

Case Report

Management of central retinal artery occlusion following successful hyperbaric oxygen therapy: case report

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ABSTRACT

Objective: This case report presents a patient with central retinal artery occlusion (CRAO) who was successfully treated with hyperbaric oxygen (HBO₂) but subsequently suffered a recurrence of his visual loss.

Methods: CRAO may be treated successfully with HBO₂ if treatment is undertaken promptly after the onset of vision loss. The goal of HBO₂ therapy is to oxygenate the ischemic inner retinal layers via diffusion from the hyperoxygenated choroidal circulation until recanalization of the central retinal artery occurs.

Results: A 71-year-old man presented with hand motion vision and fundus findings of CRAO in his left eye. Treatment with HBO₂ was initiated approximately 9.5 hours after loss of vision. The patient experienced return of vision to a near-normal level during HBO₂. His vision loss recurred, however, 15 minutes after the HBO₂ session. There was a delay to follow-up HBO₂ treatments, and the improvement of vision that resulted from these subsequent HBO₂ sessions was much less than that experienced during his initial HBO₂ treatment.

Conclusions: Recovery of vision during initial HBO₂ treatment indicated that this patient's retina had not yet suffered irreversible ischemic damage at that point in time. CRAO patients with a good result from initial HBO₂ treatment should be admitted to a stroke center and should have their visual status monitored hourly. Should vision loss recur, aggressive use of intermittent 100% normobaric and hyperbaric oxygen is indicated to preserve retinal function until central retinal artery recanalization occurs. An evidence-based management plan for such patients is presented.

INTRODUCTION

Central retinal artery occlusion (CRAO) is typically a blinding disease with very little chance of spontaneous recovery of vision unless a cilioretinal artery is present [1,2]. Loss of vision is such a disabling condition that every reasonable therapeutic measure should be undertaken to prevent the vision loss from becoming permanent. Hyperbaric oxygen therapy (HBO₂) may be useful in reversing vision loss in at least some cases of CRAO [3-12].

Approximately 60% of the retina is oxygenated by the choroid when breathing air at 1 atmosphere absolute (ATA) of pressure. [9,13,14] HBO₂ works in CRAO (if begun early enough), because hyperbaric oxygen typically allows the entire retina to be oxygenated by diffusion of oxygen from the choroidal vessels despite the vasoconstriction that occurs in retinal arteries in the presence of hyperoxia [5,13-19]. Hyperoxia does not, however, cause vasoconstriction in the choroidal vessels, so hyperbaric oxygen does not cause a reduction in choroidal blood flow [9,20]. CRAO is now an approved indication for HBO₂ as determined by the Hyperbaric Oxygen Therapy Committee of the Undersea and Hyperbaric Medical Society [4]. This group's list of recommended indications is considered the gold standard for approved indications for HBO₂ and is used by many third-party payers to make reimbursement decisions for HBO₂ therapy.

Successful HBO₂ treatment of an eye that has suffered a CRAO is dependent on three factors:

KEYWORDS: central retinal arterial occlusion; CRAO; HBO₂

- 1) hyperbaric oxygen treatment must be undertaken before irreversible damage to the retina has occurred;
- 2) the arterial occlusion is at the level of the CRA – as opposed to the small minority of individuals who present clinically as CRAO patients but actually have occlusions at the level of the ophthalmic artery, which precludes flow to the choroidal vessels as well; and
- 3) the hyperoxygenation is maintained, at least intermittently, until the CRA recanalizes. Once recanalization of the CRA occurs, blood flow to the inner layers of the retina is restored and the ischemia present during the occlusion resolves without the need for supplemental oxygen [4,5].

The optimal post-HBO₂ management for CRAO patients who have responded successfully to their initial HBO₂ therapy has not yet been defined.

REPORT OF A CASE

A 71-year-old male suffered sudden painless loss of vision in his left eye (OS) at approximately 5:30 in the afternoon. His vision loss was described as “completely black” initially, but evolved to a “uniform gray” after about two hours. Past ocular history was positive for two transient episodes of vision loss OS. The more recent of these two episodes was approximately two years prior to his presentation.

