RESEARCH ARTICLE

Varied effects exerted on sudden sensorineural hearing loss through HBO_2 therapeutic pressure

Chen Chen, MA [1]; Heng Hu, BA [2]; Rui-yong Chen, PhD [3]

[1] Hyperbaric Oxygen Department, The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital of Wannan Medical College), Wuhu, Anhui Province, China

[2] Otolaryngology Department, The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital of Wannan Medical College), Wuhu, Anhui Province, China

[3] Undersea and Hyperbaric Medical Research Department, Navy Medical Centre of PLA, Shanghai, China

CORRESPONDING AUTHOR: Rui-yong Chen – *chenruiyong@hotmail.com*

ABSTRACT

This study aimed to compare the efficacy of two commonly used therapeutic pressures, 2.0 atmospheres absolute (ATA) versus 2.2 ATA, applied in hyperbaric oxygen (HBO_2) therapy for sudden sensorineural hearing loss (SSNHL).

We retrospectively reviewed the clinical records of 160 SSNHL patients treated by typical therapy or additional HBO_2 therapy with pressure 2.0 or 2.2 ATA at Yijishan Hospital, the First Affiliated Hospital of Wannan Medical College, from February 2018 to May 2020. The pure-tone threshold audiometry results pre- and post-treatment were compared across three groups.

In the range of frequencies 250-500 Hz, P2.0 (20.92±26.11 dB, p=0.047) and P2.2 group (20.47±21.54 dB, p=0.012) both acquired higher hearing gain compared to the control group (11.94±23.32 dB). While in the range of frequencies 1,000-2,000 Hz, only the P2.2 group showed significant improvement of the hearing gain compared to the control group (19.70±21.13 dB vs.10.56±25.24 dB, p=0.015). In the range of frequencies 4,000-8,000, both the P2.0 and P2.2 groups failed to reach the desired effect.

Our results suggest that the therapeutic effect is associated with HBO_2 therapeutic pressure when applying HBO_2 treatment combined with standard medical therapy. Within the range of appropriate pressure, the higher pressure, which means higher partial pressure of oxygen, has better therapeutic efficacy for SSNHL.

KEYWORDS: audiometry; hyperbaric oxygen; pressure; sudden sensorineural hearing loss

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined as sensorineural hearing loss of more than 30 dB at three consecutive frequencies that develops within 72 hours [1]. It may lead to severe functional deficits, severely affecting the quality of life for patients with poor recovery [2]. Varieties of regimens proffered for SSNHL include topical or systemic steroids and antiviral therapy, hyperbaric oxygen (HBO_2) therapy, vasodilators and other treatments [1].

HBO_2 has been used in the treatment of SSNHL since 1979 [3] and has been shown to improve the outcome of SSNHL [4-7]. SSNHL was approved as an indication for HBO_2 therapy by The Undersea and Hyperbaric Medical Society in October 2011 [4], and in 2017 the Tenth European Consensus Conference on Hyperbaric Medicine included SSNHL as a clinical indication for HBO_2 therapy. The Academy of Otolaryngology-Head and Neck Surgery Foundation proposed HBO_2 therapy as an option for the treatment of SSNHL as both primary therapy and as salvage therapy in the Clinical Practice Guideline of Sudden Hearing Loss in the 2012 and 2019 editions [1,9].

The therapeutic pressure of HBO_2 varies from 1.6 atmospheres absolute (ATA) to 2.5 ATA in the previous studies. However, there has been little consensus regarding the optimal HBO_2 therapeutic pressure for SSNHL up to now. Clinical trials in the United States and Europe usually adopt 2.0 ATA, 2.4 ATA or 2.5 ATA; Chinese clinicians prefer lower pressure ranges from 1.6 ATA to 2.2 ATA. There is a report that states 2.5 ATA is superior to 2.0 ATA for certain frequency ranges involved [10], while evidence about efficacy comparison of 2.0 ATA and 2.2 ATA is quite limited. This study aimed to compare the efficacy of two commonly used therapeutic pressures 2.0 ATA versus 2.2 ATA for SSNHL.

METHODS

After receiving the research proposal notification of IRB approval from the hospital scientific research and new technology IRB under code n.2020014, we retrospectively analyzed the data of SSNHL patients treated at Yijishan Hospital between February 2018 and May 2020. Excluded from the study were pediatric patients; patients with pre-existing Ménière's disease; tumors; barotrauma; acoustic trauma; retrocochlear disease; patients with a history of surgery or chronic otitis in the same ear; patients who were totally deaf, with no pure tone response at all frequencies pre-treatment, still no response post-treatment, or hearing threshold at all frequencies were equal to the audiometer upper limit; (250 Hz-105 dB HL, 500 Hz-120 dB HL, 1000 Hz-120 dB HL, 2000 Hz-120 dB HL, 4000 Hz-120 dB HL, 8000 Hz-100 dB HL) post treatment; patients who did not receive pure tone audiometry re-examination.

