostaglandin, leukotriene, and thromboxane. Activation of inhibitory protein (macrocortin, limodulin and renocortin) with the help of steroids, enables their effect on phospholipase A2, thereby stopping inflammatory reaction.

With knowledge of all these effects of corticosteroids we can explain their beneficial effects in cases of ischemic edema in ischemic axon damage of optic nerve which occurs in anterior ischemic optic neuropathy.

The aforementioned possible effects of corticosteroids can account for their favorable effect in the treatment of the ischemic damage which occurs in anterior ischemic optic neuropathy. The fact that in the area of ischemic edema, the action of vasodilators is not possible, regardless of their possible effect on arteriosclerotic blood vessels, suggests that, in the acute phase, corticoptherapy is the treatment of choice, because the reduction of ischemic edema and the reduction of inflammatory reaction achieve multiple effects. In recent years, it ha been suggested that there is a need for a simultaneous thrombolytic therapy (heparin, streptokinase), which produces, along with high doses of corticosteroids, even more favorable therapeutic results (9,14,17).

It is known that in the state of neural axon ischemia there is disturbance of axoplasmatic transport, and necrosis occurs in a pronounced degree of ischemia which irreversibly damages the affected axons (18). Axons which are damaged to apoptosis degree, unfortunately, will not respond to any therapeutic treatment. But, since we have adopted the opinion that ischemia is not "all or nothing" process and that even in massive ischemias some axons remain preserved and pass through various phases which are still reversible, we can expect favorable therapeutic effects, of corticosteroids exactly in these parts of optic nerve (19). In cases of mild ischemias, when the patient reported only a couple of days since the beginning of the disease, corticosteroids can achieve a very favorable effects leading to vision recovery. In cases of severe ischemia, the possibilities for favorable effects of the therapy are smaller, but they can manifest as minimal improvement of visual acuity and expansion of visual field, which also has a favorable therapeutic effect, especially in the binocular form of anterior ischemic optic neuropathy

The application of corticosteroid therapy in cases anterior ischemic optic neuropathy caused by arteritis temporalis is of great importance and achieves its beneficial effects by means of special biochemical mechanisms. Since this disease is classified into group of autoimmune disorders, immunodepressive action of steroids, with already described anti-edematous and anti-inflammatory effects, has a special significance and justification. The inhibition of T and B lymphocyte migration, blockade of interaction between lymphocyte and macrophages, reduction of IgG globulin concentration and other action mechanisms in immunological system, give corticosteroid therapy a significant place in the treatment of anterior ischemic optic neuropathy caused by arteritis temporalis.

Unfortunately, the experiences of most of the authors who dealt with treatment of AINO caused by arteritis temporalis are unfavorable and cases of great loss of visual acuity are much more common, even with amaurosis without eyesight recovery (3,5). Taking into account the frequency of binocular cases of this disease it is clear that there are numerous cases of binocular eyesight loss, therapy causing permanent infirmity. In our group of six patients, there were three cases of binocular disease, and in the follow-up period of one year there were not any occurrences of the disease on the other eye. In cases of unilateral disease, very often, the diseases manifests on the other eye within several weeks or months (5). There is an opinion, that for this group of patients, corticosteroid therapy has a much greater significance for the prevention of the disease on the other eye. For these patients, it is recommended that they should undergo a prolonged corticosteroid therapy, up to one year, both in order to treat the acute disease and to prevent the disease of the other eye. If the disease does not occur in the other eye within four to five month this is a very favorable prognostic sign (2,8).

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ZNAČAJ PRIMENE KORTIKOSTEROIDNE TERAPIJE U LEČENJU AKUTNE PREDNJE ISHEMIČNE NEUROPATIJE VIDNOG ŽIVCA

Saša Novak, Dragan Veselinović

Klinika za očne bolesti, Klinički centar, Niš

Kratak sadržaj: *Prednja ishemična neuropatija vidnog živca je akutno ishemično oboljenje vaskularne geneze, čije lečenje zahteva urgentnu primenu odgovarajuće terapije.*
Ispitivanjem je obuhvaćeno 56 pacijenata sa akutnom formom prednje ishemične neuropatije vidnog živca, od kojih je 50 svrstano u grupu idiopatskog tipa oboljenja, dok je 6 pripadalo arteritičnoj formi bolesti.
U radu se analizira terapijski značaj i efekat opšte kortikosteroidne terapije, sa početnim terapijskim dozama od 120 mg. prednizolona.
Na osnovu promene u oštrini vida i u vidnom polju očiju zahvaćenih oboljenjem, ustanovljeno je signifikantno poboljšanje kod onih pacijenata sa idiopatskom formom oboljenja kod kojih je srovedena pravovremena kortiko terapija, u odnosu na one kod kojih ona nije primenjena ($p<0,01$). Pored primene kortiko terapije značaj u oporavku oštrine vida imalo je i vreme započete terapije, kao i stepen ishemije zahvaćenog dela vidnog živca.
U devet očiju sa arteritičnom formom oboljenja nisu postignuta zadovoljavajuća poboljšanja vidne funkcije, bez obzira na primenu opšte kortikosteroidne terapije ($p>0,05$).
U radu se diskutuje o mogućim mehanizmima povoljnog delovanja opšte kortikosteroidne terapije, o značaju ranog terapijskog delovanja i mogućoj prevenciji drugog oka.

Ključne reči: *Prednje ishemična neuropatija optikusa (PINO), terapija, kortikosteroidi*