CENTRAL RETINAL ARTERY OCCLUSION

Heather Murphy-Lavoie, Frank Butler and Catherine Hagan

Background

Central retinal artery occlusion is a relatively rare emergent condition of the eye resulting in sudden painless vision loss. This vision loss is usually dramatic and permanent and the prognosis is poor. Patients particularly at risk include those with giant cell arteritis, atherosclerosis, and thromboembolic disease, a wide variety of treatment modalities have been tried over the last one hundred years with little to no success, with the exception of hyperbaric oxygen therapy.

Rationale For Hyperbaric Oxygen Therapy (HBO) In The Management Of Central Retinal Artery Occlusion (CRAO)

The arterial blood supply to the eye is provided by the ophthalmic artery, one of the branches of cavernous portion of the internal carotid artery. Some of the branches of the ophthalmic artery (lacrimal, supraorbital, ethmoidals, medial palpebral, frontal, dorsal nasal) supply orbital structures, while others (central artery of the retina, short and long posterior ciliaries, anterior ciliaries) supply the tissues of the globe.[1] The central retinal artery enters the globe within the substance of the optic nerve and serves the inner layers of the retina through its many branches. The long posterior ciliary arteries provide blood to the choroid and the outer layers of the retina. There are approximately twenty short posterior ciliary arteries and usually two long posterior ciliary arteries. The posterior ciliary vessels originate from the ophthalmic artery and supply the entire uveal tract, cilioretinal arteries, the sclera, the margin of the cornea, and the adjacent conjunctiva. The anterior ciliary arteries also arise from the ophthalmic artery, supply the extraocular muscles, and anastamose with the posterior ciliary vessels to form the major arterial circle of the iris, which supplies the iris and ciliary body.

The visual signs and symptoms of vascular occlusive diseases of the retina are dependent on both the particular vessel occluded, the degree of occlusion, the location of the occlusion, and the presence or absence of a cilioretinal artery. In approximately 15%-30% of individuals, a cilioretinal artery is present. This artery is part of the ciliary (not retinal) arterial supply but supplies the area of the retina around the macula (central vision area.) If a cilioretinal artery is present, central vision may be preserved in central retinal artery occlusion (CRAO). The outcome of these disorders also depends on the vessel occluded and the degree of occlusion, but also on the time interval until therapy is initiated and the presence of alternate sources of oxygen to the ocular tissues.

In CRAO, the inner retinal layers (ganglion cell layer and inner nuclear layer), which are normally served by the retinal circulation, may obtain enough oxygen via diffusion from the choroidal circulation to function normally if the individual is exposed to elevated partial pressures of oxygen. Animal models have shown the choroidal supply of oxygen to the inner layers of the retina may be sufficient to maintain ganglion cell viability even when the retinal vessels have been completely obliterated.[2] Normally, the choroidal circulation supplies the majority of the oxygen to the retina. Under normoxic conditions, approximately 60% of the

retina's oxygen comes from the choroidal circulation. Under hyperoxic conditions, the choroid is capable of supplying 100% of the oxygen needed by the retina.[3]

In considering the effect of treating CRAO with supplemental oxygen, four key factors determine success: 1) therapy must be initiated before the retinal tissue is irreparably damaged; 2) the degree of occlusion of the blocked vessel may vary - this may account for why some patients respond to oxygen at lower partial pressures than others; 3) some patients may not respond to oxygen therapy, even if it is initiated promptly, if the level of occlusion is at the ophthalmic artery because in this event, the blood supply to the posterior ciliary vessels is blocked as well and there is no alternate choroidal blood supply to provide oxygenation of the inner layers of the retina; and 4) an adequate partial pressure of oxygen must be maintained to keep the retina viable until circulation is restored.

The etiology of the arterial occlusion (thrombosis, embolus, arteritis, vasospasm) has also been described as affecting outcome.[4,5] Careful classification of the factors involved in an individual case of CRAO is crucial to understanding the natural outcome and results of therapy. In the largest published series of CRAO patients, Hayreh describes the natural progression of this condition without hyperbaric oxygen therapy. He found that patients with transient CRAO (resolution of symptoms in minutes to hours) and those with cilioretinal arteries had much better outcomes than those who did not. In those patients without cilioretinal arteries, 80% had a final outcome of counting fingers or less and only 1.5% of them obtained a final vision of 20/40 or better.[5]

Recanalization occurs in retinal vessels after CRAO.[6,7] In relatively few cases, however, does this angiographic reperfusion lead to an improvement of vision.[7] The retina has the highest rate of oxygen consumption of any organ in the body at 13ml/100g/min.[8,9] Therefore, it is very sensitive to ischemia. In order to be effective, the administration of supplemental oxygen must be continued until such time as flow through the retinal artery has resumed to a level sufficient to maintain inner retinal viability under normoxic conditions.

