

## Systematic Review

# Efficacy study of hyperbaric oxygen therapy for the treatment of central retinal artery occlusion: a systematic review

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## ABSTRACT

Central Retinal Artery Occlusion (CRAO) is a rare ophthalmology emergency caused by central retinal artery embolism. Many CRAO management strategies exist. However, no treatment has consistently improved visual outcomes following CRAO. These medicines have many negative effects and unclear efficacy. HBOT has been considered for CRAO management. HBOT may minimize ischemia damage between CRAO and retinal artery recanalization, which normally occurs within 72 hours.<sup>9</sup> There is continuous disagreement about whether this treatment procedure achieves the desired visual target. The method use is PRISMA principles were followed for a systematic review. This systematic review examines HBOT's efficacy in CRAO. The search terms were "Hyperbaric Oxygen Therapy" ("HBOT") and "Central Retinal Artery Occlusion" ("CRAO"). The 5 investigations were primarily cohort retrospective. Four studies found no link between onset-to-HBOT time and visual outcome, two found no correlation between HBOT session and VA improvement, and three found no correlation between first therapy before HBOT and VA improvement. All said this therapy produced side effects. The conclusion is in this study is more investigations showed no significant link between onset-to-HBOT time, initial treatment before HBOT, and VA improvement. HBOT can produce barotrauma, ear pain, tympanic membrane rupture, and central nervous system oxygen poisoning seizures, so these must be considered.

**Keywords:** Central retinal artery occlusion, Cherry red spot, Eye stroke, Hyperbaric oxygen therapy, Sudden vision loss

## INTRODUCTION

Central Retinal Artery Occlusion (CRAO) is a rare ophthalmology emergency caused by central retinal artery embolism. CRAO causes abrupt, painless monocular vision loss that can proceed to 20/400 or worse in 80% of cases without treatment.<sup>1</sup> The incidence of acute CRAO is 8.5 per 100,000. The disease's natural development destroys vision, leaving 92% of sufferers unable to see more than movement of fingers. Only 8% may improve.<sup>2</sup> When the artery is blocked, retinal ischemia and infraction generate a pale look and a "cherry red" macula due to increased retinal visibility.<sup>3</sup> Due to its high oxygen

consumption (13 ml/100 g/minute), the retina is very sensitive to oxygen changes, making the time of ischemia the most important prognostic factor for visual outcome.<sup>1,4</sup> Risk factors include giant cell arteritis, carotid atherosclerosis, thromboembolism, hypertension, smoking, diabetes, and vasospasm. CRAO management strategies include ocular massage, anterior chamber paracentesis, intraocular pressure lowering therapies, isosorbite dinitrate, intravenous acetazolamide, mannitol, corticosteroids, thrombolytic and anticoagulant agents, and hyperbaric oxygen therapy (HBOT).<sup>6-8</sup> These treatments lower intraocular pressure to shift embolus downstream and increase vasodilation to oxygenate the ischemic inner retina. However, no treatment has

consistently improved visual outcomes following CRAO. These medicines have many negative effects and unclear efficacy.<sup>6,8</sup>

HBOT has been considered for CRAO management. HBOT may minimize ischemia damage between CRAO and retinal artery recanalization, which normally occurs within 72 hours.<sup>9</sup> This treatment method's ability to achieve the target visual goal is still debated. This study uses a systematic review to determine HBOT's visual benefits in CRAO management.

**METHODS**

**Search strategy**

A systematic review was conducted in accordance to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1).<sup>10</sup> A comprehensive literature search was performed to gather a full-length, peer-reviewed paper in English. We searched PubMed, Google Scholar, and Cochrane Library. The focus in this systematic review is to study the efficacy of HBOT treatment in CRAO. Keywords in the search matched the MeSH rule and term used are (“Hyperbaric Oxygen Therapy”) OR (“HBOT”) AND (“Central Retinal Artery Occlusion”) OR (“CRAO”).

**Inclusion Criteria**

The inclusion criteria were any studies of efficacy of HBOT in management of CRAO. The outcomes assessed includes initial VA and final VA. Given the limited number of researches, there were no limitation in patient’s demographics. Exclusion criteria included non-English article, case report, reviews, noncomparative data (Table 1).

