Case Report

DOI: 10.5582/ddt.2017.01034

Visual field improvement in non-arteritic posterior ischemic optic neuropathy in a patient treated with intravenous prostaglandin E1 and steroids

Robert Davis Steigerwalt, Jr.[1,*], Paolo Giuseppe Limoli[2], Marcella Nebbioso[3]

[1] *Via A. Brofferio 6, Rome, Italy;*
[2] *Centro Studi Ipovisione, Piazza Sempione 3, Milan, Italy;*
[3] *Department of Sense Organs, Sapienza University of Rome, P. le A. Moro 5, Rome, Italy.*

Summary **Non-arteritic posterior ischemic optic neuropathy (NA-PION) is a disorder of reduced blood flow to the retrobulbar optic nerve. There is usually an acute loss of visual acuity and field. Previous studies have noted an improvement in visual acuity and in ocular and retrobulbar blood flow with the use of a potent vasodilator of the microcirculation, prostaglandin E1 (PGE1), and steroids. The current report describes immediate improvement in the visual fields and visual acuity in a patient with NA-PION treated with intravenous PGE1 and steroids 66 hours after onset. An 89-year-old white female was first seen in December 2016 with a sudden loss of vision in the right eye. After a complete eye exam and visual fields, the patient was diagnosed with NA-PION. Treatment was immediately started with steroids and intravenous PGE1. This was repeated once again the next morning. Visual acuity in the right eye improved from 1/10 + 1 to 7/10 + 3 at 5 days. The mean deviation of the visual field improved from – 7.10 decibels (dB) with a central scotoma of – 22 dB to – 2.97 dB with a central scotoma of – 19 dB. After 2 weeks, her visual acuity was 7/10 + 1 and visual field testing of the right eye revealed a mean deviation of – 2.54 dB with a central scotoma of – 9 dB. The left eye was unchanged. In cases of NA-PION, PGE1 and steroids should be considered to immediately restore blood flow to help improve visual acuity and visual fields.**

Keywords: Non-arteritic posterior ischemic optic neuropathy, prostaglandin E1, visual field, central scotoma

1. Introduction

Posterior ischemic optic neuropathy is a disorder of reduced blood flow to the retrobulbar optic nerve, usually of acute onset. This condition can be classified as surgical, arteritic or non-arteritic (*1,2*). Use of high-dose systemic steroids to treat non-arteritic posterior ischemic optic neuropathy (NA-PION) results in improved visual acuity (*2*). Steroid therapy is not universally successful.

Prostaglandin E1 (PGE1), a powerful vasodilator of the microcirculation, improves ocular blood flow in the presence of peripheral vascular disease and diabetes (*3*). In cases of NA-PION, PGE1 was given intravenously at a dose of 1 μg/kg with steroids and was found to improve visual acuity as well as ocular and retrobulbar blood flow (*4,5*). In the current case, visual fields as well as visual acuity were improved in a patient with NA-PION treated with intravenous PGE1 and steroids 66 hours after onset.

2. Case Report

An 89-year-old white female was seen in December 2016. She had dry age-related macular degeneration in the right eye and a neovascular membrane in the left eye. One morning three days prior, she underwent ocular surgery with the Limoli retinal restoration technique on her right eye. This technique involves placing a cellular autograft in an equatorial scleral pocket of the eye (*6*). Eight hours after surgery while

**Address correspondence to:*
Dr. Robert D. Steigerwalt, Jr., Via A. Brofferio 6, Rome 00195, Italy.
E-mail: r.steigerwalt@libero.it

