

Anterior ischaemic optic neuropathy

III. Treatment, prophylaxis, and differential diagnosis

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Anterior ischaemic optic neuropathy (AION) is a serious blinding disease, with poor prognosis for the recovery of vision and a high probability that the second eye will be involved. Since we have only recently begun to understand its pathogenesis (Hayreh, 1974a,b) and most of the therapies tried so far (reviewed by Hayreh, 1974b) have made no significant difference to their visual loss, such patients are generally given up as hopeless. The main therapeutic controversy lies in the management of the non-arteritic type of AION since patients with temporal arteritis AION are invariably treated with systemic corticosteroids, primarily to prevent the involvement of the second eye. In the management of the non-arteritic type of AION, many therapies have been tried, *e.g.* anticoagulants (Lasco, 1961; Sarau and Murat, 1967), systemic corticosteroids (Foulds, 1968, 1969), subtenon vasodilators (François, Verriest, Neetens, De Rouck, and Hanssens, 1962; Calmettes, Déodati, and Béchac, 1963; Bonamour, 1966; Sarau and Murat, 1967), subtenon steroids (Bonamour, 1966; Sanders, 1971), subtenon atropine sulphate 1 per cent. (Cordes, 1937), and recently diphenylhydantoin (Burde, 1973). However, most ophthalmologists do not treat patients with the non-arteritic type of AION or try to find a treatable associated systemic or ocular disorder, *e.g.* hypertension, diabetes, anaemias, glaucoma, etc. (Hayreh, 1974a,b), but discard them with philosophical advice to accept the visual loss as a natural calamity.

In the present study, attempts were made to evaluate systemic corticosteroid therapy in AION. When patients were treated early, while they still had oedema of the optic disc, with large doses, there was visual improvement in a significant number of cases; almost all of these patients had AION due to causes other than temporal arteritis. Since the non-arteritic type of AION forms a much larger group than temporal arteritis AION, this is an important ray of hope in the gloomy picture of AION. Lowering the intraocular pressure, particularly by Diamox, has also been found to be helpful.

Material and methods

This study comprises two categories of patients:

(A) 25 patients with complete or partial AION were studied. All had a detailed initial ophthalmic examination, and the erythrocyte sedimentation rate (ESR) was estimated by the Westergren method as an emergency. If the ESR was higher than 20 mm./1st hour, a temporal artery biopsy was performed to look for evidence of temporal arteritis. A routine haematological and systemic examination was made. Stereoscopic colour photography and intravenous fluorescein angiography of the optic disc were carried out at the first attendance, or as soon as possible, in all eyes.

Systemic prednisolone 40–80 mg. daily, frequently with an initial dose of 40 units ACTH intramuscularly, was given to nineteen patients, and none to six patients. Six patients with progressive deterioration of the visual acuity or fields at a later date were given long-acting Diamox (500 mg. twice daily).

All patients were reviewed, for the first few days as inpatients and thereafter as outpatients, at variable intervals. Changes in visual acuity, visual fields (when possible), and fundus were recorded at follow-up visits, the ESR was estimated in temporal arteritis cases, and the therapy was regulated. The follow-up period in these patients varied from 3 months to 3 years, the majority being between 1 and 2½ years (mean 15 ± 9 months).

(B) Since the evaluation of these 25 cases, I have started to treat all my cases of non-arteritic AION with systemic corticosteroids, as long as oedema of the optic disc is present, giving an initial daily dose of 60–80 mg. and tapering off very gradually; 22 such patients fall into this category and have all undergone the above-mentioned investigations and follow-up studies.

Observations and discussion

In the present series the following treatments were given:

(1) *Systemic corticosteroid therapy*

To assess the efficacy of this treatment, all patients with AION in the present series were divided into three groups (Table).

GROUP I 11 patients with temporal arteritis, confirmed by temporal artery biopsy, who were given steroid therapy;

GROUP II 8 patients with no evidence of temporal arteritis who received steroid therapy;

GROUP III 6 patients with no evidence of temporal arteritis who were not given any steroid therapy.

