

## Adjunctive hyperbaric oxygen treatment for idiopathic sudden sensorineural hearing loss

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### ABSTRACT

**Introduction:** This study aims to evaluate the hearing gain efficacy from adjunctive hyperbaric oxygen (HBO<sub>2</sub>) treatment in patients with idiopathic sudden sensorineural hearing loss (ISSHL).

**Materials and Methods:** A retrospective analysis of chart reviews was performed on patients with ISSHL between January 2013 through December 2015. All patients were referred to us from our ENT Department for adjunctive hyperbaric oxygen treatment. The results were assessed through pure-tone audiometry (PTA) data change (hearing gain), both before and after HBO<sub>2</sub> treatment. Age, gender, affected ear side, HBO<sub>2</sub> treatment sessions, both before and after HBO<sub>2</sub> treatment PTA were all recorded.

**Results:** Ninety-three (93) patients with ISSHL were included in the study. The average hearing gain in this study was 17.9 dB ( $p=0.001$ ), where a total of 46 (49.46%) patients showed an improvement (hearing gain  $\geq 10$  dB) in response to HBO<sub>2</sub> treatment ( $p=0.002$ ). Patients with the poorest initial severity of hearing loss who displayed a greater degree of hearing improvement after HBO<sub>2</sub> treatment were male and in the 40- to 59-year-old age group.

**Conclusion:** This study found that adjunctive hyperbaric oxygen treatment was efficacious for patients with idiopathic sudden sensorineural hearing loss. The total average hearing gain was recorded to be 17.9 dB.

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### INTRODUCTION

Idiopathic sudden sensorineural hearing loss (ISSHL) is one otological emergency whose pathogenesis is uncertain. It is associated with either total or partial loss of a patient's hearing function [1]. A common disease, ISSHL is defined when sensorineural hearing loss at a minimum of 30 dB occurs in at least three frequencies for three days or more [2]. This loss has a significant effect on quality of life.

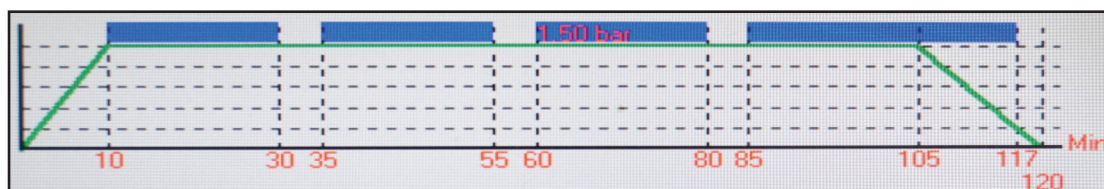
Hyperbaric oxygen treatment may improve oxygen supply to the inner ear, resulting in an improvement in a patient's hearing [3]. Systemic corticosteroid therapy is the only standard drug therapy currently in use [4].

Treatment protocols aim to decrease the inflammatory state of the inner ear while increasing blood supply and oxygenation [5-6]. Ethically, however, we cannot simply compare hyperbaric oxygen treatment with systemic corticosteroid therapy. Conventionally, we have treated ISSHL patients with systemic corticosteroid therapy while adding hyperbaric oxygen (HBO<sub>2</sub>) treatment.

In October 2011, the Undersea Hyperbaric Medical Society (UHMS) included ISSHL in its list of approved indications [7-9]. However in Taiwan, the Central Health Insurance Bureau does not pay for treatment of this indication, which means patients still must

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**KEYWORDS:** idiopathic sudden sensorineural hearing loss; ISSHL; hyperbaric oxygen;



**FIGURE 1a:** A standard 2.5 atmospheres absolute, 120-minute treatment protocol (three five-minute air breaks per session)



**FIGURES 1b, 1c:** Hyperbaric oxygen treatment chamber in Taichung Veterans General Hospital, Taiwan.

receive HBO<sub>2</sub> treatment at their own expense. We hope that through the result analysis, our objective data presentation provides a clearer reference for recommendations of HBO<sub>2</sub> treatment in ISSHL patients.

This study aimed to identify adjunctive HBO<sub>2</sub> treatment effects in patients with ISSHL. By analyzing the extent of improvement after HBO<sub>2</sub> treatment (hearing gain) in gender, age grouping, affected ear side and initial hearing loss severity, the relevance of diagnosis and treatment can be further explored.