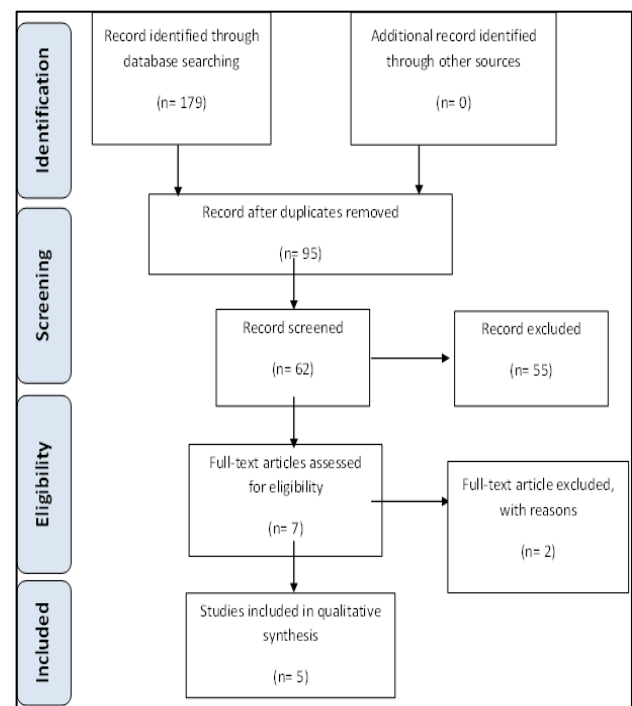
**Quality evaluation**

Assessment of study quality and risk of bias assessed using criteria developed by the Oxford Center for Evidence-based Medicine, perspicacity defined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group, and sanction made by the Agency for Healthcare Research and Quality (AHRQ). While the class of evidence is categorized into "class I" for good quality RCT, "class II" for moderate to poor quality RCT and good quality cohort, "class III" for moderate or poor-quality cohorts and case-control studies, "class IV" for the case series.

**RESULTS**

A total of 179 studies were obtained upon executing the search strategy in PubMed, Google Scholar, Clinical, Key and Cochrane Library databases. Out of these, 77 were excluded based on duplication and 40 were excluded based on title screening. Further 55 articles were excluded after reading the abstract. Full text of remaining 7 articles were

reviewed. Out of these, 2 articles were excluded upon full-text review. The final number of included studies in this systematic review was 5 studies. The first study is retrospective cohort. We analyzed 34 men and 26 women with CRAO aged 27-89 (mean, 67.5±14.4) years. In a retrospective, non-comparative study of 128 patients, 40 girls and 88 males had a mean age of 66.4±3.1 years. Third study uses retrospective investigation of 17 male and 8 female CRAO patients aged 44-89. Fourth is retroactive case-control comparison. 121 patients received HBOT in addition to satisfactory SOC (HBOT group), and 23 received only SOC without HBOT (control group). The HBOT group was substantially older than the control group (69±12 vs 60±3 years, P=0.002). Fifth prospective non-comparative study with 31 samples, 12 males and 19 females, mean age 68.3 (15-93) years. According to the first study, VA changes in the pre-COVID-19 group (n=22) and COVID-19-pandemic group (n=38) were similar (-0.53±0.58 vs -0.46±0.57 logMAR, p=0.59). Failure to equalize pressure during treatment requiring myringotomy or grommet insertion (n=25), barotrauma of grade 1 to 3 (based on the modified Teed Classification) without perforation (n=12), oxygen toxicity convulsion (during the first session while decompressing from 180 kPa to 139 kPa at 94 minutes) (n=1), confusion with agitation and aggressive behavior (n=1), sinus pain. Hypoglycemia affected three patients, two of whom had diabetes.



**Figure 1: Describing the strategy for conducting this study based on PRISMA guideline.**

In the second study, BCVA (logMAR) improved significantly following HBOT, with a mean improvement of 0.526±0.688 from 2.14±0.50 to 1.61±0.78 (P<0.000 In 67.2% of patients, visual improvement was clinically

significant (logMAR 0.3). 25.0% had final BCVAs above 1.0 logMAR. Cilioretinal arteries, branches of the short posterior ciliary artery, are seen in 15-30% of people. It supplies blood to the fovea. In these eyes, a central retinal artery occlusion (CRAO) does not impact the cilioretinal artery, preserving 20/50 or better visual acuity. Peripheral vision is still severely impaired.<sup>11</sup> One patient (0.7%) had mild epistaxis unrelated to barotrauma and stopped spontaneously; one (0.7%) had dyspnea during the session and recovered minutes later.