Table *Systemic corticosteroid therapy and final outcome of vision in patients with anterior ischaemic optic neuropathy*

Group	Systemic corticosteroid therapy	No. of patients	Visual acuity (per cent.) during follow-up		
			No change	Improvement	Deterioration
I	With therapy and temporal arteritis	11	64	9	27
II	With therapy and no temporal arteritis	8	12.5	75	12.5
III	No therapy and no temporal arteritis	6	83	17	Nil

GROUP I

These patients were usually given 40–60 mg. prednisolone orally, frequently combined with an initial dose of 40 units ACTH. The dosage and duration of the therapy was guided by the ESR level, with a rapid reduction of the dose to begin with, because of a rapid fall in the ESR at this stage, and a very slow tapering-off later. Patients with temporal arteritis required a prolonged administration of steroids because a premature stoppage or sudden reduction sometimes produced visual symptoms in the normal eye with a rise in ESR.

Usually they required a maintenance dose of 5–10 mg. daily for many months if not years to safeguard the normal eye. The steroids were still being given up to their last follow-up in six cases with temporal arteritis for 6 to 14 months (29 months in one patient). If both eyes were blind and temporal arteritis was present, the steroids were stopped as soon as the ESR settled down.

GROUP II

This group was initially started on a regime similar to that in Group I, but steroids were given only for 2 to 3 months, except for two patients with bilateral AION and some vision retained, in whom this regime was continued for 6 to 12 months by the ophthalmologist in charge.

GROUP III

These patients were followed-up like those in Groups I and II but without any steroid therapy.

The results revealed by the Table are interesting. On comparing the outcome of visual acuity in the three groups, the best outcome was in Group II where 75 per cent. showed improvement as compared to only 17 per cent. in Group III. Groups II and III are comparable, with Group III as a control for Group II. The outcome in the eyes with AION due to temporal arteritis, *i.e.* Group I, was the worst. This study thus strongly suggests that systemic corticosteroids have a beneficial effect in patients with the non-arteritic type of AION, and confirms the results of Foulds (1968, 1969). This has been further confirmed by the 22 cases in Category (B), not included in the Table. Frequent accurate recording of the visual fields by Goldmann perimetry demonstrates a much more marked and constant improvement in the visual fields during treatment. In some cases of partial AION, the central vision may show no significant change either because a central scotoma produces low visual acuity even when the visual fields improve remarkably, or because the central visual acuity remains normal in spite of marked visual field defects. This study indicates that visual fields are a much better guide in assessing improvement of AION than the central visual acuity alone. If improvement in visual acuity and/or the visual field is used as a criterion of success, then the beneficial effect of steroid therapy in Group II is even greater than that shown in the Table. It is most unfortunate that these are the cases which are usually abandoned without any treatment by ophthalmologists. The following case report is given to illustrate the efficacy of corticosteroids in Group II type of patients.

A 46-year-old man, with unstable diabetes since 1938 and on insulin, was first seen on October 31, 1973, with a history that he woke up on September 15, 1973, to find that he "could not see from the inner half of the left eye" and had a central scotoma. His visual symptoms had shown no significant change since onset other than a questionable improvement 3 to 4 days before attending the hospital. Two weeks before attending this department, he had noticed deterioration of vision in the right eye which progressed to an inferior altitudinal field defect over the next 3 to 4 days and had not subsequently changed. The patient also reported that he had had a right lateral rectus palsy for about one month 4 to 5 years earlier. His right big toe had been amputated because of gangrene on July 10, 1973. He had also been taking thyroid for the last 3 to 4 years because of hypothyroidism. He had smoked 20 to 30 cigarettes daily since the age of 25.

