Retinal artery occlusion: visual outcome after treatment with hyperbaric oxygen

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Key words
Retinal artery occlusion, hyperbaric oxygen therapy, outcome, case reports

Abstract
(Cope A, Eggert JV, O'Brien E. Retinal artery occlusion: visual outcome after treatment with hyperbaric oxygen. Diving Hyperb Med. 2011;41(3):135-8.)
Methods: We describe a case series of 11 patients with retinal artery occlusion treated with hyperbaric oxygen therapy (HBOT) at Intermountain Dixie Regional Medical Center between 2005 and 2009. We then combined data from our case series with data from two other case series to report on a combined total of 51 patients.
Results: Eight of our 11 patients achieved improved visual acuity. Analysis of the combined case series showed that 74% of patients treated with HBOT had improvement in visual acuity (*P* less than 0.0001) with 53% improving two lines or more on a modified Snellen value. The combined case series also showed that visual acuity improved in all time-from-occlusion to treatment categories, ranging from less than 8 hours to six days.
Conclusions: We recommend consideration of HBOT for patients who present with recent retinal artery occlusion. Hyperbaric centres treating these patients should consider forming a central registry of standardised data to prospectively study the results of therapy.

Introduction

Retinal artery occlusion (RAO) is characterised by a sudden, usually unilateral, painless loss of vision. Occlusion may result from thrombosis, embolus, arteritis or vasospasm.[1] Occlusion may not be complete. Many patients present with some light perception or visual loss in only one or two quadrants. Permanent visual loss generally occurs if the occlusion continues for more than a few hours. Prognosis depends on the level of occlusion, cilioretinal artery sparing and how quickly oxygen supply can be restored to the retina.[1] One explanation for variable visual loss is that the retina has a dual oxygen supply. The inner layers of the retina receive oxygen from the central retinal artery and the outer layers are supplied by the choroidal circulation from the posterior ciliary arteries.[2] Fifteen to 30% of eyes have a cilioretinal artery which branches off the posterior ciliary artery and enters the optic nerve disc separately from the central retinal artery, providing an alternate blood supply to the retina if the central retinal artery is occluded. It looks like a short hook at the edge of the disc. Another factor in explaining variability of loss is the amount of potentially salvageable tissue at the periphery of the ischaemic area, called the 'ischaemic penumbra'.[1]

The natural history of RAO is recannulation of the artery over a few days resulting in some spontaneous improvement of vision. Visual outcome has been reported in 244 consecutive patients seen from 1974 to 2000.[1] Of the ninety-nine patients presenting within seven days after RAO, 38% had some improvement of vision with no treatment. Many different treatments for RAO have been tried, none of which have shown significant improvement versus no treatment.[3–6] Hyperbaric oxygen therapy (HBOT) has been associated with improvement in visual acuity in retrospective studies.[7–10] HBOT can maintain oxygenation of the retina through the choroidal blood supply, decrease oedema and preserve compromised tissue adjacent to the ischaemic area.[2]

The purposes of our study were twofold. First, we reviewed patients with RAO treated with HBOT at our institution. Secondly, we combined our data with two other similar case series, making a total of 51 patients. Our two hypotheses were that HBOT resulted in improved visual acuity compared with the spontaneous improvement reported with no treatment and that improvement of visual acuity would be correlated with time from visual loss to treatment.

Methods

The hyperbaric chamber at Intermountain Dixie Regional Medical Center (DRMC) is located at an altitude of 811 metres above sea level, with a usual barometric pressure of about 101 kPa. DRMC is a regional referral centre for about 250,000 patients in small towns and rural areas. The next closest hyperbaric chamber is 193 km away and the closest centre that could provide angiography of the ophthalmic artery and instillation of thrombolytic therapy is 482 km away. This retrospective review was approved by the Intermountain Institutional Review Board.