Third study stated the mean VA change was -0.43 LogMAR (p=0.003). VA improved in 68% (17/25) patients. After therapy, 84% (21/25) had VA of 0.1 (1.0 logMAR) or worse and 64% (16/25) had finger counting (1.7 logMAR). The same VA was maintained after 1 week to 20 months in nine of our continued surveillance individuals. 44% (11/25) had stroke-excluding neuroimaging within a week of CRAO and 56% (14/25) within two months. 68% (17/25) received cardiovascular risk factor treatment within 2 weeks. 96% (24/25) received frequent medical exams following CRAO; one was lost to follow-up. One patient had an abrupt infarct across the right middle cerebellar peduncle after 3 HBOT sessions.

HBOT was stopped after the patient was admitted to the acute stroke unit. One patient had a fall and subdural hemorrhage 11 months following CRAO, possibly due to aspirin and dipyridamole. 92% (23/25) had no cerebrovascular incidents after CRAO. Fourth study found that HBOT improved BCVA from 2.89±0.98 logMAR to 2.15±1.07 logMAR after hyperbaric oxygen treatment (P<0.001). BCVA went from 3.04±0.82 logMAR at presentation to 2.80±1.50 logMAR in the control group. In the last follow-up, this change was not statistically significant (P=0.24). After adjusting for age, gender, and symptom duration, HBOT group had substantially higher final BCVA (2.27±1.25 logMAR) compared to control group (2.80±1.50 logMAR) (p=0.023). Three patients (0.02%) prematurely ceased hyperbaric oxygen. Two patients with ear barotrauma and one with seizures and epistaxis during treatment. Fifth study reveals a BCVA improvement, with 48.4% of patients achieving a ≥0.3 logMAR drop at 1 month. The mean referral BCVA was 1.51 (0-2.6) logMAR (around 20/600 in Snellen chart). After HBOT, the mean BCVA was 1.1 (0-2.6) logMAR (20/250 in Snellen chart). During HBOT sessions, 9 (29%) patients had an SBP ≥160 mm Hg, requiring antihypertensive medications. Six patients (19.4%) had minor barotrauma.

**Table 1: PICO Characteristic.**

Criteria	Inclusion	Exclusion
<b>Population</b>	Patients with central retinal artery occlusion	Animal study
<b>Intervention</b>	Hyperbaric Oxygen Therapy	Other method
<b>Outcome</b>	Initial visual acuity, Final visual activity complications after hyperbaric therapy	No outcome mentioned or different outcome
<b>Publication</b>	Studies published in English in peer-reviewed journals	Duplicate publications of the same study that do not report on different outcomes
<b>Study design</b>	All study design with comparative data	Case report and review articles

**Table 2: List of studies included.**

S. no.	Reference	Journal	Study design	Level of evidence
1	AU et al <sup>13</sup>	Hongkong journal of ophthalmology	Cohort retrospective study	III
2	Handanny et al <sup>2</sup>	Clinical ophthalmology	Retrospective study	III
3	Yip et al <sup>12</sup>	Hongkong journal of ophthalmology	Retrospective study	III
4	Rozenberg et al <sup>10</sup>	Royal college of ophthalmologist	Retrospective comparative study	III
5	Chiabo et al <sup>14</sup>	British journal of ophthalmologist	Prospective monocentric study	II

**Table 3: Characteristic of patients.**

S. no.	Reference	Total sample	Mean age (in years)	Gender		Mean HBOT session
				Male	Female	
1	AU et al <sup>13</sup>	60	67.5±14.4	34	26	8.6±3.2
2	Handanny et al <sup>2</sup>	128	66.4±13.1	88	40	4
3	Yip et al <sup>12</sup>	25	44 to 89	17	8	7.9±2.7
4	Rozenberg et al <sup>10</sup>	141, HBOT=121, Control=23	HBOT=69±12, Control=60±3	HBOT=81, Control=17	HBOT=40, Control=6	4
5.	Chiabi et al <sup>14</sup>	31	68.3 (range 15-93)	12 patients	12 patients	34