### Materials and methods

A retrospective analysis of chart review was performed for one hundred and five (105) patients experiencing sudden sensorineural hearing loss between January 2013 and December 2015. Eight (8) patients (one right-ear-sided and seven left-ear-sided), who had initial hearing loss of less than 30 dB – determined by PTA (pure-tone audiometry) – were deemed incompatible with the definition of ISSHL and excluded from the study. Four (4) additional patients were also excluded due to their young age (<20 years old), according to the rules of our institutional review board. This resulted in a total of ninety-three (93) patients being included for

analysis. The study was subsequently approved by the hospital individual Institutional Review Board and Ethics Committees (approval number: CE16057B).

All patients were referred from our ENT department for adjunctive hyperbaric oxygen treatment using a standard 2.5-atmospheres absolute (ATA) 120-minute protocol with three five-minute air breaks per session (Figures 1a, 1b, 1c), and treated with our ENT department standard ISSHL regimen. All patients were referred to our department, required to sign self-pay and HBO<sub>2</sub> treatment consent forms prior to treatment.

In order to avoid middle ear barotrauma, we instructed the patients in how to equalize middle ear pressure and to evaluate the efficacy of both the Valsalva and Toynbee maneuvers before HBO<sub>2</sub> treatment. If the patients were unable to equalize middle ear pressure, they would be referred back to our ENT department for tympanic membrane puncture. With appropriate education and evaluation, 28 (30%) of 93 patients experienced pain in the eardrum during the HBO<sub>2</sub> treatment pressurizing period. When this occurred, we would reduce the pressurizing speed and allow patients time to adjust. Only three patients underwent myringotomy.

Because treatment was performed at the patient's own expense, each was originally scheduled to undergo five sessions. Once treatment began, the number of treatment sessions was determined by the patient: Some received one treatment, while others received up to 15 sessions. A total of 13 patients (14.0%) received fewer than five sessions, 64 (69%) received five sessions, and 16 (17.2%) patients received more than five sessions.

Based on reports from Bennett MH, et al., as recorded in the Cochrane Database [3], there was no evidence of a beneficial effect of HBO<sub>2</sub> on chronic ISSHL or tinnitus. In our study, all patients had been experiencing acute-stage ISSHL, and most were referred from our ENT outpatient department. Because of this, comorbidities were not analyzed in this study. Sudden hearing loss was accompanied by tinnitus in 51 (54.8%) patients and vestibular symptoms (dizziness, vertigo) in 23 (24.7%); however, none of these side effects was noted to affect prognosis. ISSHL was assessed by PTA data change before and after HBO<sub>2</sub> treatment (hearing gain). Age, gender, affected ear side, HBO<sub>2</sub> sessions, along with before and after HBO<sub>2</sub> treatment PTA data were recorded. Patients were grouped according to their ages: 20-39 years old; 40-59 years old; age 60 and up.

In accordance with the American Speech and Hearing Association guidelines [5], hearing loss was defined as mild (20-39 dB hearing loss/HL), moderate (40-54 dB HL), moderate to severe (55-69 dB HL), severe (70-89 dB HL), and profound ( $\geq 90$  dB HL). Because of the small sample size in this study and the definition of ISSHL, we grouped the patients according to initial severity of hearing loss as those mild to moderate (30 to 54 dB HL), severe (55 to 89 dB HL) and profound ( $\geq 90$  dB HL).

Hearing outcome levels were determined by hearing gain in PTA change. The most lenient (and possibly the most commonly encountered definition of treatment response) is an improvement of  $\geq 10$  dB in hearing gain or an improvement of 10% to 15% in speech discrimination score [10]. Because of its relative simplicity, and its ability to be performed without any knowledge of prior hearing function or a normally hearing contralateral ear, improvement was defined as a hearing gain of  $\geq 10$  dB, steady was

**TABLE 1: Baseline characteristics of the enrolled subjects**

	N (%)	initial hearing (dB)	p-value
	93 (100)	74.9 $\pm$ 24.9 (32.0, 120.0)	
<b>gender</b>			0.192 <sup>#</sup>
male	49 (52.7)	71.7 $\pm$ 23.9 (32.0, 118.0)	
female	44 (47.3)	78.5 $\pm$ 25.7 (33.0, 120.0)	
<b>side</b>			0.876 <sup>#</sup>
left	45 (48.4)	75.4 $\pm$ 25.3 (33.0, 120.0)	
right	48 (51.6)	74.5 $\pm$ 24.7 (32.0, 120.0)	
<b>age</b>			0.701 <sup>⊕</sup>
<40	14 (15.1)	75.9 $\pm$ 30.1 (35.0, 118.0)	
40-59	52 (55.9)	72.8 $\pm$ 23.8 (32.0, 120.0)	
$\geq 60$	27 (29.0)	78.6 $\pm$ 24.5 (43.0, 120.0)	
<b>initial severity</b>			0.00 <sup>⊕*</sup>
mild to moderate	21 (22.6)	43.4 $\pm$ 7.4 (32.0, 53.0)	
severe	48 (51.6)	72.2 $\pm$ 10.9 (55.0, 88.0)	
profound	24 (25.8)	108.0 $\pm$ 11.2 (90.0, 120.0)	

# – independent t test; ⊕ –Kruskal-Wallis test; \* – p< 0.05; data were presented with mean  $\pm$  standard deviation (min, max)

defined as a hearing gain of between 0 and 10 dB, and deterioration was defined as  $\leq 0$  dB in PTA change.