Ocular examination

The visual acuity was counting fingers in both eyes, with sluggishly reacting semi-dilated pupils. Fundus examination revealed a mild degree of diabetic retinopathy in both eyes; the right optic disc showed generalized oedema, greatest in the superior temporal part and least in the inferior nasal

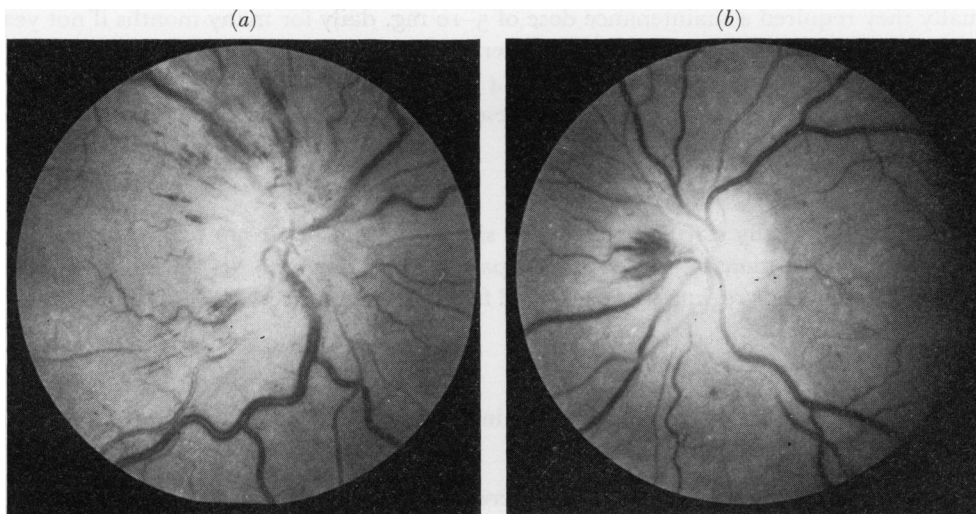
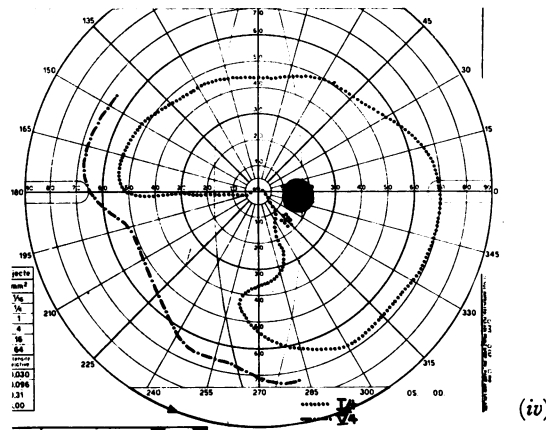
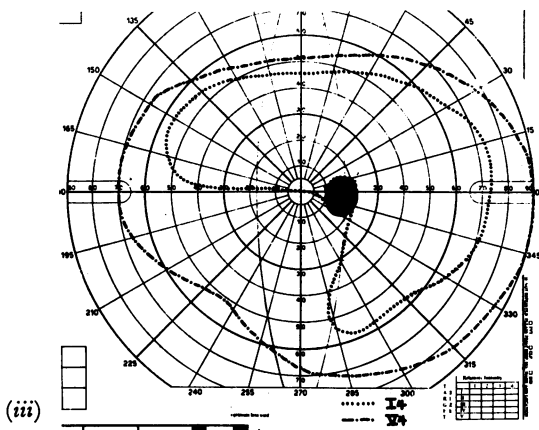
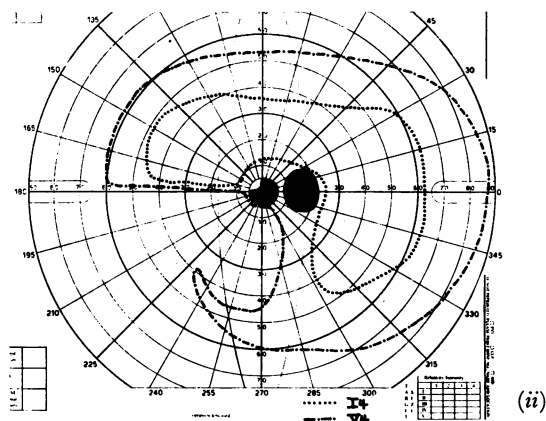
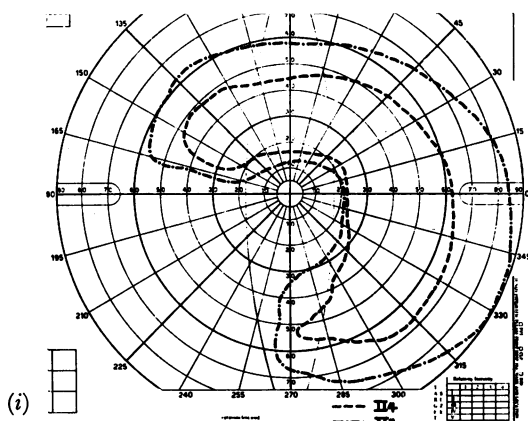


