

Early hyperbaric oxygen therapy for retinal artery occlusion

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PURPOSE. *To assess whether early hyperbaric oxygenation (HBO) treatment has a beneficial effect on visual results after retinal artery occlusion (RAO).*

METHODS. *A comparative retrospective study in which medical records of all HBO-treated RAO patients in our department were reviewed and compared with matched RAO patients not treated by HBO (from a different medical center). Mean visual acuity (VA) at completion of treatment, the presence or absence of improvement in VA between admission and discharge, and the mean change in VA between admission and discharge were noted. All patients treated by HBO had treatment no later than 8 hours after the beginning of visual symptoms.*

RESULTS. *Mean VA at discharge was 0.2981 (6/20) in the treated group and 0.1308 (6/46) in the control group ($p < 0.03$). In the treated group, 82.9% had an improvement in VA between admission and discharge, compared with 29.7% of the control group ($p < 0.00001$). Mean improvement in VA was 0.1957 in the treated group and 0.0457 in the control group ($p < 0.01$). Differences in outcome measures between treatment and control groups were found to reflect the difference between treated and untreated hypertensive patients. No difference was found between treated and untreated non-hypertensive patients.*

CONCLUSIONS. *Early HBO therapy appears to have a beneficial effect on visual outcome in patients with RAO. Further large-scale prospective controlled studies are needed to confirm this. (Eur J Ophthalmol 2001; 11: 345-50)*

KEY WORDS. *Hyperbaric oxygenation, Central retinal artery occlusion, Treatment outcome*

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INTRODUCTION

Retinal artery occlusion (RAO) is a frustrating medical event. Even in cases in which early and correct diagnosis is made and all known treatment modalities are used, the prognosis is grim. This is probably why Henkind and Chambers (1) stated that "heroic therapeutic methodology may be indicated in retinal artery occlusion".

Several reports have suggested the possibility of treating patients with RAO by hyperbaric oxygenation (HBO).

Previous publications consist mainly of reports on small numbers of patients (2-5), one report on 72 eyes treated no earlier than 12 hours (and up to 12 days) after acute visual loss (6), and a report proving the beneficial effect of early treatment (<8 hours from acute visual loss) in a small number of patients (7).

The present study was aimed at answering the question whether early HBO for RAO patients is beneficial. To answer this retrospectively, we compared 35 HBO-treated and 37 matched control RAO patients.

PATIENTS AND METHODS

Since 1989, based on previous reports (6) and our own preliminary experience (5), every RAO patient arriving in our department complaining of acute visual loss lasting up to 8 hours has been treated by HBO in the Israel Naval Hyperbaric Institute. Treatment is given in 2.8 atmosphere absolute (ATA), 100% oxygen for 90 minutes twice daily in the first three days and once daily thereafter. Treatment is discontinued when no further improvement in visual acuity (VA) is observed in three consecutive treatments.

Data were collected retrospectively and included all 35 patients treated in the Israeli Naval Hyperbaric Institute since 1989 (group A). Comparison was made with 37 matched control patients treated for RAO in a different medical center not using HBO (group B).

The study and control groups were matched for age, sex, and type of retinal artery obstruction (central or branch). Matching for VA at admission was global, as the small number of patients made personal matching impossible. Treatment outcome was assessed on the basis of final VA at discharge examination and the difference between VA at admission and discharge. Improvement in VA was defined as the patient's ability to see at least three lines better in the Snellen chart at discharge compared with admission (this change amounted to a doubling of the visual angle).

Results are presented as means \pm SD. Statistical analysis of results was based on the X² test for categorical variables, Student's t test for comparison of means, and Wilcoxon test for comparison of small groups. $p < 0.05$ was considered significant.

RESULTS

Clinical findings in the two groups are summarized in Table I. The difference between groups regarding distribution by affected eye (right or left) was not significant. Hypotensive treatments are shown in Table II. At admission, patients in both groups had a relative afferent pupillary defect in the affected eye, with granular bloodstream appearance.

In untreated patients, and in the treated ones with no improvement, a cherry-red spot developed 12 to 36 hours after the acute event. The treated patients who showed improvement did not develop a full-blown cherry-red spot. Some treated patients had no retinal edema, and others had scattered, localized edema that resolved 36-48 hours after the initial treatment. None of the patients in our series had cilioretinal artery.

This was probably because patients with cilioretinal artery who suffered RAO obstruction did not experience the severe acute visual loss that would have qualified them for our study.

Improvement in VA between admission and discharge was shown by 29 patients (82.9%) in group A compared with 11 (29.7%) in group B ($p < 0.00001$). Mean VA before treatment was 0.1025 (6/60) \pm 0.2258 (range 0 to 1.0) in group A and 0.0851 (6/70) \pm 0.1653 (range 0 to 0.71) in group B (not significant). Mean VA at discharge was 0.2981 (6/20) \pm 0.3628 (range 0 to 1.0) in group A and 0.1308 (6/46) \pm 0.2474 (range 0 to 1.0) in group B ($p < 0.03$). Mean improvement in VA was 0.1957 \pm 0.3000 (range 0 to 1.0) in group A and 0.0457 \pm 0.1498 (range -0.1 to +0.8) in group B ($p < 0.01$).

