CASE REPORT

Non-arteritic Posterior Ischaemic Optic Neuropathy Treated with Intravenous Prostaglandin E1 and Oral Corticosteroids

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ABSTRACT

Intravenous prostaglandin E1 and oral corticosteroids were used to treat the ischaemic phase of a non-arteritic posterior ischaemic optic neuropathy with immediate visual improvement. Non-arteritic posterior ischaemic optic neuropathy is a disorder of reduced blood flow to the retrobulbar optic nerve, usually of acute onset. It has been suggested that high-dose steroid therapy given soon after the onset of visual loss can result in significant visual improvement. This treatment, however, is not universally successful. The addition of a potent vasodilator to the corticosteroids could help restore ocular blood flow and improve visual acuity. This paper presents the use of prostaglandin E1 (PGE1), a powerful vasodilator of the microcirculation, to treat non-arteritic posterior ischaemic optic neuropathy. In this case report a 68-year-old white male with hereditary haemochromatosis was seen 8 hours after sudden loss of visual acuity in his left eye (OS) to 4/10. The diagnosis of non-arteritic posterior ischaemic optic neuropathy was made and he was immediately given oral corticosteroids. Intravenous PGE1 was given the next morning, 24 hours after the sudden loss of vision, once ischaemia of the optic nerve was confirmed by colour Doppler imaging. The visual acuity in the OS improved from 4/10 to 11/10 within 1 day. A visual field (VF) post treatment showed a peripheral scotoma without a central scotoma. At 12 months post treatment the vision OS remained 11/10. No complications due to the use of PGE1 were seen. The authors conclude that PGE1 should be considered in addition to steroids in cases of NA-PION to immediately restore blood flow to the optic nerve and improve visual acuity.

KEYWORDS hereditary haemochromatosis, non-arteritic posterior ischaemic optic neuropathy, prostaglandin E1 (PGE1)

INTRODUCTION

Posterior ischaemic optic neuropathy (PION) is a disorder of reduced blood flow to the retrobulbar optic nerve. It can be divided into three types: arteritic due to various vasculitides such as giant cell arteritis (GCA), non-arteritic associated with other systemic vascular diseases, and “surgical”, that is to say occurring in the perioperative period following a variety of surgical procedures.^{1,2} The use of high-dose systemic corticosteroids in a non-randomised retrospective study to treat non-arteritic posterior ischaemic optic neuropathy (NA-PION) resulted in a significant improvement in the visual acuity (VA) when compared with the untreated patients.² Steroid therapy

is, however, not universally successful. Steroids in the same study did not significantly improve the VA in the arteritic and surgical types of PION.²

Prostaglandin E1 (PGE1), a powerful vasodilator of the microcirculation, has been shown to improve ocular blood flow in the presence of peripheral vascular disease and diabetes.³ Intravenous (IV) PGE1 and steroids have been successfully used to treat 7 out of 8 cases of non-arteritic anterior ischaemic optic neuropathy (NA-AION).⁴ Since NA-PION, like NA-AION, is a disorder of reduced blood flow to the optic nerve, the use of a potent vasodilator of the microcirculation such as PGE1 may help in its treatment. This case report presents the use of oral steroids and IV PGE1 in the treatment of a NA-PION

in hereditary haemochromatosis (HH) and the rationale for their use.

CASE REPORT

A 68-year-old white male was seen in the early afternoon. Eight hours prior to the visit, on awakening in that morning, he had noted a loss of VA in his left eye (OS). He was amblyopic in the right eye (OD). He had no recent surgery and was under treatment for HH. He had no clinical symptoms of GCA. His Snellen VA was 2/10 in the OD with plano and 4/10 in the OS with $-1.25/+0.50 \times 45$. His anterior segments and intraocular pressures were normal. His optic disc and retina were normal in both eyes. A preliminary diagnosis of NA-PION in HH was made and he was immediately given 50mg of prednisone by mouth (PO). The following morning he again took 50mg of prednisone PO and had colour Doppler imaging (CDI) of both eyes. The blood flow velocity of the central retinal artery (CRA) as it enters the eye and of the ophthalmic artery (OA) within the retrobulbar portion of the optic nerve was normal in the OD and markedly reduced in the OS. The flow of the nasal and temporal posterior ciliary arteries (PCAs) was markedly reduced in the OS but normal in the OD. After a thorough explanation written consent was obtained, the patient was immediately given 60 µg of PGE1 intravenously (IV) and, after about 1 hour, noted a gradual return of the VA. The next day on ophthalmic examination the VA was unchanged at 2/10 in the OD and improved to 11/10 in the OS. The retina and optic disc were still normal in appearance and he was started on 25mg of prednisone a day for 5 days. Three days after the first infusion of PGE1, repeat CDI of the retrobulbar circulation indicated improvement from the original Doppler but a modest reduction in the flow velocity remained. The patient was given a second dose of 60 µg of PGE1 IV. A Humphrey central 30-2 VF 1 week post treatment indicated peripheral scotomas in both eyes, with a mean deviation of -10.28 OD and -6.61 OS. A thorough vascular and medical workup was done immediately after the second infusion. Minimal plaque formation at the bifurcation of the common carotid arteries on both sides was found. The blood results, including an ESR, and medical examination revealed no signs of GCA. Except for HH, no other medical problems were found and the diagnosis of NA-PION was made. At 1, 4, 6, 16, 26, and 52 weeks post treatment the patient's VA remained 11/10 in the OS with no further treatment. After 60 weeks post treatment, the patient had a new episode of NA-PION with a return of vision in the OS to 11/10 after only 1 IV of PGE1.