Patient Selection Criteria

The classic presentation of CRAO is sudden painless loss of vision in the range of light perception to counting fingers. In the case of no light perception, it must be considered that the patient may have an ophthalmic artery occlusion and therefore no choroidal blood supply either. In the case of much better visual acuity the presence of a cilioretinal artery supply is likely.

On dilated fundoscopic exam patients with CRAO will classically have a pale yellow/white appearing retina due to ischemia or necrosis. A cherry red spot may develop in the macula but may not always be present. Other physical exam findings may include: an afferent pupillary defect and boxcarring of arterioles.

Patients presenting within 24 hours of symptoms onset should be considered for hyperbaric oxygen therapy. While there are a few case reports of patients presenting after this time interval having positive results when treated with hyperbaric oxygen therapy, the majority of cases do not respond when treated beyond this point.[8,12,13,14,15,16]

While it makes intuitive sense that patients with branch occlusions and central retinal vein occlusions may also benefit from hyperbaric oxygen therapy, there is insufficient data in the literature to support this as a routine recommendation.[10,11,12]

Clinical Management

Patients who present with sudden painless loss of vision due to CRAO should be triaged "Emergent" because of the need for immediate oxygen therapy. Visual acuity should be documented as soon as possible. If decreased vision is confirmed, the emergency physician should immediately perform a fundoscopic exam, using dilation if feasible and not contraindicated. An ophthalmologist and / or neurologist should be consulted, but treatment should not be delayed awaiting their arrival. Fundoscopic findings of CRAO should trigger management as below if onset of signs and symptoms was 24 hours or less. Oxygen delivery should be titrated to patient response as follows:

1. Deliver oxygen immediately at one ATA at the highest possible FiO2
2. Refer for hyperbaric oxygen therapy if no response within 5 minutes
3. Compress to 2 ATA on 100% oxygen
4. Other adjunctive therapies to lower intraocular pressure and/or cause retinal vasodilatation may be performed as well, but should not delay compression. If vision improves, do 90 minutes at 2 ATA BID for a minimum of 3 days.
5. If no response within 5 minutes, press to the depth of visual improvement with a maximum of 2.8 ATA. If no improvement at 2.8 ATA after a 20-minute breathing period consider following a USN Table 6. If vision improves, treat at depth of improvement for 90 minutes BID.
6. For facilities without air-break capacity, it is a next best alternative to replace USN Table 6 with the Kindwall Table [2.8 ATA for 30 min, 15 min ascent to 2 ATA for 60 min., then 15 min. ascent to surface – roughly equivalent to USNTT5].
7. Continue daily BID recompression until there are three consecutive days with no visual improvement. If the patient is a non-responder, this will be the first three days of treatment.
8. If the patient responds to oxygen at 1 ATA and hyperbaric oxygen is not necessary, treat on 100% non-rebreather for 12 hours and then titrate off as tolerated.

Evidence-Based Review - HBO And CRAO

The typical presenting symptom of CRAO is a sudden and profound loss of vision. If a cilioretinal vessel to the macula is present and not affected, then central vision may be spared. Possible causes of retinal arterial occlusive disease include atherosclerosis-related thrombus, embolism, vasospasm and giant cell arteritis. A CRAO with significant visual loss is an ophthalmic emergency. Treatment should be aimed at promptly supplying oxygen to the ischemic retina at a partial pressure sufficient to maintain viability while medically assisted or spontaneous restoration of central retinal artery blood flow occurs.