FIGURE (a, b) Fundus photographs of right and left eyes respectively on October 31, 1973.

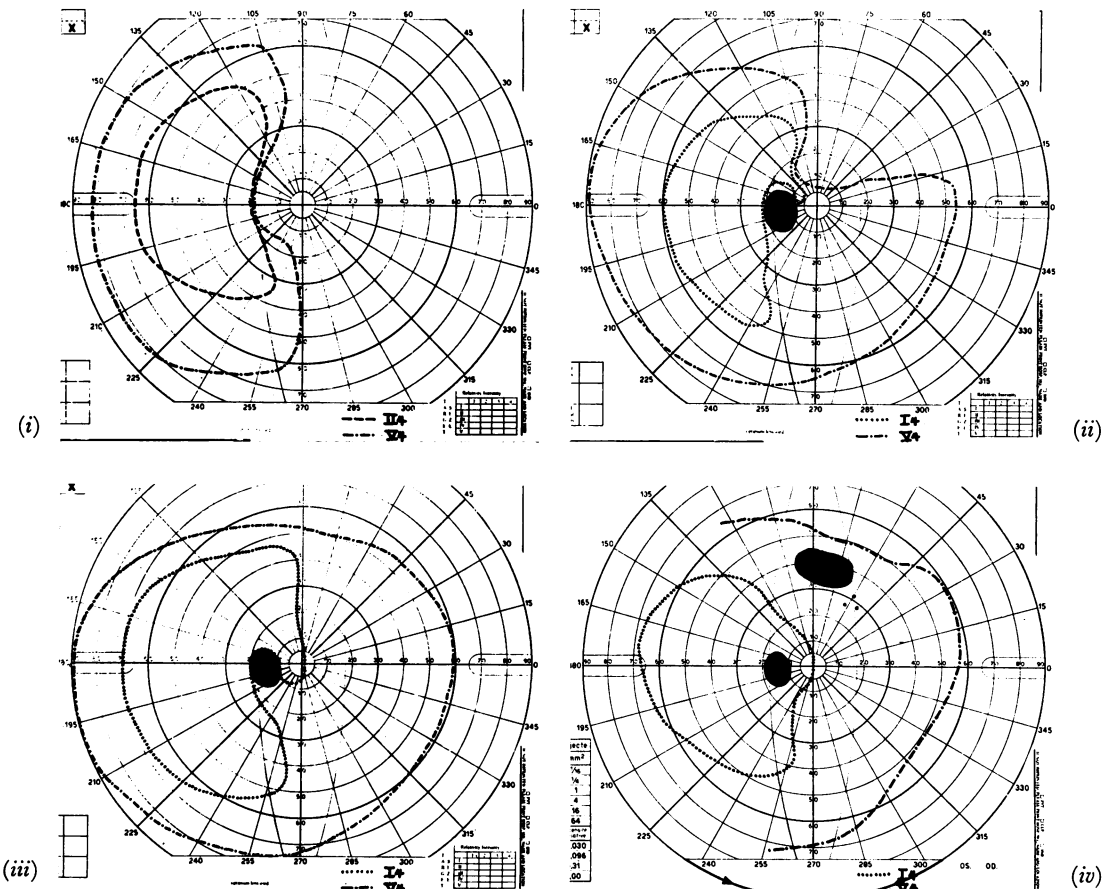


(c) Right visual fields Goldmann perimetry records on November 1, 7, and 26, 1973, and June 6, 1974