DISCUSSION

PGE1 is a safe, potent vasodilator of the peripheral vascular system (microcirculation or capillary system)

that is used to treat patients with signs and symptoms of peripheral vascular disease such as intermittent claudication and peripheral diabetic ulcers.^{3,5,6} It is the same medicine used to treat males with erectile dysfunction.⁷ A 2-day IV treatment of PGE1 causes a vasodilatation of the capillary system that can last for 4 weeks or longer in patients with peripheral vascular disease.⁸ It is well tolerated with few side effects and can be used in patients who are hypotensive. It is important to monitor the systemic blood pressure frequently (every 15–20 minutes) during its intravenous administration.^{3,5,6,8} The main mechanism of action of PGE1 is as a vasodilator of the microcirculation (capillary system). PGE1 has a direct action on the smooth muscle of the vascular wall leading to a vascular dilatation and increased flow. This vasodilatation varies according to the anatomical location and is dose dependent. PGE1 is also known to inhibit platelet aggregation.⁹ In addition to known effects of PGE1 on platelet aggregation, fibrinolysis, blood flow, and viscosity, it also inhibits monocyte and neutrophil function, suggesting anti-inflammatory effects as well. Recent research on gene expression suggests that several genes in vascular smooth muscle cells and fibroblasts are modified by PGE1 at the transcriptional level. This may contribute to tissue protection in ischaemic areas.¹⁰ These factors together promote an increase in the capillary flow. PGE1 is rapidly metabolized by oxidation during passage through the pulmonary circulation. It is excreted in the urine as metabolites within about 24 hours.⁹ This rapid elimination also contributes to its safety.

Steroids have been shown to improve the VA in NA-PION in some patients. For this reason they were immediately given to the patient. A fluorescein angiogram (FA) and perimetry were not immediately available so the patient was sent for CDI. As soon as the ischaemic component of the retrobulbar circulation was demonstrated, IV PGE1 was immediately started without attending other examinations, which would have delayed the initiation of treatment with possible permanent damage to the optic nerve. The patient had recent blood work because of his HH, which was normal. Since PION is an ischaemic disorder of the retrobulbar optic nerve, the use of a potent vasodilator to immediately re-establish blood flow could be important. PGE1 has been shown to improve ocular blood flow in patients with a decreased ocular blood flow in the presence of peripheral vascular disease and diabetes.³ It has been used with IV steroids to treat NA-AION improving the VA in 7 out of 8 patients and in 1 case of a branch retinal arterial occlusion.^{4,11} It has also been used to treat ocular ischaemia in high myopia.¹² One IV infusion of PGE1 improves peripheral blood flow for up to 4 weeks in patients with peripheral vascular disease.⁸ For these reasons, the authors decided to use PGE1 in this patient with NA-PION and the VA began to improve 1 hour after

the first infusion. Because of the prolonged effect of PGE1, it was given for only 2 days. Further treatment with PGE1 could have been administered had it been necessary but the patient here did not need it.

CDI in this case revealed generalised ischaemia of the retrobulbar circulation, with a decreased flow in the CRA, OA, and PCAs. A decreased flow of the CRA leads to inner retinal ischaemia. A decreased flow of the OA leads to an optic nerve ischaemia. A decreased flow of the PCAs would lead to a choroidal ischaemia with eventual ischaemia in the outer retina. It is certainly possible that there was choroidal as well as optic nerve ischaemia causing retinal and optic nerve visual loss in this case. A FA and indocyanine green angiogram would have been needed to evaluate the choroidal circulation but they were not immediately available and the authors did not want to delay therapy. Clinically PGE1 improves the choroidal, as well as the optic nerve and retinal circulation.^{4,11,12} In this case report PGE1 probably improved the circulation in all the sectors of the eye. Further study would need to be done in an initial acute presentation to properly understand the contribution of choroidal ischaemia to the acute loss of vision.

The Humphrey central 30-2 VF 1 week post treatment indicated peripheral scotomas in both eyes, with a mean deviation of -10.28 OD and -6.61 OS. The OD was worse than the OS but the fact that the OD was amblyopic could account for this. Also the patient may have had episodes of NA-PION in the OD in the past that could account for the scotomas in that eye. Being amblyopic in the OD he may have been unaware of these possible episodes of NA-PION. A central scotoma was not found in the OS as is usually seen in PION. However, the patient had already been treated with consequent improvement in his VA to 11/10, which could explain the lack of a central scotoma in the VF in the OS. Optic disc pallor was not seen on follow up visits. This also could be explained by the early treatment.

Steroids, in the form of prednisone, were immediately given to this patient and were continued orally for a total of 7 days. Some studies have suggested systemic corticosteroids in the form of oral prednisone to treat both NA-PION and NA-AION, and for this reason the authors began prednisone.^{2,13} However, the authors used steroids for another reason: to try to reduce ischaemia-reperfusion (I-R) injury. Ischaemia leads to tissue hypoxia, depletion of energy-rich phosphates, accumulation of metabolic waste products including reactive oxygen species, and cellular oedema, which all may cause cellular injury.^{14,15} The immediate reinstitution of blood is necessary to prevent further tissue damage but the reperfusion itself may cause further tissue damage, so-called ischaemia-reperfusion (I-R) injury. Infiltrating leukocytes are thought to play a major role in this I-R injury and I-R injury was the reason the

authors used prednisone immediately before and for a week after PGE1.^{14,15}

This is only one case report of the addition of PGE1 to the treatment of NA-PION with systemic steroids. The use of PGE1 appeared to be effective without causing any systemic or ocular side effects but more cases are necessary to evaluate its use.

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