CASE SERIES

Eleven patients with RAO were treated with HBOT at DRMC between 2005 and 2009. The referring ophthalmologist made the diagnosis and assessed visual acuity, presence of cilioretinal artery sparing and visual fields. Patients were interviewed by the treating hyperbaric physician before and after each treatment and given a hand-held standard Snellen chart to read at the recommended distance of 12 to 16 inches

from the affected eye, with the unaffected eye covered. For individuals who could not distinguish letters on the Snellen chart, (acuity worse than 20/800), visual acuity was reported as counting fingers (CF), hand motion (HM), light perception (LP), or no light perception (NLP). Time from visual loss to start of HBOT was recorded.

The medical charts in our case series were reviewed for a history of diabetes, previous eye surgery, or prescription medications for hypertension or hyperlipidaemia. The diagnosis of diabetes, high cholesterol or hypertension was based on diagnosis in the Intermountain electronic medical record or the patient taking medications for those diagnoses. HBOT was at a pressure of 243 kPa, twice daily for the first five treatments, and then daily until there was no further improvement in visual acuity. A total of 90 minutes of oxygen was given by head hood for each treatment in three 30-minute increments with a 5-minute air break in between oxygen increments.

COMBINED CASE SERIES

Two other case series in the literature were found where patients with RAO had received HBOT and the results were reported in table format with similar detail to our case series.[7,11] The data from the three case series were combined for analysis. Data for each patient in the combined case series analysis included: visual acuity, age, gender, time from onset of occlusion to beginning of treatment, number of HBOT treatments and pressures used in each treatment. Presence of cilioretinal artery sparing was unknown in the two other case series. Results reported are: percentage of patients with improved visual acuity, percentage of patients with visual acuity improved two or more increments of the modified Snellen scale and time-to-treatment versus improvement.

Visual acuity is reported in decimal values, using the table published by Holladay to convert Snellen values to decimal values.[12] Visual acuity increases by a geometric progression on a logarithmic scale. Since standard Snellen values are only listed to 20/800, Holladay calculated the values of counting fingers (CF) and hand motion (HM) by geometric progression. He gave counting fingers (CF) the Snellen value of 20/2,000, which converts to a decimal value of 0.01. Detection of hand motion (HM) was given the Snellen value of 20/20,000, which converts to a decimal value of 0.001. These values progress sequentially by a factor of 10.[12] As LP and NLP occur in consecutive order of decreasing visual acuity directly after CF and HM we arbitrarily estimated each step of decreasing visual acuity by a factor of ten. This does not presume a linear relationship. Light perception was assigned a Snellen value of 20/200,000 and a decimal value of 0.0001. NLP had a Snellen value of 20/2,000,000 and a decimal value of 0.00001. These assigned Snellen values, converted to decimal values, were used to calculate pre- and post-HBOT visual acuity for each patient included in the combined case series analysis.

STATISTICAL ANALYSIS

Statistical analysis was performed to answer two questions. Firstly, was improvement in visual acuity significantly greater than that expected by spontaneous improvement? Secondly, was improvement positively correlated with shorter time from onset of visual loss to start of HBOT?

To provide an appropriate control group allowing for the spontaneous improvement seen historically with no treatment, we used the percentage of patients improved who presented within seven days of visual loss in the report by Hayreh and Zimmerman.[1] Analysis of observed versus a 38% expected spontaneous improvement was performed using a one-tailed Z test and chi square test with a Haber correction for continuity. (Systat version 10, Systat Software Inc). A P-value of < 0.05 was accepted as significant.

Patients in the combined case series analysis were assigned to one of four time-to-treatment groups according to the time that elapsed from occlusion to the start of the first HBOT: 0 to 8 hours, 9 to 24 hours, 25 to 72 hours and more than

Table 1
Case series at DMRC; hours' delay was from onset of visual loss to start of first HBOT; chol – cholesterol