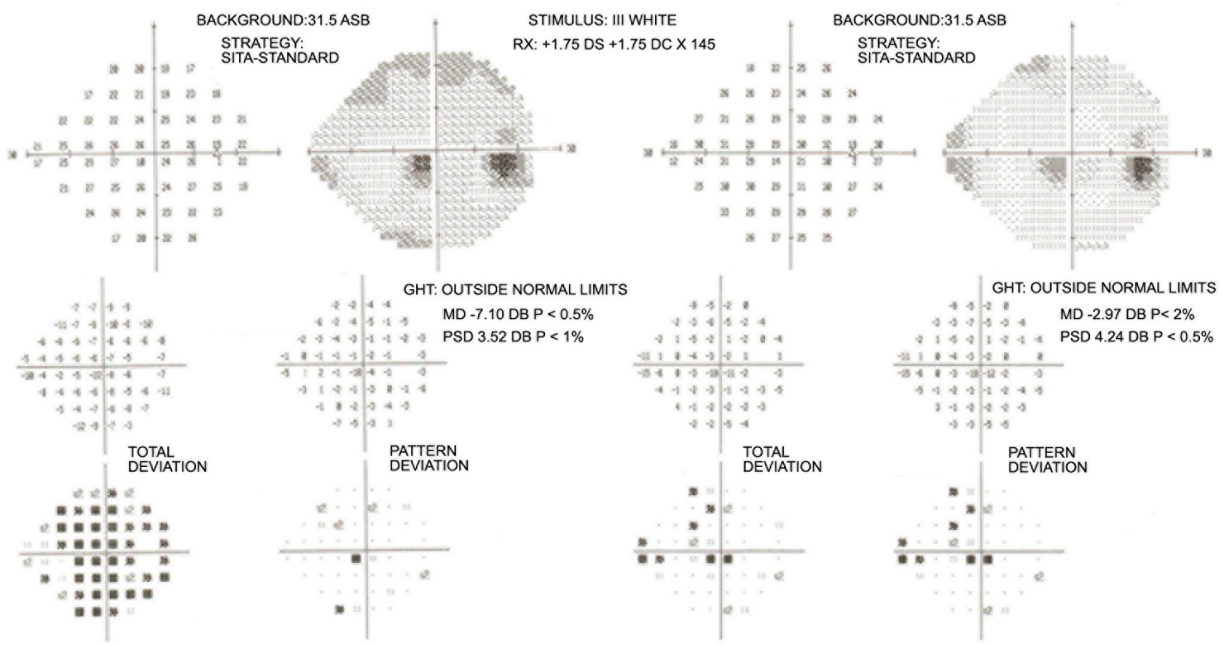

Figure 1. Visual field of the right eye on the left side before treatment and the visual field of the right eye on the right side 5 days post-treatment.

watching television in the evening, she had a sudden decrease in the visual acuity in the right eye (the eye that underwent surgery). She was examined 63 hours later. She was pseudophakic in both eyes with a visual acuity of 1/10 + 1 in the right eye according to the Early Treatment Diabetic Retinopathy Study chart and a visual acuity of 1/30 in the left eye. The intraocular pressures were normal with no signs of secondary cataracts. There were no clinical signs of giant cell arteritis. Her blood work from surgery did not indicate signs of diabetes or giant cell arteritis. A fundus exam revealed dry age-related macular degeneration in the right eye with no signs of retinal hemorrhage, inflammation or edema. Edema was present in the fundus of the left eye. The optic nerve heads were normal in both eyes with no pallor or edema. Optical coherence tomography revealed no signs of fluid in the macula in the right eye and an optical coherence tomography angiography revealed no signs of a neovascular membrane in the right eye. A neovascular membrane was present in the left eye. Humphrey central 24-2 visual field testing was immediately done. In the right eye, there was a mean deviation of – 7.10 decibels (dB) with a central scotoma of – 22 dB (Figure 1 and Table 1). The visual field in the left eye could not be tested due to lack of central fixation.