There was a significant difference ($p < 0.03$ in mean VA at admission in group A patients >55 years of age

TABLE I - MAIN CLINICAL FINDINGS IN HBO-TREATED AND UNTREATED GROUPS

	30-treated (n = 35)	Control (n = 37)	p
Sex, M/F	21/14	19/18	NS
Mean age, yrs	69.5 \pm 11.5	56.0 \pm 14.5	0.001
Cardiovascular disease, n (%)	22 (62.9)	23 (62.1)	NS
Diabetes mellitus, n (%)	6 (17.1)	5 (13.5)	NS
Arterial hypertension, n (%)	22 (62.9)	13 (35.1)	0.02
RAO central/branch, n (%)	29/6 (82.9/17.1)	31/6 (83.8/16.2)	NS

(0.0304 [6/200] \pm 0.0800 [range 0 to 0.33]) and those \leq 54 years of age (0.1788 [6/34] \pm 0.0300 [range 0 to 1.0]). There was no significant difference in VA at discharge between group A patients \geq 55 years of age (0.2068 [6/30] \pm 0.3157 range 0 to 1.0) and those \leq 54 years of age (0.3949 [6/15] \pm 0.3900 range 0.005 to 1.000). Mean improvement in VA in group A was 0.1764 \pm 0.3100 (range 0 to 1.0) for patients \geq 55 years and 0.2316 \pm 0.300 (range 0 to 1.0) for those \leq 54 years (not significant).

Group A patient \geq 55 years had a significantly greater improvement ($p < 0.03$) in VA (0.1764 \pm 0.3097 (range 0 to 1.0) than group B patients in the same age group (0.0255 \pm 0.0800 (range -0.1 to +0.3).

In group A, mean VA at admission was 0.1708 (6/36) \pm 0.3300 (range 0 to 1.0) for patients without arterial hypertension (HTN) versus 0.0621 (6/100) \pm 0.1235 (range 0 to 0.5) for patients with HTN (not significant). VA at discharge was 0.2126 (6/28) \pm 0.3343 (range 0 to 1.0) for patients without HTN versus 0.3487 (6/17) \pm 0.3768 (range 0 to 1.0) for those with HTN (not significant). Improvement in VA was 0.042 \pm 0.0580 (range 0 to 0.17) for patients without HTN versus 0.2864 \pm 0.3472 (range 0 to 1.0) for those with HTN ($p < 0.005$).

In group B, there were no significant differences in VA at admission between patients with and without HTN (0.0122 [6/490] \pm 0.3000 [range 0 to 1.0] versus 0.1246 [6/50] \pm 0.1940 [range 0.706]) or at discharge (0.0203 [6/300] \pm 0.0327 [range 0 to 0.1] versus 0.1407 [6/45] \pm 0.2900 [range 0 to 1.0]), nor any real difference in improvement in VA between patients with and without HTN (0.0661 \pm 0.1835 [range -0.1 to +0.8] versus 0.0081 \pm 0.0200 [range 0 to 0.07]).

Among non-HTN patients, no difference was found between groups A and B in mean VA at admission

(0.1708 [6/35] \pm 0.3300 [range 0 to 1.0] versus 0.1246 [6/48] \pm 0.1940 [range 0 to 0.706]; $p = 0.3$), mean VA at discharge (0.2126 [6/28] \pm 0.3343 [range 0 to 1.0] versus 0.1407 [6/43] \pm 0.2910 [range 0 to 1.0]; $p = 0.3$), and mean change in VA (0.0418 \pm 0.0583 [range 0 to 0.17] versus 0.0661 \pm 0.1835 [range -0.1 to +0.8]; $p=0.09$).

Among HTN patients, no significant difference was found in mean VA at admission (0.0621 [6/100] \pm 0.1235 [range 0 to 0.5] versus 0.0122 [6/500] \pm 0.2980 [range 0 to 0.1]; $p>0.05$), but mean VA at discharge (0.3487 [6/18] \pm 0.3768 [range 0 to 1.0] versus 0.0203 [6/300] \pm 0.0327 [range 0 to 0.1]; $p < 0.00001$) and mean change in VA (0.2860 \pm 0.3472 [range 0 to 1.0] versus 0.0081 \pm 0.2000 [range 0 to 0.07]; $p < 0.00001$) both showed highly significant differences in favor of the treatment group.

DISCUSSION

The theoretical rationale for HBO treatment in RAO is based on the increase in diffusion distance of oxygen caused by extreme hyperoxemia in HBO breathing conditions. Diffusion distance increases 3-fold for a 10-fold increase in oxygen tension (8), and breathing 100% oxygen under normobaric conditions enables oxygen, because of the increase in oxygen diffusion distance, to reach the inner retina from the choroid by diffusion (9, 10). During hyperbaric treatment at 2 ATA breathing 100% oxygen, There is an 11- to 14-fold increase in oxygen arterial pressure. At this high oxygen pressure its diffusion distance increases sufficiently to permit a full supply of retinal oxygen needs by diffusion from the choroid (2, 11).

