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Hyperbaric Oxygen in Post STroke Patients (HOST): A Feasibility Study

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Abstract: Background: Hyperbaric Oxygen treatment (HBOT) has been shown to improve the outcome of selected stroke patients. Our objective was to assess the feasibility of HBOT in daily practice in unselected stroke patients, especially their commuting ability to our center. **Methods**: This is an explorative, interventional, prospective monocentric study on post-stroke patients having completed their in-hospital stroke rehabilitation. We aimed at including 10 participants able to complete 40 daily HBOT (2.0 ATA). Effectiveness was assessed using the National Institutes of Health Stroke Score (NIHSS) pre- and post-HBOT. **Results:** 13 patients, 12 males, median age of 61, had to be recruited. Among the 3 drop-out patients, 2 never started HBOT one withdrew after 5 sessions because of travelling distance. Post stroke time was 4-251 months. Among the 10 patients with entire program, 8 improved their NIHSS by a mean of 1,3 (1-4), while in 2 it remained unchanged. There were no serious adverse events and no deleterious effects. **Conclusions:** HBO was shown feasible for unselected and mobile post-stroke patients with complete standard rehabilitation. In the absence of major safety concern, HBOT seems an interesting option with the potential to further improve residual stroke severity.

Keywords: post-stroke; hyperbaric oxygen therapy; sequelae; feasibility; out-patient

1. Introduction

HBOT is a well-known treatment in many as listed by the European Committee for Hyperbaric Medicine [1] In recent time much have been discovered regarding its mode of action. From High oxygen flow improving oxygen delivery to hypoxic tissues, we know that its action is mainly dependent of the free oxygen radicals that are produced. These free oxygen radicals have a great impact on cellular processes, transcription factors, mitochondrial function, oxidative stress, and inflammation [2].

Lately, HBO has been proposed for the treatment of chronic stroke [3]. In Switzerland, we have only two hyperbaric facilities functioning in accordance with the European Code of Good Practice of Hyperbaric Oxygen Therapy [4]. The aim of the present study was to assess the feasibility of HBOT in daily practice for highly motivated ambulant patients after they had had intensive and comprehensive rehabilitation program and were interested in innovative means to further increase their neurological impairments. We wanted also to know if these patients were able and enough motivated to travel daily from another city, traveling distance up to 110 Km.

2. Materials and Methods

After approval by of the local ethical committee (EKNZ, Nr. 2017-02131), patients with stroke sequelae who had completed a standardized in-hospital stroke rehabilitation program. Patients were asked if they were interested in participating in HBOT as an additional therapeutic approach. All patients who met the inclusion and exclusion criteria were included in the study. After a successful

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pressure test, patients signed an informed consent form. Some patients had to travel from another city to be treated in our outpatient center. Recruitment (2018-2021) was stopped when 10 patients successfully completed HBOT as foreseen.

Table 1. Inclusion/Exclusion criteria.

Inclusion	Exclusion
Ischemic stroke with residual defects	Inability to understand the informed consent form
Conclusive brain CT or brain MRI	Inability to put on a face mask
Uneventful pressure test 0,5 ATA	Claustrophobia
	Uncontrolled epilepsy
	Dementia or psychological disorder
	Previous pneumothorax
	Positive pregnancy test
	Anticonception measures during HBO
	Unsuccessful pressure test 0,5 ATA

All patients were treated in our multiplace chamber to a pressure of 2.0 ATA according to the European Code of Good Practice. One treatment lasted 2 hours with 90 minutes of oxygen, 5-minutes air brake after 45 minutes as a prevention against neurological toxicity due to high-pressure oxygen inhalation. Oxygen was provided with a tight face mask.

Potential visual side effects were assessed using the Snellen chart, before, immediately after 40 HBO and 3 months later. Possible Ear Nose Throat side effects were assessed with an interview and a digital otoscopy before and after each single HBO treatment.

Base line neurological assessment was done with NIHSS and was repeated after 40 sessions as well as three months later. It was done by a trained neurological physician. A further neurological assessment was done by the hyperbaric physician using a Rivermead mobility index (RMI) before the start of HBO, then weekly and again 3 months later. Patients' compliance was daily assessed with an attendance list filled by the hyperbaric technician.

The levels of stroke severity as measured by the NIHS scoring system were:

- 01–04 = minor stroke
- 5–15 = moderate stroke
- 15–20 = moderate/severe stroke
- 21–42 = severe stroke

3. Results

Our patients had a mean age of 61 years, 1 female, 12 men and the mean time from Stroke to the start of HBOT was 43 months. The mean age of the patients who fulfilled the entire program was 60 years and the mean time from stroke to the start of HBOT was 52 months, 31 months if we exclude patient 2.