### Statistical analysis

All data were reported as mean  $\pm$  standard deviation (SD) for continuous variables or number (percentage) for categorical variables. Comparisons were performed using the independent t-test or Kruskal-Wallis test for continuous variables in normal or non-normal distribution, respectively, while the chi-square test was used for categorical variables. Trends in improvement, depending on initial severity with sex, age, and affected ear side, respectively, were analyzed. Statistical significance was set at p<0.05. Statistical analysis was performed using the SPSS version 18.0 (SPSS, Chicago, Illinois, U.S.).

### RESULTS

A total of 93 patients (49 males, 44 females) with ISSHL were included. Mean age of the patients was 52.8 years old (range: 21–84 years of age). Hearing loss was right-sided in 45 (48.4%) of the patients and left-sided in 48 (51.6%) (Table 1). Gender, different side affected ear, age group, and initial severity of hearing loss classi-

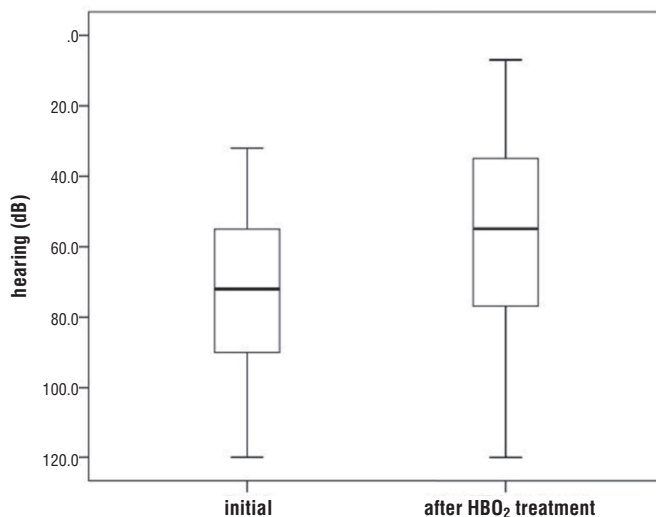
**TABLE 2: Hearing gain after HBO<sub>2</sub> treatment**

group	hearing gain (dB)			p- value
gender	male	female		0.899#
	17.7 ± 24.9	18.3± 21.8		
side	left	right		0.600#
	16.7± 26.0	19.3± 20.3		
age	<40	40-59	≥60	0.917⊕
	16.0± 20.5	19.5± 26.5	16.0± 18.2	
initial severity	mild to moderate	severe	profound	0.480⊕
	9.4± 10.0	21.7± 26.8	18.0± 22.7	

Hearing gain showed no significant difference in gender, affected ear side, age grouping, and initial severity of hearing loss.

All values present with mean ± sd; #: independent t test;

⊕: Kruskal-Wallis test

**FIGURE 2: Hearing comparison**

Comparison of hearing between initial and post-HBO<sub>2</sub> treatment ( $p=0.001$ ).

fication showed no significant difference in hearing gain after HBO<sub>2</sub> treatment was completed (Table 2).

The average hearing gain was 19.3 dB for right-sided patients and 16.7 dB for left-sided patients, with the total average hearing gain recorded at 17.9 dB. For all patients before HBO<sub>2</sub> treatment, mean hearing loss was shown to be PTA:  $74.9 \pm 24.9$  dB, whereas after HBO<sub>2</sub> treatment hearing loss – PTA:  $57.0 \pm 29.5$  dB – displayed a significant improvement ( $p=0.001$ ) (Figure 2).

For patients affected in the right ear, 27 showed improvement ( $\geq 10$  dB) in hearing gain, while 11 remained steady (between 0 and 10 dB), and seven (7) displayed deterioration ( $\leq 0$  dB). For patients affected in the left ear, 19 showed improvement in hearing gain, 17 remained steady, and 12 displayed deterioration. A total of 46 (49.46%) patients showed an improvement in hearing gain ( $p=0.002$ ) during this study as determined by the chi-square test (Figure 3-1). Initial severity of hearing loss and response (improvement, steady, deterioration) after HBO<sub>2</sub> treatment was not associated ( $p=0.522$ ) (Figure 3-2).