Traditional therapeutic regimens for CRAO have been aimed at promoting a downstream movement of the embolus by lowering intraocular pressure and producing vasodilatation. These measures include ocular massage, anterior chamber paracentesis, intraocular pressure lowering medications, vasodilators, and oral diuretics.[7,8,17] These treatment modalities have been relatively unsuccessful.[7,17,18] Acute obstruction of the central retinal artery, even when treated promptly, typically results in severe, permanent visual loss[5,7] Hayreh stated that no currently used therapy is efficacious for CRAO.[5,19]

More recent treatment modalities include thrombolytic agents[20,21,22] and surgical removal or the embolus or thrombus.[23,24] One study reporting the limited success of thrombolytics used in conjunction with intraocular-pressure lowering medications, anterior chamber paracentesis, and methylprednisolone included only patients seen within 48 hours of onset of symptoms and noted that all eight patients in whom visual acuity improved had symptoms for less than 12 hours.[21]

Supplemental oxygen therapy has been used in conjunction with the above regimens. When retinal arterial flow is interrupted, the retinal tissue undergoes a period of ischemia. Blood flow is usually re-established via recanalization, but if ischemia and hypoxia have resulted in cell death and necrosis in the inner layers of the retinal supplied by the retinal artery, vision may not return when blood flow is re-established.[25] The period of time during which the tissue is ischemic, yet capable of recovery, is called the ischemic penumbra.[25]

Supplemental oxygen need not always be provided at hyperbaric pressures to successfully reverse retinal ischemia in CRAO. One patient suffered a CRAO in his only seeing eye and presented within approximately one hour of vision loss to the Emergency Department, where he was found to have vision of 20/400 and fundus findings typical of a CRAO. He was treated with oxygen supplied by a non-rebreathing mask at one atmosphere in the ED, and his vision quickly improved to the 20/25 level. After a period of approximately 5 minutes, the supplemental oxygen was removed, whereupon vision equally quickly returned to 20/400. This process was repeated several times to confirm the efficacy of the supplemental oxygen with the same results. The patient was then hospitalized, anticoagulated, and maintained on supplemental oxygen for approximately 18 hours, after which his central retinal artery presumably recanalized, since removal of the supplemental oxygen at that point no longer caused a drop in vision. He was discharged with a visual acuity of 20/25 in his only seeing eye.[26]

Patz reported improvement in two CRAO patients given oxygen at 1 ATA. One patient received oxygen after a four-hour delay to therapy and improvement was maintained after oxygen was discontinued 4 hours later. The second patient improved significantly after a delay to treatment of 90 minutes and maintained this improvement when oxygen was discontinued 3 hours later. In both patients, early discontinuation of oxygen was followed by deterioration of vision within minutes and visual recovery when oxygen breathing was resumed shortly thereafter. This phenomenon was observed several times in both patients.[2]

Stone et al reported two patients with CRAO of greater than 6 hours duration treated with intermittent carbogen (95% oxygen and 5% CO2), retrobulbar anesthesia, and anterior chamber paracentesis. The first patient had vision loss of 6 hours duration. His vision improved from hand motion to 20/20 on the above therapy, with carbogen being administered for 10 minutes every

hour. The second patient presented 8 hours after onset of visual loss and had improvement from finger counting to 20/25. Carbogen was administered 10 minutes every hour for 48 hours.[17]

Of note is that carbon dioxide was added to the oxygen to help prevent retinal vasoconstriction in the cases above. Elevated partial pressures of oxygen cause retinal artery vasoconstriction.[27,28,29] Carbon dioxide is added to the gas mix in carbogen to counter this effect through its vasodilatation of retinal vessels. If the mechanism of improved oxygenation to the retina is diffusion from the choroidal circulation, however, then the addition of carbon dioxide should be of little benefit, since unlike retinal blood flow, choroidal blood flow is not significantly affected by changes in oxygen tension.[3,29] The hyperoxygenation of the choriocapillaris was noted to more than offset the reduced retinal blood flow as observed by the appearance of arterialized bright red blood in the retinal veins during HBO.[27]

The study published by Augsberger and Magargal in 1980 was notable in that it demonstrated the criticality of the time to oxygen treatment in successful outcome. They used paracentesis, ocular massage, carbogen, acetazolamide, and aspirin to treat 34 consecutive cases of CRAO. Twelve of the 34 patients were successfully treated, with 7 of the 12 having been treated within 24 hours of onset of symptoms. The longest delay to treatment in which treatment was considered successful was 72 hours. The average delay to therapy in the patients with successful outcomes was 21.1 hours, compared to 58.6 hours in those who did not improve. Carbogen inhalation was conducted for 10 minutes every hour during waking hours and 10 minutes every 4 hours at night and continued for 48-72 hours in these patients.[14]