Pertinent medical history included a history of aortic valve replacement in 1998 and estrogen therapy for prostate cancer. There was no history of hypertension, hyperlipidemia, or diabetes mellitus noted. When seen in the eye clinic at 8:00 p.m. the same evening, his vision was found to be hand motion at five feet. He had fundus findings typical of CRAO, and he was treated with ocular massage, timolol drops, and acetazolamide without improvement. The patient was subsequently referred for emergent HBO₂.

HBO₂ was undertaken at approximately 3:00 a.m. the next morning, 9.5 hours after the onset of visual loss. During this initial HBO₂ session (2.4 ATA for 115 minutes), the patient reported that his vision returned to normal except for “a single small dark spot” near the center of his vision in the left eye. Objective measurement of his vision was not documented at that time. This recovery persisted throughout the HBO₂ session, but 15 minutes after returning to 1 ATA and resuming air breathing, his vision loss recurred. He was not treated with either a second HBO₂ session or supplemental normobaric oxygen at that time.

The patient was seen several hours later the same morning in the eye clinic of the referring hospital. He reported no improvement of vision since his recurrence of vision loss shortly after exiting the chamber. His vision OS was again found to be hand motion at five feet. Vision in the right eye was 20/20. Fundus exam OS revealed a cup/disc ratio of 0.3, with 1+ optic disc pallor noted. There were no retinal hemorrhages. The retinal arterioles were markedly narrowed and segmented throughout. Although there was no significant retinal whitening at this point, intravenous fluorescein angiogram (IVFA) performed that morning confirmed a CRAO OS. Visual fields were not done because of the patient’s anticipated difficulty in maintaining central fixation with his reduced level of visual acuity. Repeat HBO₂ was felt to be indicated because of the initial success with this treatment modality, and the patient was referred for follow-up HBO₂. A medical workup for systemic diseases associated with CRAO was undertaken as well.

The patient’s second HBO₂ session was undertaken approximately six hours after surfacing from his first treatment. He underwent five additional HBO₂ sessions (details regarding the depths and times of these five follow-up treatments are not available) over the next three days. There was no improvement of vision equivalent to the marked improvement that occurred during the initial HBO₂ session, although the patient did notice some improvement in his peripheral field OS, especially superiorly.

His visual acuity at follow-up on 15 October 2008 was count fingers (distance not specified), with the patient using his peripheral vision to achieve that level of visual acuity. There was a 2+ afferent pupillary defect (APD) OS. His work-up for systemic diseases was negative except for his known cardiac valvular disease.

DISCUSSION

Observations from the literature

In an animal model, the retina can tolerate complete loss of blood flow to the central retinal artery and choroid for 105 minutes before retinal cell death occurs [21]. In the clinical setting of CRAO, however, obstruction of retinal blood flow may not be complete [22,23]. This difference between the animal model studied and the clinical situation may be responsible for reports of visual recovery with HBO₂ despite

delays to treatment well beyond the 105-minute time window described by Hayreh and often quoted in the ophthalmology literature.

No interventions, including HBO₂, are of benefit once retinal cell death has occurred [5]. The central retinal artery typically recanalizes hours to days after the occlusion in CRAO [2,22], but vision will not return if blood flow is re-established to a non-functioning retina [23]. Observed times for presumed or observed retinal recanalization reported in the literature range from 4.5 hours to 72 hours [5,14]. Since CRAO is typically a painless disorder and the patient may be unaware of vision loss because of good vision in the fellow eye, many affected patients do not seek medical attention immediately and have already suffered irreversible retinal damage by the time they present for evaluation. This fact, as well as the general lack of awareness in the ophthalmology and emergency medicine communities about the effectiveness of HBO₂ in CRAO as well as the paucity of hyperbaric chambers that are willing to provide 24-hour emergency treatment, all contribute to HBO₂ being very much underused in CRAO at this point in time. HBO₂ is not even mentioned as a treatment option in the 2016 American Academy of Ophthalmology Preferred Practice Pattern for CRAO [24].