part (Fig. 1a). There were flame-shaped haemorrhages in the optic disc and peripapillary region—greatest in the superior temporal area. The disc was slightly hyperaemic, and there was no pallor. The left optic disc showed slight pallor in the temporal part, mild oedema, and one flame-shaped haemorrhage nasally (Fig. 1b). The visual fields showed nasal hemianopia with central scotoma in the left eye (typical of lateral posterior ciliary artery occlusion—Hayreh, 1970) (Fig. 1c) and an inferior nasal quadrantric field defect with central scotoma in the right (Fig. 1d). The patient was diagnosed as suffering from bilateral AION and was admitted to the hospital. In consultation with the diabetic department, he was given oral prednisone 15 mg. four times daily and long-acting Diamox 500 mg. twice daily on November 1, 1973.

Follow-up

On November 6, 1973 the visual acuity in both eyes was 6/120; this had improved to 6/30 left and 6/60 right by November 19. On November 26, both eyes individually could see better than 6/30, while the binocular vision was 6/21. When he was seen on January 14, 1974, the visual acuities were 6/18 and 6/24, with scotomas, in right and left eyes respectively. They did not improve any further. Changes in the visual fields are shown in Figs 1c and d, which demonstrate a very noticeable progressive improvement up to November 26, 1973, and have since been stationary. The improvement in the visual acuity, though considerable, was not as evident because of the presence of small central scotomata in both eyes.



(d): Left visual fields Goldmann perimetry records on November 1, 7, and 26, 1973, and June 6, 1974

Oedema of the optic disc in the right eye started to subside on November 6, and in the left eye no significant change in the disc was seen till November 19. On November 26, the right disc showed only a slight degree of oedema while the left disc showed none. No marked pallor was visible in either disc. On January 14, 1974, both discs were almost uniformly pale, with well-defined edges.

The patient was taking 60 mg. prednisone daily up to November 21 when the dose was decreased by 5 mg. daily to 30 mg. daily; he was discharged on November 26. The steroids were stopped on December 15, 1973, by gradually tapering off the dose.

During the administration of the corticosteroids, the diabetic department continuously supervised the patient's diabetes, but was unable to control it, as he was not at all co-operative, and, surprisingly, had frequent attacks of hypoglycaemia.

Comment

This case clearly illustrates the great usefulness of corticosteroids in improving visual loss in AION, it demonstrates the remarkable capacity of the optic nerve fibres to recover their function, for treatment was not started until 6 weeks after the onset of the ischaemic process in one eye (2 weeks in the other). Visual loss in ischaemia, therefore, should not be regarded as irreversible, and every possible effort must be made to resuscitate the nerve fibres. This case also points the twin morals that all visual problems in the diabetic should not be ascribed to diabetic retinopathy, and that diabetes is not necessarily a contraindication for steroid therapy.

(2) *Diamox*

The purpose of giving Diamox is to lower intraocular pressure to improve the perfusion pressure in the vessels of the optic nerve head, and to improve the imbalance between the intraocular pressure and perfusion pressure—the most important factor in the pathogenesis of AION (Hayreh, 1974a). In the present series Diamox was given to six patients in the form of long-acting Diamox 500 mg. twice daily. It was given mainly in cases with a progressive loss of vision or visual fields after the initial insult and damage to the optic nerve head. The pretreatment intraocular pressure in all of them was less than 20 mm.Hg on applanation tonometry. Further deterioration was prevented. Angiography in some of these patients showed a poor perfusion pressure in the posterior ciliary artery system even in the contralateral normal eye. Thus, intravenous fluorescein angiography can be of assistance in identifying the patients who could benefit from Diamox. This small trial has given some encouraging results with this therapy, which requires to be used in conjunction with systemic steroids during the initial stages of AION.