**Table 4. Outcome characteristics.**

S. no.	Reference	Clinical outcomes	Complications
1.	AU et al <sup>13</sup>	Visual acuity (VA) improvement	Middle ear barotrauma without perforation, Convulsion secondary to oxygen toxicity, Confusion with agitation and aggressive behavior, Sinus pain, Shortness of breath.
2	Handanny et al <sup>2</sup>	Visual acuity (VA) improvement pre-HBOT and post-HBOT	Middle ear barotrauma, Otaglia without barotrauma, Mild epistaxis unrelated to barotrauma, Dyspnea.
3.	Yip et al <sup>12</sup>	Visual acuity (VA) improvement	Tinnitus, Otaglia with suspected hemotimpanum, Acute stroke with an acute infarct over the right middle cerebellar peduncle, subdural hemorrhage.
4.	Rozenberg et al <sup>10</sup>	Visual acuity (VA) improvement	Barotrauma, Seizure, Epistaxis.
5.	Chianbo et al <sup>14</sup>	Visual acuity (VA) improvement Fluorescence angiography (FA)	Barotrauma, Arterial hypertension during the session.

**Table 5. Characteristic of outcome of studies.**

S. no.	Reference	Outcome measure	
		Visual acuity (VA) improvement	
		Mean Initial BCVA (LogMAR)	Mean final BCVA(LogMAR)
1	AU et al <sup>13</sup>	1.87±0.25 (range, 0.7-2.0) logMAR (Snellen equivalent to 20/1400)	1.41±0.63 (range, 0.1-2.0) logMAR (Snellen equivalent to 20/500)
2	Handanny et al <sup>2</sup>	2.14±0.50 LogMAR	1.62±0.78
3	Yip et al <sup>12</sup>	The mean LogMAR 2.02 (range, 1.3-3.0)	84% (21/25) had VA of 0.1 (1.0 logMAR) or worse 64% (16/25) had VA of finger counting (1.7 logMAR) or worse.
4	Rozenberg et al <sup>10</sup>	Control group: 3.04±0.8 HBOT group: 2.89±0.98	Control group: 2.80±1.5 HBOT group: 1.5±1.07
5	Chianbo et al <sup>14</sup>	1.51 (0-2.6) logMAR (or approximately 20/600 in Snellen chart)	1.1 (0-2.6) logMAR (logarithm of the minimum angle of resolution) (20/250 in Snellen chart)

**DISCUSSION**

The poor prognosis associated with a CRAO diagnosis is primarily due to the high sensitivity of retinal tissue to ischemia; retinal tissue has the maximum oxygen consumption rate per unit mass in the human body. Vision loss is commonly observed in patients with CRAO which results in the loss of viability of the inner retinal layers, which are normally supplied by retinal circulation. Nevertheless, if sufficient oxygen can diffuse through the choroidal circulation, these layers can maintain their viability.<sup>7</sup> Recently HBOT has been approved by the

Undersea and Hyperbaric Medical Society (UHMS) for treatment of CRAO due to evidence of significant efficacy.<sup>3</sup> According to the American Heart Association's

level IIb evidence classification, hyperbaric oxygen therapy for CRAO is effective. Reasonable to strong evidence supports its application. Although deemed

acceptable and secure, its confirmation by level I studies is lacking.<sup>9</sup> No alternative therapies exhibit comparable efficacy. However, HBOT continues to be a subject of debate among numerous ophthalmologists.<sup>8</sup> In this systematic review, we review some studies using HBOT and focus on such functional outcome such as VA and complications. Hyperbaric oxygen therapy (HBOT) is only beneficial if the macula affected by ischemia has not yet undergone irreversible anoxic changes, which are observed as cherry red spot. HBOT may be effective for non-arteritic CRAO, especially if the patients receive early treatment with salvageable vision. HBOT can provide oxygen to the ischemic retina, even if it is not completely necrotic. This treatment can reverse the pre-infarction state and greatly enhance the visual outcome, with a clinically significant improvement rate of 86%. As previously mentioned, the duration from ischemia to infarction in humans cannot be accurately anticipated and is influenced by numerous factors. Thus, while it is important to minimize the time delay between symptoms and treatment, the existence of necrosis or cherry red spot is a separate factor that can predict the effectiveness of HBOT.<sup>2</sup>