One remarkable case described a patient with angiographically documented obstruction of both the central retinal artery and his temporal posterior ciliary artery.[7] He presented after 5 hours of visual loss with minimal light perception vision. In addition to ocular massage, anterior chamber paracentesis, timolol, and acetazolamide, he was given carbogen for 10 minutes every hour around the clock. His vision did not improve significantly during his three days of hospitalization, but improved spontaneously approximately 96 hours after onset of vision loss. His vision in the affected eye was documented to be 20/30 one week after discharge. Although the authors of this case report do not necessarily ascribe his recovery to any one of treatments used,[7] the role of supplemental oxygen in maintaining retinal viability must be considered. Rarely patients with CRAO improve spontaneously.[7]

If hyperoxia at one atmosphere is not effective in reversing vision loss in CRAO, emergent compression and 100% oxygen breathing should be undertaken. Phillips et al reported a 71 year-old white female patient with CRAO in whom surface oxygen was ineffective in restoring "total" vision loss of approximately 2 hours duration.[30] Initial treatment with supplemental oxygen at one atmosphere did not reverse this vision loss. The patient was then recompressed on 100% oxygen. As she passed 15 feet during her descent, light perception was restored and the end of the first air break at 2.4 ATA reported full vision. She was discharged with a visual acuity of 20/30 in her only seeing eye and a 2+ afferent papillary defect noted prior to treatment had resolved after treatment.

The timing of HBO therapy is critical in CRAO. There is a threshold of time beyond which ischemic tissue can no longer recover from a hypoxic event even if reperfusion occurs.[3] Hayreh

et al reported a study in which the ophthalmic artery of rhesus monkeys was completely occluded for varying periods of time. Retinas exposed to greater than 105 minutes without blood flow showed permanent damage. If the duration of occlusion was kept to less than 97 minutes, the retinas returned to normal when evaluated by multiple different tests.[31]

In the clinical setting of CRAO, however, some residual retinal blood flow has been detected by fluorescein angiogram.[6,14] This may help explain the great variability in visual outcome with different time delays until treatment. Ideally, the shorter the time delay until treatment, including HBO, the better the likelihood of recovering ischemic retina that is threatened but viable.[3,14,42] Ophthalmology literature includes cases in which humans with a CRAO have regained significant vision even when treatment was delayed for periods of up to two weeks[34] with the strongest evidence for symptomatic improvement in cases with less than 12 hours of delay.[3,8,16,32] It is impossible for the clinician to predict who may recover spontaneously or who may suffer irreversible vision loss.[35]

Hertzog et al reported a series of 17 patients with CRAO treated with HBO. They retrospectively divided patients into 4 treatment groups based on the time to onset of treatment and noted that HBO seemed useful in preserving visual function when applied within the first 8 hours from the onset of visual impairment. The patients in this study were treated for 105 minutes of oxygen at 2.0 ATA three times a day until they ceased to show improvement in visual acuity or for 3-4 days if no improvement occurred, receiving a mean of 29.3 hours of HBO early in the study and 34.6 hours later in the study. The authors point out that the colloquialism "Time is Muscle" used in management of myocardial infarctions can be changed to "Time is Vision" in CRAO.[8]

Another paper demonstrated success in treating three cases of CRAO presenting shortly after symptom onset. One patients treated 90 minutes after onset of visual loss had vision improve from light perception to counting fingers after the first 10 minutes of HBO with subsequent improvement to 20/70 following five days of two 90-minute HBO treatments at 2.5 ATA daily for 5 days. Another presented 40 minutes after visual loss and improved from hand movement to 20/20 after 12 treatments at 2.5ATA in 9 days. A third patient presented 4 hours after the onset of symptoms with finger-counting vision. He received ten 90-minute HBO treatments at 2.5 ATA with gradual improvement of visual acuity to the 20/30 level. A last patient who was treated with HBO 6 hours after symptom onset showed no significant improvement in vision.[32]

In 2001, Beiran published a retrospective controlled trial of 35 patients treated with hyperbaric oxygen therapy compared to 37 matched controls from another facility where hyperbaric oxygen was not available.[33] All patients were treated within 8 hours of symptom onset and none of the patients included in the trial had a cilioretinal artery. The patients in the hyperbaric group received 2.8ATA for 90 minutes BID for the first three days and then once daily until no further improvement for 3 consecutive days. In the hyperbaric group, 82% of the patients improved compared to only 29.7% of patients in the control group. Improvement was defined as reading at least 3 lines better on Snellen chart compared to admission. The mean visual acuity for the hyperbaric group at discharge was 6/20 in metric or about 20/70 in feet.