Patients were divided into three groups: the control group; group P2.0 (20.92± 26.11 dB) and group P2.2 (20.47±21.54 dB) based on their treatment protocol. The control group received medication recommended by the Guideline of Sudden Hearing Loss [1] over 10 days, including intravenous methylprednisolone 80mg once daily, ginaton injection 105mg once daily, Vitamin B1 tablet 10mg three times daily, and mecobalamin 0.5mg three times daily. Groups P2.0 and P2.2 received HBO_2 therapy in addition to routine pharmacotherapy, with hyperbaric exposures of 2.0 ATA and 2.2 ATA respectively. Both groups received seven to 10 daily sessions in a multiplace hyperbaric chamber. Each session consisted of 60-minute periods of inhalation of 100% oxygen interspersed with a 10-minute air break after 30 minutes of O_2 inhalation.

Pure-tone threshold audiometry was conducted pre- and post-treatment by a certified audiologist. According to degree of hearing loss and the frequency involved, type of audiometry curve is divided into four categories:

- ascending (hearing decreases below 1000 Hz, hearing loss ≥ 20 dB at 250 and 500 Hz);
- descending(hearing decreases above 2000 Hz and hearing loss ≥ 20 dB at 4000 and 8000 Hz);
- flat (hearing loss at all frequencies, average hearing threshold ≤80 dB); and
- total deafness(hearing loss at all frequencies, average hearing threshold ≥80 dB)[11].

The pure-tone average (PTA) for low-frequency descending-type hearing loss was the average threshold at 250 and 500 Hz. The PTA for high-frequency descending type hearing loss was the mean threshold at 4000 and 8000 Hz. PTA was calculated as an average threshold measured at 500, 1,000, 2,000, 4,000 Hz for full-frequency hearing loss. According to PTA pre- and post-treatment, the therapeutic effect is divided into four categories:

- ineffective (hearing gain less than 15 dB),
- effective (hearing gain between 15 dB and 30 dB),
- obvious (hearing gain more than 30 dB); and
- cured (impaired frequency hearing returns to normal/ healthy ear levels/pre-disease level) [11].

All statistical analyses were operated with SPSS 22.0 software at an alpha level of $p \le 0.05$. Count data were expressed as mean ± SD. The normal distribution test and analysis of variance (ANOVA) were adopted to check data normality and homogeneity variance. Baseline characteristics were compared across groups using multiple t-tests or the Mann-Whitney U test for non-normal distribution. The Kruskal-Wallis test was applied in the comparison of efficacy among the three groups, with the higher rank associated with better prognosis: "ineffective" was assigned to 1; "effective" was assigned to 2; "obvious" was assigned to 3; and "cured" was assigned to 4. Then the average effective rank was calculated. The sex distribution, type and severity of disease were data compared across the groups using Pearson's $\chi 2$ test. The hearing gain after treatment was compared across the groups using the Mann-Whitney U test.

RESULTS

A total of 160 patients with SSNHL were included. Characteristics of the three groups are summarized in Table 1. No statistically significant differences were shown between three groups except the sex, which is not a prognostic factor of SSNHL [12].

The audiometric thresholds at each frequency pre- and post-treatment among the three groups are shown in Table 2.

The effective rates of the control group, P2.0 group and P2.2 group were 41.67%, 46.15% and 45.76% respectively. Although the average rank of the P2.0 group and P2.2 groups was higher than that of the control group, there was no statistical difference in efficacy among the three groups (Table 3).

For further analysis, the hearing gain for PTA was calculated. The P2.2 group obtained the highest mean hearing gain of PTA (19.47±18.50), followed by the P2.0 group (18.94±21.42). The control group acquired

TABLE 1. Characteristics of patients

characteristics	control group (n=36)	P2.0 group (n=65)	P2.2 group (n=59)	p value
age, years	46.14±18.77	46.52±16.02	47.46±16.00	0.92
sex	7/29	37/27	42/16	<0.001
male	7	37	42	
female	29	27	16	
affected ear				0.82
left	19	32	32	
right	17	32	26	
course of disease (days)	9.72±15.58	7.19±6.21	9.36±12.50	0.94
type of audiometry curve				0.19
ascending	8	4	5	
descending	9	16	18	
flat	13	21	19	
total deafness	6	23	16	
severity of disease				0.18
mild (PTA: 20-40 dB)	2	2	6	
moderate (PTA: 41-60 dB)	13	12	15	
severe (PTA: 61-90 dB)	5	17	16	
profound (PTA >90 dB)	16	34	22	

