CRITICAL REVIEW FORM:
THERAPY ARTICLES

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Citation: Rozenberg, A et al., (2021). Hyperbaric oxygen treatment for non-arteritic central retinal artery occlusion retrospective comparative analysis from two Tertiary Medical Centres. *Eye*, *36*(6), 1261–1265. https://doi.org/10.1038/s41433-021-01617-8

Study Objective:
To compare visual outcomes of patients treated for non-arteritic CRAO in a tertiary medical center that used hyperbaric oxygen therapy in addition to standard of care management to a tertiary center that does not have HBOT and only used standard of care.

Study Methodology:
The study was a retrospective comparison study including data from two tertiary medical centers in Israel. Medical records of all patients diagnosed with non-arteritic CRAO without patent cilioretinal artery between January 2010-December 2018 from the two tertiary medical centers were reviewed for this study. One tertiary center had HBOT and the other did not. There were 134 patients in the study, 121 patients received HBOT + standard of care vs 23 patients who received standard of care only. There was a BCVA and ophthalmologic exam completed initially, post HBOT/at discharge, and at follow up visit which then compared between the two groups.

GUIDE	COMMENTS
I. Are the results valid?	
A. Did experimental and control groups begin the study with a similar prognosis	No, There was a significant difference in average age of subjects in both groups as well as duration of symptoms prior to initiation of management which both could be confounding. Both control group and HBOT group had non-arteritic CRAO without patent cilioretinal artery. They were otherwise similar in baseline characteristic (Table 1).
1. Were patients randomized?	No, it was retrospective comparison study
2. Was randomization concealed (blinded)? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	Randomization was not part of the study as it was a retrospective comparison study

3. Were patients analyzed in the groups to which they were randomized?	Patients were analyzed retrospectively, and visual outcomes compared based on if they received HBOT + SOC or just SOC.
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	Patients of both groups had similar systemic risk factors. There was significant difference in average age between control group and HBOT group. Average age 60 (control) vs 69 (HBOT). Also, significant difference in duration of symptoms prior to treatment onset. HBOT 9hrs, Control 19hr. Outside of duration of symptoms clinical exam similar between groups
5. Were patients aware of group allocation?	N/A
6. Were clinicians aware of group allocation?	N/A
7. Were outcome assessors aware of group allocation?	N/A
8. Was follow-up complete?	Follow up was completed and patients received another BCVA and ophthalmologic exam. The mean follow-up time was 12.9 ± 34 months for the treatment group (HBOT) and 51.5 ± 57 months for the control group. BCVA remained statistically significant at last follow up in HBOT group
What are the results ?	
1. How large was the treatment effect?	There was a significant improvement in best corrected visual acuity in the group that received HBOT. **2.89 ± 0.98 logMAR at presentation to 2.15 ± 1.07 logMAR** (p=0.001) upon the end of hyperbaric oxygen treatment and remained significant at the end of follow-up. Control Group BCVAchanged from **3.04 ± 0.82 logMAR at presentation to 2.80 ± 1.50 logMAR** (p=0.24) With adjustment for age, gender and the duration of symptoms, final BCVA was significantly better in the

	HBOT group compared to the control group **2.27 ± 1.25 logMAR and 2.80 ± 1.50 logMAR respectively (P = 0.023)** Both groups had similar percent of patients that had VA improved to 20/200. There was no significant change in control receiving only SOC.
2. How precise was the estimate of the treatment effect? (CI's?)	No CI's were provided by the authors.
III **How can I apply the results to patient care?**	
1. Were the study patients similar to my patient?	Study patients were from one of two tertiary centers in Israel. Some similar risk factors there would likely be some differences in baseline health, weight. However, the disease process should remain similar between study patients and our patients.
2. Were all clinically important outcomes considered?	When discussing CRAO the major concern is vision loss and this study focused on visual outcomes. Specifically, if use of HBOT will lead to improved visual outcomes. No report of harms from HBOT (O2 toxicity, barotrauma, confinement anxiety) No cost assessment. No patient preference
3. Are the likely treatment benefits worth the potential harm and costs?	HBOT has a low risk for harm and did demonstrate improvement in visual outcome compared to SOC alone. However, cost and accessibility may be two obstacles. In addition, there is no evidence of clinically meaningful improvement when noting that the WHO considers blindness a **best-corrected visual acuity worse than 1.3 LogMAR and the malority of patients were >2.0 logMar**

Limitations: This study had several limitations. First off, the control group had only 23 patients compared to 121 patients in HBOT group which could skew results due to small sample size. Also SOC management was left open to ophthalmologist discretion and it was not standardized. It is a retrospective non-randomized study

Clinical Bottom Line: This retrospective comparison study demonstrates HBOT may have a statistically significant improvement in logMAR visual outcomes in patients with non-arteritic CRAO though a questionably meaningful one. Larger prospective RCT's are needed to determine any benefit from HBOT. Also, accessibility and cost have to be considered. Current evidence presented here is insufficient to consider HBOT as a standard of care.