As with oxygen administration at one ATA, hyperbaric oxygen must be started within the time interval that retinal tissue can still recover.[7] Reports, which describe failure of HBO,

sometimes fail to note the delay to therapy,[28] and HBO therapy in these cases may have been started after the time window for successful treatment had passed. Miyake reported on 53 cases of CRAO and 19 branch occlusions treated with HBO over a 13 year period. He found no significant difference between time to treatment and response to HBO; however, only 3 of these patients received HBO within 24 hours of symptom onset. Overall 44% of his patients showed improvement of at least 2 levels on the visual acuity scale after treatment with HBO despite this delay to treatment. Unfortunately, no distinction was made between patients with cilioretinal arteries and transient occlusions and those without.[15]

These cases make it apparent that some patients with CRAO can be treated successfully with hyperoxia, either at 1 ATA or with HBO. Patients with sudden painless loss of vision should report to the nearest medical facility as soon as possible. Triage nurses should be aware that sudden painless loss of vision of less than 24 hours duration is an emergency that should be triaged for immediate examination by the emergency physician. If the patient is found to have exam findings consistent with CRAO, the patient should immediately be started on the highest possible fraction of inspired oxygen.[2,7,14,17,35] Visual recovery should occur within minutes if surface oxygen is to be sufficient. If vision is not restored, there should be consideration (ideally in consultation with ophthalmology and neurology) of emergent referral to the nearest recompression facility and the patient should bemaintained on supplemental oxygen at the highest possible FiO_2 until arrival.

Based on the American Heart Association classification of evidence, treatment of CRAO with hyperbaric oxygen therapy is level IIb. There is fair to good evidence to support its use with retrospective case series but no prospective randomized controlled trials. It is acceptable, safe, considered efficacious but lacks confirmation of efficacy by level 1 studies. There is no evidence of harm and consistently positive results. In addition, there are no alternative therapies with similar outcomes.[18,19] The relatively rare incidence of this condition does not lend itself to randomized controlled trials as evidenced by the paucity of trials for other therapies in treating this condition. As of 2006, a Medline search revealed only 2 very small randomized controlled trials for all of the proposed therapies. The hopeless and recalcitrant nature of this condition when left untreated mandates we utilize all potentially helpful treatments including hyperbaric oxygen therapy.

Utilization Review

The optimum number of treatments will vary depending on the severity and duration of the patient's symptoms and the degree of response to treatment. The majority of patients will stabilize within one week of symptom onset. Utilization review is recommended for patients treated for more than three days after clinical plateau and no further improvement.

Economic Impact

There are no formal cost analyses for this condition in the literature; however, the treatment cost for a hyperbaric oxygen therapy is approximately $500 per 90-minute treatment (based on 2006 Medicare reimbursement rates). If each CRAO patient received 14 treatments the cost would be $7000 per patient. This is a very reasonable price to pay to restore a patient's vision.