TABLE 2. The audiometric thresholds pre- and post-treatment among groups

group	frequencies 250-500		frequencies 1000-2000		frequencies 4000-8000	
	PTA pre-treatment	PTA post-treatmt.	PTA pre-treatment	PTA post-treatmt.	PTA pre-treatment	PTA post-treatmt.
control	60.28±29.71 range: 12.5-112.5	48.33±31.90 range:5-112.5	68.33±32.54 range: 10-120	57.78±33.73 range: 2.5-120	71.60±34.25 range: 10-115	61.25±36.46 range: 2.5-115
P2.0	67.62±31.07 range: 7.5-112.5	46.69±29.87 range: 5-107.5	73.81±28.90 range: 17.5-120	55.85±29.48 range: 10-120	76.19±24.17 range: 0-110	63.65±26.63 range: 0-110
P2.2	59.36±33.19 range: 7.5-112.5	38.90±27.71 range: 0-102.5	65.47±32.70 range: 13-120	45.76±27.94 range: 5-100	71.82±26.74 range: 12.5-110	59.62±25.89 range: 5-102.5

TABLE 3. Comparison of treatment effect between groups

group	ineffective	effective	obvious	cured	average rank
control	21	9	2	4	76.75
P2.0	35	10	18	2	81.90
P2.2	32	10	13	4	81.25

$\chi 2 = 0.38$, df* = 2, $p = 0.827$ * degree of freedom

TABLE 4. The hearing gain of PTA between the groups

group	PTA before treatment	PTA after treatment	hearing gain	p-value
control	77.46±26.25	63.26±32.45	14.20±24.15	0.306
P2.0	80.06±21.77	61.12±25.88	18.94±21.42	
P2.2	73.60±24.59	54.13±22.35	19.47±18.50	

TABLE 5. Hearing gain among different frequency of three groups

group	hearing gain in the range of frequencies 250-500Hz (dB)	p	hearing gain in the range of frequencies 1000-2000Hz(dB)	p	hearing gain in the range of frequencies 4000-8000Hz(dB)	p
control	11.94±23.32		10.56±25.24		10.35±21.51	
P2.0	20.92±26.11*	0.047	17.96±25.25	0.197	12.55±17.03	0.78
P2.2	20.47±21. 54*	0.012	19.70±21.13*	0.015	12.20±15.25	0.625

*: the difference was statistically significant compared to the control group

the minimum (14.20±24.15). However, this did not reach statistical difference (Table 4).

Consequently, we focused on analyzing the hearing gain among different frequency of the three groups. As presented in Table 4, in range of frequencies 250-500Hz, P2.0 group (20.92±26.11 dB, $p<0.05$) and P2.2 group (20.47±21. 54 dB, p=0.01) both acquired higher hearing gain compared to the control group (11.94±23.32 dB). While in the range of frequencies 1000-2000 Hz, only the P2.2 group was shown to significantly enhance the hearing gain in comparison with the control group (19.70±21.13 vs. 10.56±25.24 dB, p=0.015). In the range of frequencies 4000-8000, both the P2.0 and P2.2 groups failed to reach the desired effect (Table 5).

DISCUSSION

Factors influencing the efficacy of HBO_2 in the treatment of SSNHL, such as the number of sessions and intervention time, has been intensively studied [2,13-15], while the relationship between therapeutic pressure and effect is still obscure. To our best knowledge, only three studies have reported the relationship between therapeutic pressure and effect [10,16,17]. Desloovere applied HBO_2 as salvage treatment at 1.5 ATA and 2.5 ATA. The outcome of patients with 2.5-ATA HBO_2 showed higher mean hearing gain than those with 1.5-ATA HBO_2 or the control [16]. It suggested that efficacy of HBO_2 for SSNHL was better at higher pressure when used as salvage treatment. However, the most effective pressure of HBO_2 when applied as initial therapy is unknown. Zong reported that patients who received HBO_2 as initial therapy at 2.2 ATA gained a higher effective rate compared to patients who received HBO_2 at 2.0 ATA and the control group (86.67%, 60%, 33.33% respectively) after 20 daily sessions [17]. Our results showed no significant differences in the effective rate between the 2.2-ATA and 2.0-ATA HBO_2 treatment groups, but the number of sessions in our study (seven to 10 daily sessions) may be insufficient to fully reflect the efficacy of HBO_2 in the treatment of SSNHL. Krajcovicova adopted HBO_2 as the initial therapy for 10-20 daily sessions and found that 2.0-ATA pressure brought higher hearing gain in the range of frequencies 1000-2000 compared to 2.5 ATA [10].