Handanny et al observed that cherry red spots at CRAO at presentation in two-thirds of patients and baseline BCVA increase the chance of poor visual outcome (discharge logMAR) by 16.488 ([4.857–55.979],  $P=0.0001$ ) and 3.993 ([1.277–12.490],  $P=0.017$ ), respectively. The BCVA improvement was considerably greater in patients lacking cherry red spots at presentation ( $0.973\pm 0.782$  vs  $0.300\pm 0.506$ ,  $P=0.0001$ ). The cherry red spot can indicate retinal tissue injury and oxygen deficiency. Thus, cherry red spot can quantify disease duration and intensity. Hyper-oxygenation can restore damage till cherry red spot emerges, regardless of time. However, Rozenberg found no significant correlation between a cherry red spot at presentation or diabetic retinopathy with the final VA ( $P=0.45$ ,  $P=0.23$ , respectively) and clinical characteristics at presentation and HBOT group BCVA.<sup>10</sup> Yip et al found cherry red spots on fundal examination in 23 of 25 patients, however they did not report a link with BCVA.<sup>12</sup> Sunny et al and Chiabo et al did not report cherry red spot and BCVA improvement.<sup>13,14</sup>

Numerous studies have shown that HBOT treats CRAO. HBOT helps CRAO sufferers keep vision. The Undersea and Hyperbaric Medicine Society recommends HBOT for visual recovery of CRAO with onset within 8-24 hours. 15 Opinions vary on when HBOT is beneficial. Delays under 12 hours are the greatest evidence, according to Butler et al (2011) in Soares, et al (2017). HBOT works best when started within eight hours of visual impairment.<sup>9</sup> Kraisorpnornsan et al. (2020) found that HBOT after 24 hours after visual loss had poor visual outcomes.<sup>15</sup>

In our systematic review, four of five stated there's no such significant correlation between onset-to-HBOT time and visual outcome was identified. Yip et al (2020) found that no such significant correlation between visual outcome and door to door time ( $p=0.77$ ), age ( $p=0.46$ ), onset-to-HBOT time ( $p=0.46$ ). But most likely it was caused to the inclusion of patients with shorter onset-to-HBOT time only and the small sample size.<sup>12</sup> Rozenberg et al also stated that no correlation was found between the time to the first hyperbaric oxygen treatment and BCVA at the end of treatment ( $P=0.32$  Within the HBOT group, the mean time between the onset of symptoms and the first hyperbaric oxygen treatment was  $9.1\pm 5$  hours). The mean final BCVA of patients that underwent the first hyperbaric oxygen treatment within 6 hours from the onset of symptoms was  $2.44\pm 1.14$  logMAR while the mean final BCVA of the patient who underwent the first treatment between 6 and 24 hours was  $2.18\pm 1.31$  logMAR ( $P=0.30$ ).<sup>10</sup> In Handanny the meantime delay from symptoms to treatment was  $7.8\pm 3.8$  hours. Time delay from symptoms to treatment between patients with cherry red spot (mean  $8.1\pm 3.7$  hours, range 3-19) and without cherry red spot (mean  $6.8\pm 3.7$  hours, range 1-20) ( $P=0.06$ ). Thus, they were not statistically significant in this model.<sup>2</sup> Sunny CL Au et al, did not state because they only included subjects with symptoms onset of  $\leq 6$  hours, and all of their best-corrected VA improved significantly after HBOT,  $2.14\pm 0.50$  logMAR (Snellen equivalent to hand

movement) to  $1.61\pm 0.78$  logMAR Snellen equivalent to 20/800) [ $p<0.0001$ ].<sup>13</sup> In the study by Chiabo et al time between the first ocular symptoms and the first HBOT session was  $<12$  hours in 10 (32.3%) patient. They found there's no association between the onset of the first symptoms and HBOT initiation and BCVA improvement ( $p=1.000$ ).<sup>14</sup>

The median number of sessions finished in a given amount of time is another metric that may be used to evaluate the effectiveness of HBOT. Throughout the course of the research, 10.5 hours of therapy were provided on average. The severity and length of a patient's symptoms, as well as how effectively those symptoms are responding to HBOT treatments, will determine how many HBOT sessions are necessary, according to the Undersea and Hyperbaric Medical Society. Additionally, a recent meta-analysis of seven randomized controlled trials revealed that, in line with the study's findings (251 eyes, with the most beneficial treatment period exceeding 9 hours), the median number of HBOT sessions was three.1 According to the study's findings, treatment durations of more than 9 hours boosted the therapeutic efficacy of the intervention.<sup>9</sup> In one of the case presentations that a CRAO patient who had hyperbaric oxygen therapy for a total of 13.5 hours saw considerable improvement in his or her VA after getting the treatment.<sup>16</sup>