References

1. Cibis, GW, Beaver HA, Johns K et al. Basic and Clinical Science Course: Fundamentals and Principles of Ophthalmology. American Academy of Ophthalmology, San Francisco 2006; 38-40.
2. Patz A. Oxygen inhalation in retinal arterial occlusion. *Am J Ophthalmol* 1955; 40: 789-795.
3. Li HK, Dejean BJ, Tang RA. Reversal of visual loss with hyperbaric oxygen treatment in a patient with Susac Syndrome. *Ophthalmology* 1996; 103(12): 2091-2098.
4. Stone R, Zink H, Klingele T, Burde R. Visual recovery after central retinal artery occlusion: Two cases. *Ann Ophthalmol* 1977; 9: 445-450.
5. Hayreh SS, Zimmerman MB. Central retinal artery occlusion: Visual outcome. *Am J Ophthalmol* 2005; 140: 376-391.
6. David NJ, Norton EWD, Gass JD, Beauchamp J. Fluorescein angiography in central retinal artery occlusion. *Arch Ophthal* 1967; 77: 619-29.
7. Duker JS, Brown GC. Recovery following acute obstruction of the retinal and choroidal circulations. *Retina* 1988; 8(4): 257-260.
8. Hertzog LM, Meyer GW, Carson S, Strauss MB, Hart GB. Central retinal artery occlusion treated with hyperbaric oxygen. *J Hyperbaric Medicine* 1992; 7: 33-42.
9. Jain KK. Textbook of Hyperbaric Medicine. Hogrefe&Huber, 4th edition revised 2004; 383-392.
10. Roy M, Bartow W, Ambrus J, Fauci A, Collier B, Titus J. Retinal leakage in retinal vein occlusion: Reduction after hyperbaric oxygen. *Ophthalmologica* 1989; 198: 78-83.
11. Miyake Y, Awaya S, Takahashi H, et al. Hyperbaric oxygen and acetazolamide improve visual acuity in patients with cystoid macular edema by different mechanisms. *Arch Ophthalmol* 1993; 111: 1605-1606.
12. Murphy-Lavoie, H, Harch, P, VanMeter, K. Effect of hyperbaric oxygen on central retinal artery occlusion. UHMS Scientific Assembly, Australia, 2004.
13. Anderson B, Saltzman H, Heyman A. The effects of hyperbaric oxygenation on retinal arterial occlusion. *Arch Ophthal* 1965; 73: 315-319.
14. Augsburger JJ, Magargal LE. Visual prognosis following treatment of acute central retinal artery obstruction. *Br J Ophthalmol* 1980; 64: 913-917.
15. Miyake Y, Horiguchi M, Matsuura M, et al. Hyperbaric oxygen therapy in 72 eyes with retinal arterial occlusion. 9th International symposium on underwater and hyperbaric physiology. Undersea and hyperbaric medical society, Bethesda, MD, 1987; 949-953.
16. Yotsukura J, Adachi-Usami E. Correlation of electroretinographic changes with visual prognosis in central retinal artery occlusion. *Ophthalmologica* 1993; 207: 13-18.
17. Stone R, Zink H, Klingele T, Burde R. Visual recovery after central retinal artery occlusion: Two Cases. Ann Ophthalmol 1977; 9: 445-450.
18. Neubauer AS, Mueller AJ, Schriever S, Gruterich M, Ulbig M, Kampik A. Minimally invasive therapy for clinically complete central retinal artery occlusion--results and meta-analysis of literature. *Klin Monatsbl Augenheilkd* 2000 Jul; 217(1):30-6. German.
19. Hayreh SS, Podhajsky P. Ocular neovascularization with retinal vascular occlusion: II. Occurrence in central retinal and branch retinal artery occlusion. *Arch Ophthalmol* 1982;100: 1581-1596.
20. Weber J, Remonda L, Mattle HP et al. Selective intra-arterial fibrinolysis of acute central retinal artery occlusion. *Stroke* 1998; 29: 2076-2079.
21. Rumelt S, Dorenboim Y, Rehany U. Aggressive systematic treatment for central retinal artery occlusion. *Am J Ophthalmol* 1999; 128: 733-738.
22. Petterson JA, Hill MD, Demchuk AM et al. Intra-arterial thrombolysis for retinal artery occlusion: The Calgary experience. *Can J Neurol Sci* 2005; 32: 507-511.
23. Garcia-Arumi J, Martinez-Castillo V, Boixadera A, Fonollosa A, Corcostgui B. Surgical embolus removal in retinal artery occlusion. Br J Ophthalmol 2006; 90:1252-1255.
24. Tang WM, Han DP. A study of surgical approaches to retinal vascular occlusions. *Arch Ophthalmol* 2000; 118: 138-143.
25. Mangat HS. Retinal artery occlusion. *Surv Ophthalmol* 1995; 40: 145-156.