I would therefore recommend the following regime in patients with AION:

(i) Patients with AION due to temporal arteritis should be given systemic corticosteroids to safeguard the second eye; they should be given high doses, *e.g.* up to 80 mg. daily or even more, of prednisolone orally to begin with, the dose being regulated by the ESR level. In addition, they should be given Diamox to lower the intraocular pressure as much as possible, to help the perfusion of the blood vessels in the optic nerve head. The outcome in these cases is not good, but additional Diamox treatment is worth a trial for about 4 weeks from the onset of AION. The dosage of steroids is guided by the ESR level and should be continued till the ESR remains normal even on stopping the steroids and there are no symptoms.

(ii) In AION not due to temporal arteritis, systemic corticosteroids should be administered in an initial dose of 60–80 mg. daily, thereafter slowly tapered so that the treatment is continued for about 2 months, *i.e.* during the time when the disc shows oedema. Reduction of oedema by the steroids would relieve the pressure on the disc capillaries and restore some circulation in the vessels of the optic nerve head. At the same time the administration of

Diamox to lower the intraocular pressure as far as possible would help further perfusion of the vessels. In ischaemia of the optic nerve fibres, the function of the fibres may be impaired for some time before they undergo irreversible damage, just as a starving man, unable to do his work but still alive, can be restored to normal functional capacity with the restoration of an adequate food supply. *Thus, the fact that a person has marked loss of vision with oedema of the optic disc does not mean that his loss of vision is irreversible unless all resuscitation methods have failed.* Once optic atrophy has been established, steroids are of no use, although Diamox has been found helpful in some cases to prevent a poor perfusion pressure in arteriosclerotic posterior ciliary arteries from causing further deterioration.

Prophylactic measures against AION

Since AION, particularly in temporal arteritis, is a blinding disease with poor prognosis for recovery of vision, and the second eye is likely to be involved after the first, it is worth considering possible preventive measures.

These can be considered under the two following major causes of AION.

(1) Temporal arteritis AION

Preventive measures should include early and adequate systemic corticosteroid therapy. The following should indicate that such therapy is needed.

- (a) Early diagnosis of temporal arteritis before it has produced any ocular symptoms.
- (b) Development of AION should be anticipated in all patients with temporal arteritis and polymyalgia rheumatica.
- (c) Amaurosis fugax should be considered a danger signal.
- (d) If a patient is seen with AION in one eye, the therapy should be started immediately even if the diagnosis of temporal arteritis is not definite. *This is an ophthalmic emergency.*

(2) Arteriosclerotic AION

In patients with marked cardiovascular disease, the following features make them specially vulnerable to AION.

- (a) Hypertension, evidence of marked arteriosclerosis and carotid artery disease, tendency to systemic arterial hypotension, congestive heart failure, myocardial ischaemia, anaesthesia, and surgical or nonsurgical shock.
- (b) Very low ophthalmodynamometric pressure in the ophthalmic artery or easily induced pulsation with a gentle pressure on the eyeball may be indirect evidence of poor perfusion in the posterior ciliary arteries.
- (c) Amaurosis fugax, usually considered to be due to migrating emboli in the retinal arteries. In the absence of any ophthalmoscopic evidence for such emboli, posterior ciliary artery ischaemia may be responsible. Moreover emboli can also become lodged in the posterior ciliary arteries. *Attacks of altitudinal hemianopia would be very highly suggestive of an impending AION.*
- (d) Any tendency to raised intraocular pressure or glaucoma. In these patients the chance of developing AION should be anticipated because any sudden imbalance between the perfusion pressure in posterior ciliary arteries and intraocular pressure will precipitate AION.