HBO₂ is not always required to restore retinal function in CRAO. The use of normobaric hyperoxia has been shown to restore vision and prevent retinal cell death in some CRAO patients [14,25]. When normobaric oxygen is able to improve retinal oxygenation sufficiently for significant improvement in vision to occur, the improvement in vision usually occurs within several minutes. Vision is likewise typically lost rapidly when supplemental oxygen is removed [14,25]. Patz reported two CRAO patients treated with supplemental oxygen at 1 ATA. The first had a four-hour delay after visual loss had occurred before oxygen was administered, but still improved from 4/200 to 20/70. This improvement was maintained after supplemental oxygen therapy was discontinued four hours later. The second patient was treated with supplemental normobaric oxygen after a delay of 90 minutes after the onset of vision loss. Once oxygen was begun, vision improved from no light perception to 20/200. This improvement in vision was maintained when oxygen was discontinued three hours later. In both patients, early discontinuation of oxygen was followed by recurrent vision loss within minutes. As soon as

supplemental oxygen was resumed, however, the improvements in vision were restored. This phenomenon was observed several times in both patients [5,14]. Intermittent supplemental normobaric oxygen given 10 minutes of every hour has also been shown to prevent retinal cell death in some CRAO patients. Patients in two case series were given carbogen, a mixture of 95% oxygen and 5% carbon dioxide. These patients' vision did not always improve during the periods of oxygen administration, but vision returned to normal or near-normal levels hours to days later when the CRA recanalized [26,27]. Return of normal or near-normal vision is a reliable indicator of adequate retinal oxygenation and viability when supplemental normobaric oxygen is breathed, but there is no assurance that retinal cell death will be prevented (or has not already occurred) if intermittent hyperoxia does not produce improvement in vision during the period of hyperoxia.

Air breaks are useful in preventing the onset of pulmonary oxygen toxicity, which may complicate hyperoxic therapy, either at one atmosphere or in a hyperbaric setting [28]. The duration of hyperoxia required to cause pulmonary oxygen toxicity is a function of the partial pressure of inspired oxygen. The higher the partial pressure of oxygen, the more rapid the onset of pulmonary toxicity. No benefit has been documented from providing oxygen at a higher partial pressure than that sufficient to produce normalization of vision in CRAO patients

HBO₂ has been shown to restore vision and prevent retinal cell death in CRAO after normobaric oxygen has been ineffective [8]. The optimal HBO₂ regimen for the initial treatment of CRAO with hyperbaric oxygen has not been well defined and may, in fact, vary based on the degree of CRA occlusion and the degree to which the individual patient's retina is oxygenated by the choroidal circulation. With the objective of providing treatment at relatively lower partial pressures of oxygen if that is effective in restoring vision, a stepwise approach that begins with a treatment pressure of 2.0 ATA and proceeds to a pressure of 2.8 ATA has been recommended [6].

As mentioned previously, however, no benefit from either normobaric hyperoxia or HBO₂ will be obtained if the occlusion is at the level of the ophthalmic artery or if retinal cell death has occurred before the initiation of hyperoxic therapy [5,6].

Comments on this case

The interval from onset of symptoms to initial recompression was 9.5 hours in this patient. Hertzog and colleagues have documented that improvement of vision in CRAO is more likely if HBO₂ is undertaken within eight hours of vision loss [2]. The presence of the classic fundus finding of a “cherry-red spot” has been reported to be an indication that ischemia has been present for some time and to be an unfavorable prognostic indicator [3]. The time interval before damage to the retina becomes irreversible varies, however, as a function of the degree of CRA obstruction, as noted previously. This patient had a good return of vision at depth during his initial HBO₂ treatment, which provides clinical evidence that his retina was still viable when HBO₂ was undertaken. The decrease in vision shortly after HBO₂ was terminated indicates that:

- 1) his CRA had not recanalized at that point; and
- 2) that the amount of oxygen reaching the inner layers of the retina from his choroidal circulation while breathing room air was not sufficient to sustain retinal function.

Supplemental oxygen breathing at 1 atmosphere was not attempted, and it is unknown whether this intervention would have resulted in an immediate return of vision or, when used intermittently as described above, would have resulted in return of vision at the point of time that his retina recanalized.

The interval from the end of his first treatment to the start of the second HBO₂ session was approximately six hours. The failure of the patient's vision to improve at depth during the second HBO₂ session and subsequent treatments indicates that at some point between the end of his first treatment and the beginning of the second, irreversible retinal damage occurred.