The patient was diagnosed with NA-PION. The experimental nature of the treatment was explained and after written consent was obtained, treatment was immediately begun 66 hours after onset. PGE1 comes as a liquid in vials of 20 µg and is given intravenously in physiologic solution at a dose of 1 µg/kg. The patient weighed 68 kilograms and was started on 60 µg of PGE1 administered intravenously over 1 hour. Subjectively, she noted a gradual return in the visual acuity in the right eye the same evening after treatment. The following morning, PGE1 was administered again intravenously and the patient was started on 25 mg of prednisone once a day for 5 days. Five days after the first treatment, she was examined. Visual acuity in the right eye was 7/10 + 3. There was no change in the left eye. Other results of the exam, including the fundus, remained the same. Visual field testing of the right eye revealed a mean deviation of – 2.97 dB with a central scotoma of – 19 dB (Figure 1 and Table 1). Two weeks later, visual acuity was 7/10 + 1 and visual field testing of the right eye revealed a mean deviation of – 2.54 dB with a central scotoma of – 9 dB (Figure 2 and Table 1). The patient was continued on 60 µg of PGE1 in the form of a skin cream for systemic absorption every 2 weeks. One, 4 and 7 months (at the time of this report), her vision was stable and she continued to use PGE1 skin cream every 2 weeks.

Table 1. Visual acuity and Humphrey 24.2 visual fields of the right eye before and after treatment with prostaglandin E1 (PGE1)

Date	Visual Acuity	Mean Deviation	Central Scotoma
Initial visit (T0)	1/10 + 1	– 7.10 dB	– 22 dB
After 5 days (T5)	7/10 + 3	– 2.97 dB	– 19 dB
After 2 weeks (T2ws)	7/10 + 1	– 2.54 dB	– 9 dB

dB: decibels.

3. Discussion

The purpose of this case report is to present further evidence, which includes improvement in visual fields,

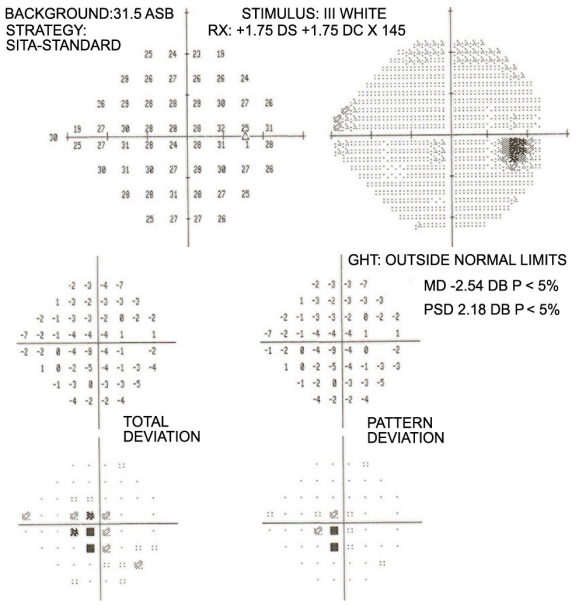

Figure 2. Visual field of the right eye 2 weeks post-treatment.

for the use of intravenous PGE1 and steroids in the treatment of NA-PION. The authors also intend to describe how that treatment, even though it was delayed up to 66 hours after onset, was still beneficial.

NA-PION is a disorder of reduced blood flow to the retrobulbar optic nerve (*1,2,5*). The use of a potent vasodilator, PGE1, to immediately re-establish blood flow could be important (*3,7*). PGE1 given intravenously at a dose of 1 µg/kg together with steroids has been successfully used to treat cases of NA-PION and acute non-arteritic anterior ischemic optic neuropathy (NA-AION) (*4,5,8*). PGE1 has helped in the treatment of acute arteritic anterior ischemic optic neuropathy when given with high-dose steroids (*9*). In the current case, intravenous PGE1 and steroids were immediately started as soon as the patient was diagnosed with NA-PION, resulting in an improvement in visual fields and visual acuity. This is the first report of improvement in visual fields in NA-PION and is further evidence for this therapy. Based on the authors' clinical experience with cases of NA-AION, PGE1 must be given immediately, *i.e*. within 12 hours, to be effective. In the current case involving NA-PION, the therapy was effective even after 66 hours, so this therapy should be attempted. One intravenous infusion of PGE1 improves peripheral blood flow for up to 4 weeks in patients with peripheral vascular disease (*3,7*). Because of this, PGE1 was given only 2 times over 2 days and was effective. Repeated treatments could lead to systemic hypotension. The dosage is 1 µg/kg in physiologic solution over 1 hour. Higher dosages could also lead to systemic hypotension. PGE1 is well-tolerated and causes few adverse reactions, so it can be used in patients who are hypotensive. Systemic blood pressure needs to be monitored frequently during its intravenous administration (*3,7*). The main mechanism of action of PGE1 is *via* vasodilatation of the microcirculation. PGE1 has a direct action on the smooth muscle of the vascular wall, leading to a vascular dilatation and increased 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. This rapid elimination also contributes to its safety (*10*).