3.1. Neurology

Table 2. Effect of 40 sessions HBO at 2.0 ATA in rehabilitated post-stroke patients.

Patient # and (age)	Time to stroke in months	NIHSS Before HBOT	NIHSS 3 months after HBOT	RMI before HBOT	RMI after 10 HBOT	RMI after 20 HBOT	RMI after 30 HBOT	RMI after 40 HBOT	RMI 3 months after HBOT
1 (57)	65	4	3	14	14	14	14	14	14
2 (86)	251	3	2	13	14	14	14	14	14
3 (63)	60	5	2	15	14	15	15	15	15

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4	(69)	14	8	8	9	9	6	8	-	8
5	(58)	4	3	Withdraw						
6	(75)	12	4	4	12	13	13	13	15	15
7	(60)	19		withdraw						
8	(69)	7	6	withdraw						
9	(65)	18	4	3	19	14	15	15	15	15
10	(35)	47	6	2	15	15	15	15	15	15
11	(66)	15	3	2	13	13	13	14	14	14
12	(57)	21	3	2	15	15	15	15	15	15
13	(34)	17	4	3	15	15	15	15	15	15

Table 3. Details of NIHSS changes.

Patient	Changes of NIHSS score 3 months after 40 HBOT	Patients reporting
1	4 ↗ 3 facial palsy ↔ with 1 left arm motricity ↗ from 2 to 1 left leg motricity ↔ with 1	Less fatigue, improved supination,
2	3 ↗ 2 ataxia extremities ↔ with 2 dysarthria improved from 1 to 0	Psychological state very good, left arm better, walking unchanged
3	5 ↗ 2 facial palsy ↔ with 1 motricity right leg ↔ with 1 ataxia right leg improved ↗ from 2 to 0 sensibility ↗ from1 to 0.	Does not know if it was helpful, sensibility clearly better
4	8 ↔ 8 orientation ↔ with 1 visual field ↔ with 2 motricity ↔ with 1 ataxia ↗ from 1 to 0 sensibility ↘ from 0 to 1 language ↔ with 1 dysarthria ↔ with 1 neglect ↔ with 1	
6	4 ↔ 4 motricity left leg ↔ with 1 ataxia left ↔ with 2 sensibility left ↔ with 1	Patient feels he can walk better
9	4 ↗ 3 facial paresis ↗ from 1 minimal to 0 motricity right leg ↔ with 1 ataxia right ↔ with 1	

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	dysarthria ↗ from 1 light to 0	
10	6 ↗ 2 compliance with order improved from 1 to 0 motricity right leg and arm ↗ from 1 to 0	Clear improvement, still improving, does not know if it is due to HBO
11	E ↗ 2 ↔ motricity right leg with 1 ataxia right leg ↗ from 2 to 1	Found treatment very good and felt that his right leg had improved
12	3 ↗ 2 motricity right leg ↗ from 1 to 0 ataxia right leg ↗ from 1 to 0	The patient sees no effect of HBO, function of the hand is a bit improving but it cannot be objectivated with the NIHSS score. Handwriting slightly improved
13	4 ↗ 3 motricity right Arm ↗ from 1 to 0.	No effect on tiredness, right arm feels heavy but does not sink anymore when held in horizontal position

↔ = unchanged, ↗ = improved, ↘ = worse.

8 of the 10 patients who completed the study showed some improvement with HBO in the NIHS scale, in 2 patients there was no effect. There was no improvement in self-reported RMI.

There were no signs of acute oxygen brain toxicity.

3.2. Visual acuity

Table 4. Visual side effects of hyperbaric oxygen at 2.0 ATA in Stroke patients.

Patient	Glasses	Snellen chart before HBOT		Snellen chart after 40 HBOT		Snellen chart 3 months after HBOT	
		Left	Right	Left	Right	Left	Right
1	Yes	1.08	0.96	1.08	0.96	0.96	0.84
	No	0.12	0.12	0.12	0.12	0.12	0.12
2	Yes	0.84	1.2	0.9	1.0	0.84	1.2
	No	0.36	0.24	0.5	0.6	0.48	0.48
3	Yes	-	-	-	-	-	-
	No	0.8	0.8	0.8	0.9	0.8	0.9
4	Yes	-	-	-	-	-	-
	No	0.96	0.96	0.84	0.72	0.84	0.72
6	Yes	0.36	0.48	0.72	0.72	0.7	0.7