No	Sex	Age	Delay (hrs)	Diabetic	High chol	High BP	Prev. eye surgery	Treatments total #	Acuity before HBOT	Acuity after HBOT	Increments of improvement
1	M	58	9	Yes	Yes	No	No	6	0.00001	0.0001	1.0
2	F	81	6	No	Yes	No	Yes	5	0.00001	0.001	2.0
3	F	55	8	No	No	Yes	No	5	0.00001	0.001	2.0
4	M	71	72	Yes	Yes	Yes	No	5	0.00001	0.001	2.0
5	M	22	24	Yes	No	No	Yes	5	0.00001	0.4	9.0
6	M	75	18	No	Yes	Yes	No	5	0.0001	0.25	6.5
7	F	66	6	No	Yes	Yes	No	5	0.001	0.001	0.0
8	M	78	24	No	Yes	Yes	No	7	0.001	0.4	7.0
9	M	65	5	No	Yes	Yes	Yes	21	0.01	0.25	4.5
10	F	24	144	No	Yes	Yes	No	5	0.05	0.05	0.0
11	F	75	72	No	No	Yes	No	10	0.4	0.4	0.0

72 hours. Any improvement versus time-to-treatment was analysed using the MANOVA test from the Systat program. A *P*-value of < 0.05 was accepted as significant.

Results

DRMC CASE SERIES

Eleven patients were referred from their ophthalmologist for sudden, unilateral, painless loss of vision diagnosed as retinal artery occlusion. All patients received a minimum of five HBOT (Table 1). HBOT was well tolerated with no significant side effects such as barotrauma or oxygen toxicity symptoms.

Data collected on the 11 patients treated at DRMC are shown in Table 1 and the main clinical features are summarised here. Five of the patients with unilateral loss presented with NLP. One improved to LP (Patient #1). Three patients improved to HM (#2,3,4) and one to 20/50 (#5). One patient presented with LP only (#6). He improved to 20/80. Two patients presented with HM only. One did not improve (#7) and one improved to 20/50 (#8). One patient presented with CF (#9). He improved to 20/80. One patient (#10) presented with NLP in the upper half of the affected eye, but overall visual acuity of 20/400 in the eye. Visual acuity did not change after treatment, but visual fields were regained except for a small central scotoma. One patient with a patent cilioretinal artery (#11) presented with a black band across the center of the eye. Visual acuity was unchanged at 20/50, but the band was about 50% smaller in size after HBOT.

We did not see any significant trends between improvement in visual acuity and a diagnosis of diabetes, hyperlipidemia, hypertension or previous eye surgery. The data are included to facilitate future detailed case series reports.

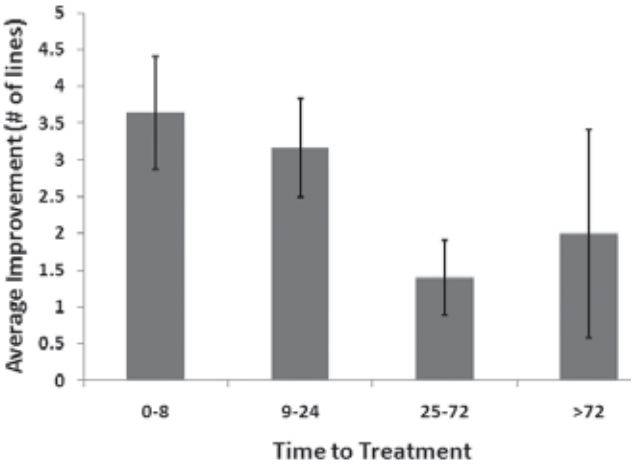
COMBINED CASE SERIES ANALYSIS

The total number of patients treated with HBOT in the combined case series is 51; 11 at DMRC, 19 and 21 respectively in the other two case series.[7,11]

Visual acuity

There was a similar distribution of initial visual acuity to those reported by Hayreh and Zimmerman: two had acuity of 20/50 to 20/100; six had acuity of 20/200 to 20/400 and 43 had vision worse than 20/400. HBOT was associated with improvement in visual acuity independent of the time-to-treatment category (t_{50} = –4.372, $P < 0.001$). Thirty-eight of the fifty-one (75%) of patients who received HBOT had any improvement in visual acuity, which is significant compared to expected spontaneous improvement of 38% (Z score = –4.19, $P < 0.001$; Chi square = 3.841, $P < 0.001$). Twenty-eight patients improved by two incremental values or better on the modified Snellen scale (Z score = –1.92, $P < 0.05$).