The current patient had poor vision in the left eye because of a neovascular membrane. Ischemic episodes in NA-AION and NA-PION are known to reoccur in the affected eye or in the other eye (*5,11*). To avoid another episode in the good eye, the authors wanted to maintain vasodilatation of the microcirculation with PGE1 without resorting to intravenous treatments. Accordingly, the patient continued to receive 60 µg of PGE1 in a skin cream. The PGE1 concentration in this cream is 20 µg/cc. Three cc of cream, for a total dosage of 60 µg of PGE1, is applied in repeated individual doses over 2 hours to the inner surface of the forearm, spread and allowed to dry. This allows for systemic absorption over 2 hours. This is done every 2 weeks. This is a compound pharmacy preparation that has been patented by one of the authors (RDS).

Steroids, in the form of prednisone, were given orally to the current patient for 5 days. Systemic steroids have been used to treat NA-PION and NA-AION (*2,12*). Steroid therapy is, however, not universally accepted. A more recent study using high-dose systemic steroid treatment in acute NA-AION noted no visual or anatomic benefit and some serious complications due to steroids (*13*). However, the current authors used steroids for another reason: to try to reduce ischemia-reperfusion injury. Ischemia leads to tissue hypoxia, depletion of energy-rich phosphates, accumulation of metabolic waste products including reactive oxygen species and cellular edema, all of which may cause cellular injury (*14,15*). The immediate resumption of blood flow is necessary to prevent further tissue damage but the reperfusion itself may cause further tissue damage *via* reperfusion injury. Infiltrating leukocytes are thought to play a major role in this ischemia-reperfusion injury (*14,15*), and this was why the current authors administered 25 mg of prednisone along with PGE1 during the first 5 days.

Surgery with the Limoli retinal restoration technique was done 8 hours prior to the loss of vision. This technique involves fashioning a scleral pocket at the equator of the eye filled with adipose stromal cells derived from orbital fat, platelets from platelet-rich plasma and adipose-derived stem cells from abdominal adipose tissue. This is meant to bring nutrition to the choroid and retina (*6*). Upon examination of the patient after the visual loss, there were no signs of unusual ocular or orbital inflammation due to the surgery. The authors do not think that the surgery was the cause of NA-PION.

In the current case, visual field testing was possible before treatment without an unusual delay in treatment, so this testing was done immediately. The Humphrey visual field improved after treatment, with a reduction in the mean deviation from – 7.10 to – 2.54 dB. The central scotoma improved from – 22 to – 9 dB (Table 1 and Figures 1 and 2). This paralleled the improvement in the visual acuity from 1/10- to 7/10 + 1, which is consistent with her age-related macular degeneration. In another case of NA-PION, vision improved to 11/10 with no central scotoma on visual fields tested only after treatment (*5*). In that case, treatment was administered within 24 hours and there was no age-related macular degeneration. In the current case, improvement in visual fields and the central scotoma are evidence of the benefit of therapy even though it started 66 hours after onset.

This case report describes the beneficial use of intravenous PGE1 and steroids in the treatment of NA-PION even though that treatment started 66 hours after onset. The addition of steroids may help to reduce damage from ischemia-reperfusion injury, but this point needs to be evaluated further. In order to provide the complete clinical picture, use of PGE1 was continued in the form of a skin cream every 2 weeks to avoid recurrence; however, this approach also needs to be properly studied.

Conflicts of interest

One of the authors, RDS, has a financial interest in the prostaglandin E1 skin cream mentioned in this case report. The other authors have no proprietary or financial interests in or conflicts of interest with regard to the products mentioned in this study. The authors alone are responsible for the contents and writing of the paper.