Defining optimal management of CRAO patients after a successful initial HBO₂ treatment

The challenge that this case highlights is the need to define as precisely as possible the optimal management of a patient who has sustained a CRAO and has had a good response during his or her initial HBO₂ treatment. The fact that the patient experienced significant recovery of vision during the initial HBO₂ treatment indicates that:

- 1) the patient was fortunate enough to have a hyperbaric oxygen chamber in his vicinity that is willing to treat emergency patients. Many hyperbaric chambers will not accept emergency patients on the basis of organizational business decisions [29]; and that
- 2) the inner retinal layers were capable of recovery at the time that the HBO₂ treatment was initiated.

The guiding principles of management for such patients, whose vision can be saved with proper management, are to closely monitor visual function and to provide supplemental oxygen at a partial pressure sufficiently high to maintain retinal viability without inducing pulmonary oxygen toxicity until the CRA recanalizes. After recanalization occurs, supplemental oxygen is no longer needed to maintain the patient's visual recovery.

Following the successful initial HBO₂ session, the patient should be kept in the chamber treatment area and his or her vision checked after 15 minutes of air breathing at 1 ATA. Since the need for immediate HBO₂ often precludes pretreatment ophthalmic consultation, vision should be measured as precisely as possible in the Emergency Department as well as during and after the HBO₂ treatment. A near vision card is a good option for checking central visual acuity if a standard eye chart is not available. Since measurement of the peripheral visual field is difficult in these settings, the subjective input of the patient is important. If the patient has a definite but subjective improvement in his or her peripheral vision with the initial HBO₂ treatment, that should be considered a positive response.

Patients with sustained good visual recovery at the 15-minute point after their initial HBO₂ treatment should be admitted immediately to a nearby hospital, ideally a stroke center, so that they can be evaluated for potential associated systemic disease and to determine the ongoing risk for further cerebrovascular ischemic events [24]. Vision should be monitored hourly and documented. In the hospital setting, the best way to check visual acuity at the bedside is with a near vision card, making sure to use the patient's refractive prescription with a reading correction (that is – their bifocals or reading glasses). Emergent ophthalmology consultation should also be obtained and an intravenous fluorescein angiogram performed to assess the status of the CRA. If the patient's visual recovery is sustained for 24 hours and the systemic and cerebrovascular evaluation has

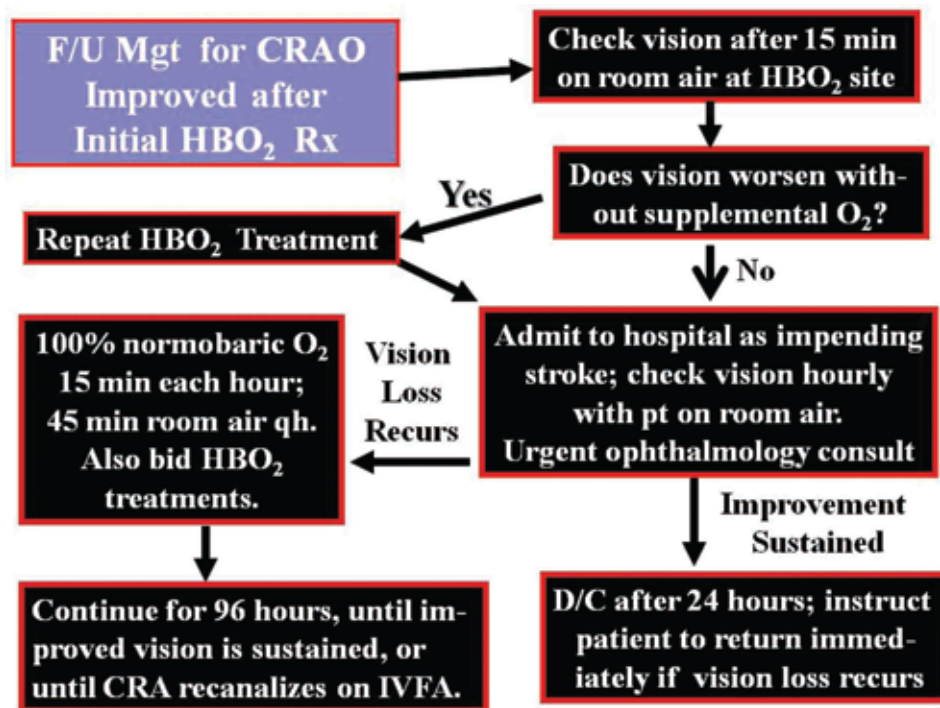


FIGURE 1: Recommended follow-up management of CRAO patients who have had good recovery of vision from their initial HBO₂ treatment

bid – twice a day; CRA – central retinal artery; CRAO – central retinal artery occlusion; D/C - discharge; F/U – follow-up; HBO₂ – hyperbaric oxygen; IVFA – intravenous fluorescein angiogram; min - minutes; O₂ – oxygen; Pt – patient; QH – every hour; Rx – treatment

been completed, he or she may be discharged with instructions to return immediately if vision loss recurs.