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	No	**0.24**	**0.36**	**0.24**	**0.24**	**0.5**	**0.5**
9	**Yes**	**0.96**	**0.72**	**1.08**	**0.72**	**0.96**	**0.72**
	No	**<0.1**	**<0.1**	**<0.1**	**<0.1**	**0.12**	**0.12**
10	**Yes**	**0.6**	**1.08**	**0.6**	**0.84**	**0.6**	**1.08**
	No	**0.36**	**0.72**	**0.36**	**0.8**	**0.36**	**0.72**
11	**Yes**	**-**	**-**	**-**	**-**	**-**	**-**
	No	**0.96**	**1.2**	**0.84**	**1.2**	**0.96**	**1.2**
12	**Yes**	**-**	**-**	**-**	**-**	**-**	**-**
	No	**0.84**	**0.6**	**o.84**	**1.2**	**1.2**	**1.2**
13	**Yes**	**-**	**-**	**-**	**-**	**-**	**-**
	No	**0.96**	**1.2**	**0.84**	**0.84**	**0.8**	**1.0**

We could not detect a shift towards myopia in our patients.

3.3. Pressure related effect

Patient Number 10 had difficulties in equalizing and had to pause HBOT, he resumed HBOT after one week and fulfilled the program as scheduled. In this case digital otoscopy showed a transitory barotrauma of the eardrum staged as Teed 2 which had normalized after one week.

3.4. Compliance

13 patients were recruited.

Patient Number 5 was examined by the neurologist and started HBO as scheduled but after 5 sessions commuting to our center had become too time consuming for him, therefore he decided to withdraw from the study.

Patient Number 7 and 8 signed the informed consent. Patient 7 did not show up to first neurological examination, patient 8 was examined by the neurologist but never showed up to HBO.

In total, 10 out of 11 patients who started HBOT completed 40 HBOT as prescribed.

4. Discussion

Our study confirms that 40 HBOT are well tolerated in unselected patients with mild to moderate post-stroke residual symptoms. All patients except two patients (patient 4, 6) had an improvement of their neurological symptoms according to NIHSS but not according to RMI. This is probably because our patients suffered only from mild stroke and were therefore not suited for RMI.

We did not select our post-stroke patients and had no advanced imaging information regarding their potential of neuroplasticity and were surprised by the relatively high rate of positive response to HBOT. Even without a control group, we attributed the improvement as a HBOT effect. It is well known that spontaneous improvements can occur in some stroke patients after one or two years. However, in our sample this was the case in 8 of 10 patients [5].

Rosario et al [6] as well as Schiavo et al. [7] had similar results regarding the feasibility of HBOT at 2.0 ATA in their prospective series on unselected post stroke patients. They also found that these patients were strongly motivated to collaborate with the physicians in a hyperbaric center dedicated to outpatients. Churchill et al. [8] came to the same conclusion with a protocol involving 60 consecutive sessions. They noted that even 6 months after HBO, 90% of their patients were willing to repeat HBO.

Several researchers have pointed out the plasticity potential of the post stroke brain. They could show that there is a penumbra of dormant neurons around the stroke area and that it can regain some functionality after HBOT. This has been demonstrated with PET scans [9] and more recently with diverse technology using functional MRI [10].

In a first study, Efrati et al. found that HBOT [3] can improve neuroplasticity in post-stroke patients. Later [11] they suggested that the existence of a large penumbra could be an indicator of responsiveness to HBOT.

According to the literature up to 57% of HBOT induced myopia can be expected using compression rates of 2.2-2.5 ATA. [12]. Using 1.5 ATA, Churchill et al. found only 3 out of 55 patients with a myopic shift [8]. In our small study with 2.0 ATA, we did not find any case of such myopia, maybe because we treated only 10 patients.

HBOT can provoke from 0.2% [13] up to 10% of mild barotrauma [14]. Our study is in accordance with the literature with one out of 10 patients with a mild barotrauma.

5. Conclusion

Extensive HBOT treatments in post-stroke patients are feasible in an outpatient setting with minor and reversible side effects, even if patients must commute daily to the hyperbaric facility. HBOT seems to have the potential to improve their clinical state. However, there is an urgent need to select potential responders with imaging techniques and better assess the role of HBOT. This can only be done with prospective controlled studies.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee Ethikkommission Nordwest- und Zentralschweiz, project ID 2017-02131, dated 24.1.2018.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: available in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics.

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Conflicts of Interest: M.G. is head of Hyperbaric Center Basel, J.S. was founder of the of Hyperbaric Center Basel. Both are involved in daily hyperbaric treatments.

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