References

1. Sadda SR, Nee M, Miller NR, Biousse V, Newman NJ, Kouzis A. Clinical spectrum of posterior ischemic optic neuropathy. Am J Ophthalmol. 2001; 132:743-750.
2. Hayreh SS. Posterior ischemic optic neuropathy: Clinical features, pathogenesis, and management. Eye. 2004; 18:1188-1206.
3. Steigerwalt RD Jr., Belcaro GV, Christopoulos V, Incandela L, Cesarone MR, De Sanctis MT. Ocular and orbital blood flow velocity in patients with peripheral vascular disease and diabetes treated with intravenous prostaglandin E1. J Ocul Pharmacol Ther. 2001; 17:529-535.
4. Steigerwalt RD, Cesarone MR, Belcaro G, De Angelis M, Pascarella A, Nebbioso M. Non-arteritic posterior ischemic optic neuropathy treated with intravenous prostaglandin E1 and oral corticosteroids. Neuro-Ophthalmology. 2011; 35:81-84.
5. Steigerwalt RD Jr, Pascarella A, De Angelis M, Grimaldi G, Nebbioso M. Three episodes of non-arteritic posterior ischemic optic neuropathy in the same patient treated with intravenous prostaglandin E1. Drug Discov Ther. 2016; 10:177-180.
6. Limoli PG, Limoli C, Vingolo EM, Scalinci SZ, Nebbioso M. Cell surgery and growth factors in dry age-related macular degeneration: Visual prognosis and morphological study. Oncotarget. 2016; 7:46913-46923.
7. Cesarone MR, Belcaro G, Nicolaides AN, Griffin M, Geroulakos G, Ramaswami G, Cazaubon M, Barsotti A, Vasdekis S, Christopoulos D, Agus G, Bavera P, Mondani P, Ippolito E, Flenda F. Treatment of severe intermittent claudication: ORACLE-PGE1 short term study. A randomised 40-week study. Evaluation of efficacy and costs. Minerva Cardioangiol. 2002; 50:683-690.
8. Steigerwalt RD Jr, Cesarone MR, Belcaro G, Pascarella A, De Angelis M, Bacci S. Nonarteritic anterior ischemic optic neuropathy treated with intravenous prostaglandin E1 and steroids. Int J Angiol. 2008; 17:193-196.
9. Steigerwalt RD Jr, Cesarone MR, Belcaro G, Pascarella A, De Angelis M, Gattegna R, Nebbioso M. Arteritic anterior ischemic optic neuropathy treated with intravenous prostaglandin E1 and steroids. Int J Angiol. 2010; 19:113-115.
10. Parfitt K. Prostaglandins. In: Martingale: The Complete Drug Reference (Parfitt K, ed.). Pharmaceutical Press, London, UK, 1999; pp. 1411-1413.
11. Arnold AC. The 14th Hoyt Lecture: Ischemic optic neuropathy: The evolving profile, 1966-2015. J Neuroophthalmol. 2016; 36:208-215.
12. Hayreh SS, Zimmerman MB. Non-arteritic anterior ischemic optic neuropathy: Role of systemic corticosteroid therapy. Graefes Arch Clin Exp Ophthalmol. 2008; 246:1029-1046.
13. Rebolleda G, Perez-Lòpez M, Casas-LLera P, Contreras I, Munoz-Negrete FJ. Visual and anatomical outcomes of non-arteritic anterior ischemic optic neuropathy with high-dose systemic corticosteroids. Graefes Arch Clin Exp Ophthalmol. 2013; 1:255-260.
14. Collard CD, Gelman S. Pathophysiology, clinical manifestations and prevention of ischemia-reperfusion injury. Anesthesiology. 2001; 94:1133-1138.
15. Kurokawa T, Takagi H. Mechanisms and prevention of ischemia-reperfusion injury. Transplant Proc. 1999; 31:1775-1776.

(Received June 25, 2017; Revised August 8, 2017; Accepted August 10, 2017)