If the patient’s vision loss recurs, however, while the patient is breathing normobaric air during the 15-minute waiting period in the hyperbaric chamber area, the initial successful HBO₂ treatment should be repeated if feasible. Following the second HBO₂ treatment, the patient should be admitted to a hospital, as described above.

If vision loss is still present or recurs while breathing room air in the hospital, normobaric supplemental oxygen should be started at the highest oxygen fraction attainable. Near-100% inspired fraction of oxygen is achievable using an oxygen mask with a reservoir bag and an oxygen flow rate of 15 liters/minute. The supplemental oxygen should be continued for 15 minutes, then stopped. Oxygen breathing periods should be alternated with 45-minute periods of air breathing. This pattern of intermittency was derived from that

used in reports of success in treating CRAO with intermittent carbogen (a mixture of oxygen and carbon dioxide) [2,26,27]. Supplemental oxygen is not breathed during the 45-minute air breaks because:

- 1) air breaks are needed to reduce the likelihood of pulmonary oxygen toxicity; and
- 2) the retina can survive 45 minutes without supplemental oxygen – as long as oxygen breathing is used at hourly intervals to restore the oxygen supply to the ischemic inner retinal layers [2,26,27].

These alternating periods of 15 minutes of supplemental oxygen breathing and 45 minutes of room air breathing should be continued around the clock and supplemented with twice-a-day HBO₂ treatments [12]. While this is admittedly an intensive regimen for both staff and patient, in the specific setting of an eye that is at risk but potentially salvageable, it is a reasonable course of action to undertake. Although this treatment is recommended up to a maximum of 96 hours, recanal-

ization of the CRA typically occurs well before this time, sometimes within just a few hours [8]. Emergent ophthalmology consultation should also be obtained and an intravenous fluorescein angiogram performed to assess the status of the CRA. Intermittent 100% oxygen breathing should be continued during the ophthalmic consultation.

The regimen above should be continued until either the improvement in vision is stable without supplemental normobaric or hyperbaric oxygen or until the consulting ophthalmologist and the hyperbaric physician decide that retinal cell death has occurred and that further oxygen therapy is futile. The longest interval from onset of visual loss in CRAO until spontaneous recovery of vision in a patient who was managed with intermittent hyperoxia was reported by Duker. He described a CRAO patient who presented five hours after the onset of visual loss and who was then given carbogen for 10 minutes every hour around the clock for four days. There was no improvement of vision during the oxygen administration periods, but at 96 hours after initial loss of vision, his vision returned spontaneously and was sustained at 20/30 one week after recovery [2].

The algorithm in Figure 1 summarizes the evidence-based management outlined above in a therapeutic approach that optimizes the likelihood of a good outcome in patients who have suffered a CRAO and have had a good recovery of vision during their initial HBO₂ treatment. This treatment protocol has been developed in response to the case described in the present report. Whether its use would have improved the out-

come for the patient reported is unknown, but this approach incorporates established principles of hyperbaric oxygen therapy and evidence from previously published reports in which variations of this protocol have produced good results in CRAO patients.

The efficacy of this treatment plan is again contingent upon a demonstrated positive clinical response during the first HBO₂ session – which is clinical evidence of retinal viability. Additional clinical experience is needed to further refine the management of this subset of CRAO patients who have the potential for a good visual recovery. ■

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Disclosures

Dr. Murphy-Lavoie and Dr. Van Hoesen are attending physicians at hyperbaric oxygen facilities.

Disclaimers

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Release

This document was reviewed by the Public Affairs Office and the Operational Security Office at the U.S. Army Institute of Surgical Research. It is approved for unlimited public release.

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