TABLE II - HYPOTENSIVE TREATMENTS IN HBO-TREATED AND UNTREATED GROUPS

	HBO-treated (n = 35)	Control (n = 37)	p
External massage, n (%)	17 (48.6)	30 (89.2)	NS
Retrobulbar block, n (%)	2 (5.7)	5 (14.4)	NS
Timolol maleate, n (%)	12 (34.2)	29 (78.3)	0.00047
Acetazolamide, n (%)	24 (68.6)	33 (89.2)	0.03
Paracentesis, n (%)	1 (2.9)	9 (24.3)	0.01

Oxygen is a potent vasoconstrictor of retinal arteries (12, 13). Nevertheless the oxygen content of retinal cells under HBO is much higher than with normotensive breathing, on account of the extremely high oxygen tension and concentration in arterial blood under these conditions (12, 14). Thus, the expected beneficial effect of HBO on RAO is based on its ability to provide a temporary alternate route for oxygen delivery to the retina until recanalization takes place. Of course, this treatment must be instituted early, before irreversible damage to the retina occurs.

Experimental dog models showed that the damage to the retina caused by total clamping of the central retinal artery was reversible, as proved by electrophysiologic studies, for up to 100 minutes, but irreversible thereafter (11). In clinical reports about patients, the estimated maximal time for HBO application to be effective after acute visual loss was about 6 to 8 hours (5-7). Two reports on recurrent RAO in patients with known pathologies that explain these events showed a favorable effect of HBO in each event (15, 16).

It is therefore our policy now to treat with HBO every RAO patient arriving at our department <8 hours after the acute visual loss.

In the present study we tried to evaluate the beneficial effect of HBO on RAO patients by comparing clinical data. Because most of our RAO patients were referred from other medical centers and were followed up, after their acute hospital stay, in their original centers, we were unable to provide long-term follow-up and needed to rely on short-term results. Although we are well aware of this shortcoming, we believe that in the light of the fact that the control population was compared with the study population within the same time frame and did not differ in its basic characteristics, the significant differences in treatment outcome measures probably reflect a true effect attributable to HBO.

We noted a beneficial effect of early HBO treatment in cases of RAO. This could be attributed to the significantly better visual results and higher improvement rate in VA in patients with HTN. This advantage was proved both when comparing HTN and non-HTN patients in group A and comparing HTN patients in group A with those in group B. Treatment results were no better in treated than untreated non-HTN patients.

Studies testing the changes caused by HBO in ar-

teries of compromised circulation in human and animal models have found a unique phenomenon given the name "Robin Hood effect". In these models the vasoconstrictive effect of HBO was observed only in healthy tissues. In the compromised tissue vasoconstriction did not take place because the hypoperfusion did not permit high oxygen partial pressure. When the hypoperfused tissue was reperfused, a vasoconstrictive effect was observed in it, just like healthy tissue. In acute ischemic situations treated by HBO, this effect caused oxygen to move away from tissues rich in oxygen (by vasoconstriction) into tissues poor in oxygen (whose vasculature was not constricted), resembling the noble deeds of Robin Hood (18-20).

This may help explain our observation about HBO's beneficial effect being restricted to hypertensive patients. The net effect of HBO on retinal oxygen supply is the result of two contradictory mechanisms: high oxygen concentration in plasma and vasoconstriction. A beneficial net effect is achieved when the influence of the high oxygen concentration is stronger than that of vasoconstriction.

The arterial vasculature of HTN patients is chronically constricted as part of the HFN cardiovascular atheromatous process (and as proved in the eye by the HFN retinopathy). The chronically constricted vasculature may act like the compromised tissues in the models mentioned. When HBO is applied unlike the normal reaction of vasoconstriction, these abnormally constricted vessels do not constrict further, both because oxygen reaches them less and because they are basically already fully constricted. Because of this, the elevated oxygen concentration has fully effect, so the ischemic retinal tissue receives a more meaningful additional oxygen supply in HTN than in non-HTN patients.

The use of hypotensive agents (timolol maleate, acetazolamide) and paracentesis has a weaker beneficial effect on final VA than HBO, as proved by the fact that although these means were used significantly more in group B, final VA was better in group A. In the same group, older (≥ 55 years) patients benefited from treatment no less than younger (≤ 54 years) ones. In fact, older patients seem to benefit even more from HBO for RAO than younger people, as suggested by the comparison of treated and untreated old patients and old and young patients in the treatment group.

The present report confirms, on a larger scale, the

proposed conclusion of two earlier reports about the importance, of HBO being applied as early as possible after the acute visual loss (5, 7). The general impression of improvement, not confirmed statistically in other reports, is probably the result of later HBO having only a partial or no effect (4, 6, 17).

We believe the present findings strongly support the beneficial effect of early HBO application for RAO patients with HTN (up to 8 hours after acute visual loss). This is true even in cases with poor initial VA and older age (≥ 55 years). HBO is superior to hypotensive

agents and paracentesis in its effect on VA in cases of RAO. No conclusions can be drawn from the present study whether HBO is more useful than retrobulbar block, rebreathing, or eyeball massage.

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