26. Butler FK. The eye in the wilderness. Wilderness Medicine. Auerbach PS, ed: St Louis, Mosby; Fifth Edition, in press for 2006.
27. Saltzman HA, Hart L, Sieker HO, Duffy EJ. Retinal vascular response to hyperbaric oxygenation. *JAMA* 1965; 191(4): 114-116.
28. Haddad HM, Leopold IH. Effect of hyperbaric oxygenation on microcirculation: Use in therapy of retinal vascular disorders. *Invest Ophthalmol* 1965; 4: 1141-1151.
29. Yu DY, Cringle SJ. Retinal degeneration and local oxygen metabolism. *Exp Eye Res* 2005; 80: 745-751.
30. Phillips D, Diaz C, Atwell G, Chimiak J, Ullman S et al. Care of sudden blindness: A case report of acute central retinal artery occlusion reversed with hyperbaric oxygen therapy. *Undersea Hyperbaric Med* 1999; 26 (supplement): 23-24 (abstract).
31. Hayreh SS, Kolder HE, Weingeist TA. Central retinal artery occlusion and retinal tolerance time. *Ophthalmology* 1980; 87(1): 75-78.
32. Beiran I, Reissman P, Scharf J, Nahum Z, Miller B. Hyperbaric oxygenation combined with nifedipine treatment for recent-onset retinal artery occlusion. *Eur J Ophthalmol* 1993; 3(2): 89-94.
33. Beiran I, Goldenberg I, Adir Y, Tamir A, Shupak A, Miller B. Early hyperbaric oxygen therapy for retinal artery occlusion. *Eur J Ophthalmol* 2001 Oct-Dec; 11(4): 345-50.
34. Matsuo T. Multiple occlusive retinal arteritis in both eyes of a patient with rheumatoid arthritis. *Jpn J Ophthalmol* 2001; 45: 662-664.
35. Perkins SA, Magargal LE, Augsburger JJ, Sanborn GE. The idling retina: Reversible visual loss in central retinal artery obstruction. *Ann Ophthalmol* 1987; 19: 3-6.
36. Gool VJ, De Jong H. Hyperbaric oxygen treatment in vascular insufficiency of the retina and optic nerve. In Ledingham IM, ed. Proceedings of the 2nd international congress on clinical and applies hyperbaric medicine. Livingstone, Edinburgh 1964; 447-460.
37. Takahashi K, Shima T, Yamamuro M. Hyperbaric oxygenation following stellate ganglion block in patients with retinal artery occlusion. In Smith G ed. Proceedings of the 6th international congress on hyperbaric medicine. University of Aberdeen Press, Aberdeen 1977; 211-215.
38. Pallotta R, Anceschi S, Costagliola N et al. Recovery from blindness through hyperbaric oxygen in a case of thrombosis on the central retinal artery. *Ann Med Nav* 1978; 83: 591-592.
39. Sasaki K, Fukuda M, Otani S et al. High pressure oxygen therapy in ocular diseases: With special reference to the effect of concomitantly used stellate ganglion block. *Jpn J Anesth* 1978; 27: 170-176.
40. Szuki H, Inie J, Horiuchi T. Hyperbaric oxygen therapy in ophthalmology. Part I: Incipient insufficiency of the retinal circulation. *J Clin Ophthalmol* 1980; 34: 335-343.
41. Krasnov MM, Kharlap SI, Pereverzina OK et al. Hyperbaric oxygen in the treatment of vascular disease of the retina. In Yefunny SN ed. Abstracts of the 7th international congress on hyperbaric medicine. USSR Academy of Sciences, Moscow 1981; 301-302.
42. Zhang XZ, Cao JQ. Observations on therapeutic results in 80 cases of central serous retinopathy treated with hyperbaric oxygenation. Presented at the 5th Chinese conference on hyperbaric medicine, Fuzhow, China 1986, Sept 26-29.
43. Desola J. Hyperbaric oxygen therapy in acute occlusive retinopathies. In Schmutz J ed. Proceedings of the 1st Swiss symposium on hyperbaric medicine. Foundation for Hyperbaric Medicine, Basel 1987; 333.
44. Kindwall EP, Goldmann RW. Hyperbaric medicine procedures. St. Luke's Medical Center, Milwaukee 1988.
45. Aisenbrey S, Krott R, Heller R et al. Hyperbaric oxygen therapy in retinal artery occlusion. *Ophthalmologe* 2000; 97: 461-467.
46. Weinberger AWA, Siekmann UPF, Wolf S et al. Treatment of acute central retinal artery occlusion (CRAO) by hyperbaric oxygenation therapy (HBO)—a pilot study with 21 patients. *Klin Monatsbl Augenheilkd* 2002; 219: 728-734.
47. Imai E, Kunikata H, Udono T et al. Branch artery occlusion: A complication of iron-deficiency anemia in a young adult with a rectal carcinoid. *Tohoku J Exp Med* 2004; 203: 141-144.
48. Hirayama Y, Matsunaga N, Tashiro J et al. Bifemelane in the treatment of central retinal artery or vein obstruction. Clin Ther 1990; 12: 230-235.