In our study the 2.0 ATA pressure did not showed superiority compared to 2.2 ATA in the range of frequencies 1000-2000 Hz. We may infer that beyond a certain range of pressure the benefit brought by the higher pressure is no longer valid. Our results showed the 2.2-ATA HBO_2 treatment brought higher hearing gain in the range of 1000-2000 Hz than the control. The HBO_2 groups had no significant benefits over the control group at either 2.0 or 2.2 ATA in terms of hearing improvement at 4000-8000 Hz.

Since our study adopted therapeutic pressures of 2.0 ATA and 2.2 ATA only, the efficacy of a higher HBO_2 pressure protocol (such as a 2.4 ATA or 2.5 ATA) requires further investigation. The question of whether there is a linear relationship between the efficacy of hyperbaric oxygen and therapeutic pressure or a specific pressure range only requires further research.

The pathological mechanism of SSNHL is unclear. Theories include vascular occlusion, endolymphatic hydrops, viral infection, systemic immune-mediated mechanisms and others [18-20]. Although there are several theories, it may be a combination of multiple mechanisms. The paradox between the organ of Corti's sparse blood supply [21] and high requirement for oxygen supplies (especially the stria vascularis and organ of Corti [22]) plays a key role in the pathological process of SSNHL [23]. Hypoxia of the stria vascularis may lead to Na+/K+ pumps dysfunction and endolymphatic hydrops, which could cause low-tone hearing loss [24]. Hypoxia of the organ of Corti may bring about hair cell-cilia fusion, synaptic, dendritic swelling and persistent depolarization [23].

HBO_2 could exert great influence in oxygen transport, hemodynamics and the inner ear pressure regulating system, enhancing the volume of dissolved oxygen in plasma as well as partial pressure of oxygen in the inner ear [25,26]. HBO_2 at 1.6 ATA increases perilymph partial pressure of oxygen 9.4-fold, prolonging the diffusion distance of oxygen; this allows for more efficient oxygen transport from perilymph to the cochlea and structures within it [27,28]. A greater oxygen supply to the stria vascularis could make Na+/K+ pumps perform better in maintaining high potassium and low sodium levels in the endolymph, promoting electrophysiological functional recovery of the inner ear [29], thus relieving endolymphatic hydrops. Additionally, the changing pressure press under HBO_2 facilitates the process of endolymph outflow to the cerebrospinal fluid [26].

It is thus inferred that the electrophysiological function of inner ears can be recovered by strengthening the perilymph oxygen partial pressure while relieving capillary endothelial cell edema, combined with higher therapeutic pressure, higher partial pressure of oxygen, longer diffusion distance and more efficient dissolution of oxygen. It can be concluded that with the joint efforts of the mechanisms mentioned above, a pressure variation of even 0.2 ATA can have a different effect.

Higher-pressure HBO_2 may induce more oxidative stress, which is associated with the duration and therapeutic pressure of exposure [30-32]. Körpınar and colleagues showed that the level of serum malondialdehyde (MDA) increased and the superoxide dismutase (SOD) activity decreased after three sessions of HBO_2 treatments, while after 15 sessions of HBO_2 treatments, the level of MDA and SOD activity returned to normal in both the P2.0 and P2.4 groups [33]. There is great variability in threshold improvement in the present study (and other similar studies in the literature), demonstrating substantial interindividual differences in response to HBO_2 treatment. This may reflect the balance of oxidative stress and efficacy of HBO2 in different individuals with different pathological processes. It suggests that close observation of patients' hearing recovery and real-time adjustment of each treatment plan may achieve a more effective curative outcome.

Limitations

A limitation is that the number of sessions and sample size in our study may be insufficient to fully reflect the efficacy of HBO_2 in the treatment of SSNHL. Another limitation is that the protocol did not include higher therapeutic pressures, such as 2.4 and 2.5 ATA. Moreover, the pure-tone threshold audiometry was not followed up after discharge.

CONCLUSION

Our results indicate that the therapeutic efficacy of HBO_2 treatment for SSNHL is associated with the therapeutic pressure applied. A 2.2-ATA HBO_2 protocol appears to be more beneficial in hearing gain than a 2.0-ATA protocol at 1000-2000 Hz frequencies. Further clinical trials are needed to identify the most suitable hyperbaric protocol (i.e., therapeutic pressure, exposure duration and number of sessions) for SSNHL.

Conflict of interest statement

The authors have declared no conflicts of interest.

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