We found that, two of five study stated that there's no correlation between HBOT session and VA improvement. The mean number of HBOT sessions in Sunny et al study received was  $8.6\pm 3.2$  (range, 1-10), but they didn't report is there any correlation between number of session and therapeutic efficacy.<sup>13</sup> Meanwhile, in a study did by Yip et al, mean number of HBOT session was  $7.9\pm 2.7$  and there's no factor were associated between VA improvement and number of HBOT session.<sup>12</sup> Handanny use the average number of HBOT sessions,  $4.0\pm 1.2$ . Treatment was given in 2–2.4 ATA (absolute atmosphere), 100% oxygen, 90-minute sessions, three times in the first 24 hours and once daily thereafter. Treatment was discontinued when no further improvement in BCVA was observed in two consecutive treatments. All HBOT sessions were performed in a multiplace hyperbaric chamber. They also stated number of HBOT sessions were not statistically significant in their model.2 In Rozenberg et al study, they also use the same HBOT protocol as Handanny the HBOT group received a median of 4 hyperbaric oxygen treatments (range 2-8) and all of them got significantly better final BCVA. They didn't report whether any significant relation between number of HBOT session and VA improvement.<sup>10</sup>

Chiabo et al using the protocol where the patients underwent their first 90 min HBOT session at 2.5 ATA in a HAUX Comex hyperbaric chamber. After the session, patients were referred to the radiology department to undergo contrast-enhanced cervical and cerebral CT-scan to rule out any cerebral stroke or internal carotid dissection. If contrast-enhanced CT scan was

unremarkable, the patients received two daily 90 min HBOT sessions for 15 days in an outpatient basis. Retinal revascularisation was assessed by fluorescein angiography (FA). In case of retinal reperfusion, HBOT was discontinued, and a final ophthalmological follow-up was scheduled at day 30. Otherwise, HBOT was continued with two daily sessions and FA was repeated on day 21. All patients were seen at day 30 for the final ophthalmological examination. Patients received a mean number of 33.9 (13-56) hyperbaric sessions. All patients received two daily HBOT sessions except three patients who only received one daily session between 17 March 2020 and 20 April 2020 due to the COVID-19 lockdown. Fifteen (48.4%) patients achieved the main outcome measure. But they didn't report any correlation between number of session and the efficacy of HBOT.<sup>14</sup>

CRAO treatment includes acute therapy to improve VA and subsequent therapies to prevent ischemia.<sup>17</sup> No gold standard VA-boosting therapy has been shown after CRAO.<sup>18</sup> Acute therapy within three hours of injury may prevent irreparable retinal ischemia. Extension to 61-2 hours is possible, however treatment after 12 hours is unsuccessful. Most CRAO treatments are given 12 to 24 hours after vision loss, limiting their acute treatment effectiveness.<sup>1</sup> A few studies reveal that because to center limitations, patients frequently got ophthalmology treatments before HBOT referral.<sup>2,15</sup> Early treatment included anterior chamber paracentesis, ocular massage, oral acetazolamide, rt-PA, Aspirin, Bevacizumab, Enoxaparin, Brimonidine, and Timolol eye drops.<sup>2,10,14</sup>

CRAO patients with symptom onset  $\leq 6$  hours who failed emergency bedside ocular therapy were referred to HBOT in the first study. Thus, all trial participants received first therapy. The author did not discuss the treatment or link initial treatment before HBOT to VA improvement.<sup>13</sup> The second Hadanny study found that 10 patients received aspirin, 59 received paracentesis, 36 received ocular massage, 28 received PO acetazolamide, 20 received eye, and 0 received brimonidione. They said age, sex, anti-aggregation and anti-coagulation drugs, long-term medical disorders, IOP, other funduscopy findings, paracentesis and eye massage, or HBOT sessions did not affect BCVA improvement.<sup>2</sup> The third study found that 12 patients received rebreathing bag therapy, 15 received ocular massage therapy, 3 received Diamox 250 mg peroral, 10 received 500 mg peroral, 2 received aphagan P, 1 received normobaric oxygen therapy, 9 received timolol, and 1 received xalacom. The referring ophthalmologist treated before transfer. The study found no link between initial treatment before HBOT and VA improvement.<sup>12</sup> In Rozenberg et al (2022), all patients received conventional care ocular massage, anterior chamber paracentesis, oral aspirin, oral acetazolamide, or topical beta-blocker as determined by a competent ophthalmologist. This study likewise found no link between pre-HBOT treatment and VA improvement.<sup>10</sup> Chiabo et al found that referral with anti-platelets improved visual performance ( $p=0.044$ ) in their sixth research. Antiplatelet therapy may reduce