Figure 1
Time-to-treatment and improvement in visual acuity; error bars are 1 standard error



Time-to-treatment and improvement

Figure 1 shows the average improvement in visual acuity by time-to-treatment categories. Seventeen patients were treated within 8 hours of visual loss and 13 improved. Twenty of 25 patients treated within 9–24 hours after visual loss improved. Four of five patients treated within 25–72 hours improved and two of four patients treated between 73 and 144 hours of visual loss improved.

Discussion

The natural history of RAO is that of irreversible visual loss that traditional treatments have not been successful in regaining, though occasionally there will be spontaneous improvement in vision with no treatment. Of the 99 patients presenting within seven days after RAO reviewed by Hayreh and Zimmerman, 38% had some improvement of vision with no treatment, this being less likely the worse the presenting visual loss.[1] Of 84 patients with visual acuity of counting fingers or less, 15 had cilioretinal artery sparing, and in 10 of these, visual acuity improved spontaneously, whereas only 15 of 69 patients without cilioretinal artery sparing showed improvement.[1]

Local intra-arterial fibrinolysis does not appear to improve outcome more than conservative therapy and has been associated with 37.1% adverse reactions.[6] Treatments such as ocular massage or pharmacologic agents to reduce intra-ocular pressure have failed to improve outcome. Effectiveness of HBOT needs to be measured against spontaneous improvement observed with no treatment. We believe that comparing our combined case series of HBOT patients to the 99 patients reported by Hayreh and Zimmerman is useful and valid.[1] The improved visual acuity following HBOT was significant versus no treatment.

Analysis of our combined case series demonstrated a clear

trend towards poorer recovery if patients presented more than 24 hours following visual loss. Because of the small number of patients in the delayed treatment groups, the results were not statistically significant. Most clinicians believe that the sooner oxygen is restored to ischaemic tissue, the better the outcome. Hayreh et al cite their study in rhesus monkeys showing that RAO lasting for 240 minutes resulted in massive irreversible damage.[13] Patients may not present with complete occlusion proximal to branching of the posterior ciliary arteries and consequentially have a longer interval to irreversible damage. Butler et al cite several case studies reporting patients regaining vision with HBOT treatment delays of up to two weeks, but feel the best evidence is with a delay of less than 12 hour.[2] Hertzog et al noted HBOT was most useful when started within 8 hours of onset of visual loss.[7] Beiran treated all patients with HBOT within 8 hours of symptom onset and found 82% of HBOT patients improved versus 29.7% of no-HBOT controls.[8] Butler et al summarised selection criteria for emergent HBOT.[2] Criteria included patients who presented within 24 hours of acute painless vision loss, had visual acuity of 20/200 or worse with pinhole testing, age over 40 years and no history of recent eye surgery, trauma or "*flashes or floaters prior to visual loss*".[2] Even without an exact linear relationship, our data support those selection criteria, as visual recovery drops dramatically when patients present more than 24 hours following visual loss.

Retinal artery occlusion is an uncommon event and most hyperbaric chambers treat only a few such patients annually. A central registry for RAO would be an effective way to further broaden and strengthen therapy results. The entries should include gender, age, presence of cilioretinal artery, visual acuity before and after HBOT, time from symptom onset to treatment, number of treatments and treatment pressure. Additional data for co-morbidities such as diabetes, hyperlipidaemia, hypertension and prior eye surgery would be useful and may help predict which individuals are more likely to respond to hyperbaric oxygen therapy.

Conclusions

Eight of 11 patients treated for RAO with HBOT between 2005 and 2009 had some improvement in vision. No trends related to co-morbidities such as diabetes, hyperlipidemia, hypertension or previous eye surgery were seen. A combined case series analysis of our data with two other case series concluded that a significantly increased proportion of patients treated with HBOT had improvement in visual acuity compared to historical controls and that visual acuity improved in all time-delay categories. Chances of recovery were much less if patients presented more than 24 h after visual loss, but only nine patients presented after 24 h. We recommend consideration of HBOT for patients who present with recent RAO and hyperbaric centres treating these patients should consider forming a central registry of standardised data to prospectively study their results.

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