Preventive measures should include:

- (1) Prevention of a sudden fall in systemic arterial blood pressure, *e.g.* hypotensive anaesthesia, sudden lowering of blood pressure, congestive heart failure, etc.

- (2) Medical therapy to improve systemic circulatory haemodynamics.
- (3) Prevention of a sudden rise in intraocular pressure, *e.g.* angle closure, and after ocular surgery (*e.g.* cataract extraction and retinal detachment).
- (4) Keeping intraocular pressure as low as possible by medical means, *e.g.* by miotics and Diamox.
- (5) In every patient with a sudden onset of visual disturbance on recovering from shock, AION should be considered as a first possibility.
- (6) If AION does develop in these eyes, there should be awareness of the occurrence of such a lesion, and immediate institution of systemic corticosteroids to reduce oedema of the disc and assist the residual circulation in the optic nerve head, for the survival of the nerve fibres. This can help towards the recovery of vision. I am stressing this point because these cases are so often dismissed as hopeless and not worth treating.

Differential diagnosis

AION, which is usually seen in persons past middle age, has the following essential features:

- (1) Visual disorders consisting of disturbance of visual acuity and/or the presence of a variety of visual field defects.
- (2) Oedema of the optic disc, which may be uniform or more marked in one sector during early stages, and is followed by sectoral or complete optic atrophy a month or two later.

From these two components of AION, it is evident that AION needs to be differentiated from a large number of ocular, optic disc, optic nerve, intracranial, vascular, and systemic diseases which can produce one or more of the following:

- (1) Sudden or rapid loss of all or part of the vision in one or both eyes, preceded by presence or absence of amaurosis fugax.
- (2) Unilateral or bilateral oedema of the optic disc associated with visual disorders and a variety of visual field defects.
- (3) Partial or complete unilateral or bilateral optic atrophy associated with visual disorders and a variety of visual field defects.

It is beyond the scope of this work to discuss all of the conditions that may show one or more of these three features, because there are so many conditions that can present with these characteristics. However, I should like to stress that, in patients who present for the first time with sectoral or complete optic atrophy of unknown aetiology, AION should be considered as one of the diseases in differential diagnosis, particularly in elderly individuals. This is because about two months after the onset of AION every patient has no oedema of the disc but has optic atrophy (Hayreh, 1974a,b). Lessell (1974) recently stated "I am always dubious of the diagnosis [of AION] if there has been no phase of disc swelling. A surprising number of those patients who do not have swelling have turned out to have metastatic tumours of the optic nerve." This is a highly misleading and dangerous statement. As mentioned above, unless and until the patient with AION is seen during the early oedematous phase, the short-lived oedema of the optic disc may be completely missed. Thus, many patients with AION may be seen for the first time during the stage of optic atrophy. To imply that metastatic tumours of the optic nerve are a more common cause of optic atrophy than AION does not make sense to me, because the occurrence of such tumours is exceptional whereas AION is not rare. Unfortunately, many cases of AION are being missed because of lack of awareness of this disorder.

Summary

The effects of systemic corticosteroid therapy on anterior ischaemic optic neuropathy (AION) were investigated by dividing the cases into three groups:

GROUP I: AION due to temporal arteritis.

GROUPS II AND III: AION *not* due to temporal arteritis.

Groups I and II were treated identically by corticosteroids. No medication was given to Group III. The results showed the best visual outcome in Group II patients, of whom 75 per cent. showed visual improvement as compared to only 17 per cent. in Group III. The outcome was worst in Group I. It is therefore recommended that all patients with AION should be treated as soon as possible with systemic corticosteroids, with a starting dose of at least 60 to 80 mg. prednisolone, thereafter slowly tapered to continue the treatment so long as the optic disc shows oedema in cases without temporal arteritis, and as long as indicated in temporal arteritis cases. Diamox was found useful in preventing further deterioration of vision in late cases with optic atrophy, and it is suggested that it should also be given in acute cases to lower the intraocular pressure and improve the vascular perfusion of the optic disc. The treatment of and prophylactic measures against AION are discussed.

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