thrombus size, improving residual arterial flow and enabling hyperbaric oxygenation of the inner retinal layers.<sup>14</sup> Three studies found no correlation between first treatment before HBOT and VA improvement, one found no correlation, and the fifth identified an association between antiplatelets and visual improvement.

HBOT is usually well-tolerated. Its side effects are mostly moderate and temporary.<sup>19</sup> Middle ear barotrauma and oxygen convulsion are the most prevalent side effects, at 5.5%.<sup>1</sup> Middle ear barotrauma occurs when the patient cannot balance the pressure difference between the middle ear and the outer world, even with natural or strong motions. This usually happens during hyperbaric oxygen therapy compression. Middle ear barotrauma is unavoidable due to the pressure difference between the external environment and the middle ear. This treatment may cause minor discomfort to severe ear pain, fullness, hearing loss, tinnitus, or bleeding.<sup>20</sup> Teaching patients auto inflating procedures like the Valsalva and Toynbee maneuver, which opens the Eustachian tubes and equalizes pressure, can avoid it. Other therapies include nasal decongestants and prophylactic myringotomy or tympanostomy tubes to minimize middle ear congestion and swelling.<sup>12</sup> Seek medical consultation and action immediately after HBOT exposure to avoid these risks. An emergency needle myringotomy or tympanostomy breathing tubes may be needed if a patient cannot equalize during an urgent clinical hyperbaric treatment.<sup>21</sup> Hyperbaric therapy should be avoided until symptoms are gone and otoscopic evaluation is normal.

HBOT, unlike paracentesis and ocular massage, is non-invasive, safe, and versatile and has been shown to be safe for CRAO patients.<sup>14</sup> Rapid and inexpensive paracentesis and ocular massage are beneficial. Ocular massage is periodic digital pressure on the affected eye to manually expel aqueous fluid. Relieving digital pressure lowers intraocular pressure (IOP), increasing retinal perfusion pressure and retinal artery dilatation. This treatment may cause the retinal embolus to migrate downstream and worsen symptoms. Anterior chamber paracentesis removes aqueous fluid from the front of the eye. When CRAO occurs within 24 hours and intra-arterial thrombolysis is not possible, this technique is performed. The 1-2 hours needed to restore normal pressure in a deflated anterior chamber limits anterior chamber paracentesis.<sup>22</sup> Five of systematic reviews found side effects from this therapy. Barotrauma with and without perforation, seizure, convulsion, confusion, anxiety, aggression, sinus pain, shortness of breath, cerebrovascular stroke, otalgia, epistaxis, tinnitus, subdural hemorrhage, arterial hypertension. Barotrauma occurred in 33 patients (55%) after HBOT in the first study. The second trial found 7 (5.5%) individuals with barotrauma, otalgia without barotrauma, epistaxis, and dyspnea. In the third research, 7 of 25 individuals experienced otalgia and mild tinnitus. Three patients (0.02%) in the fourth study have barotrauma, seizures, and

epistaxis. Six (19.4%) patients had minor barotrauma and 29% had hypertension in the fifth study.

## CONCLUSION

According to our study results, a certain individual studies suggest that early treatment of patients with CRAO using HBOT and numbers of HBOT session related with improvement of their final VA. But in we found that more studies stated there's no significant correlation between onset-to-HBOT time, initial treatment before HBOT towards improvement of VA. In order to gain a deeper understanding of the effectiveness of HBOT in treating CRAO, it is necessary to conduct large randomized studies. However, it is equally important to carefully consider the potential negative effects of HBOT, such as barotrauma, ear pain, tympanic membrane rupture, and seizures caused by oxygen toxicity in the central nervous system.

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