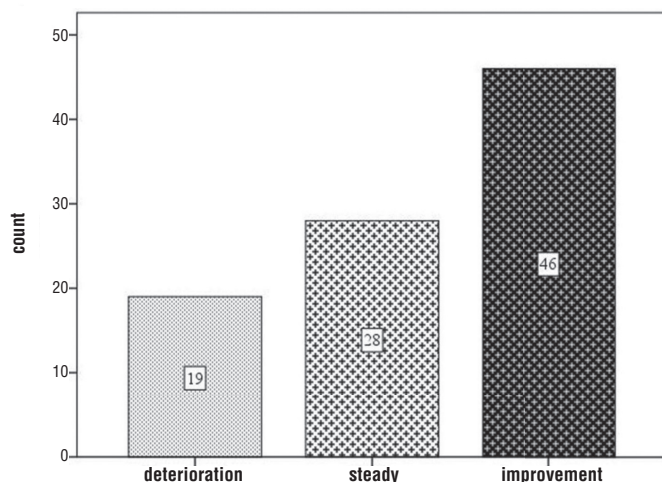
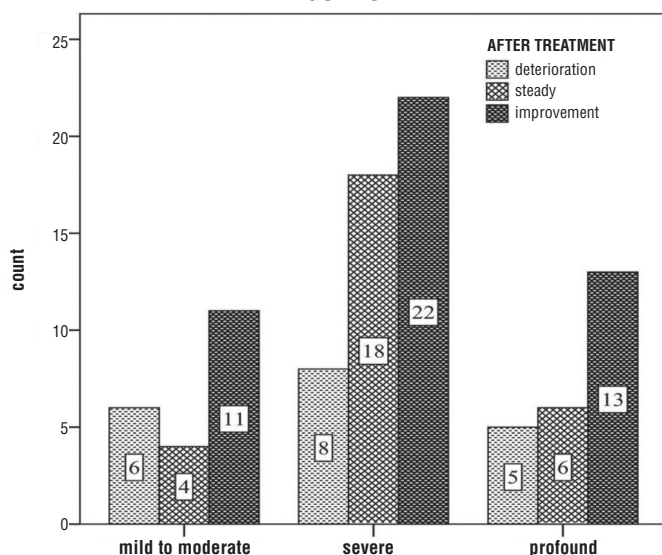
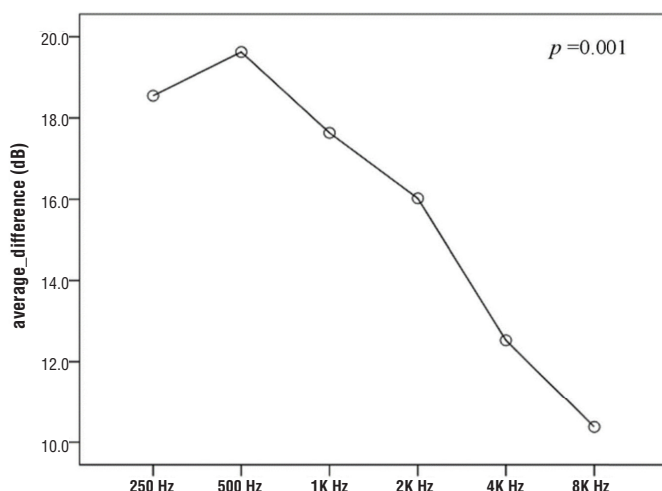
The analysis of the affected frequencies is presented in Table 3. Hearing gain showed a significant difference ( $p=0.000-0.006$ ) in different affected frequencies (250 Hz, 500 Hz, 1k Hz, 2k Hz, 4k Hz, 8k Hz). For patients with hearing loss of  $\geq 30$  dB in different affected frequencies, there are significant treatment effects in before-after data, especially in low frequencies (Figure 3-3). The initial PTA evaluation revealed that 21 (22.6%) of the patients displayed mild to moderate hearing loss, whereas 48 (51.6%) had severe hearing loss, and 24 (25.8%) had profound hearing loss (Table 1).

There was no statistical significance between the initial severity of hearing loss before HBO<sub>2</sub> treatment, and hearing gain after HBO<sub>2</sub> treatment (Table 2). An improvement in response after HBO<sub>2</sub> treatment was found in 11 (52.4%) patients, 22 (45.8%) patients, and 13 (54.2%) patients respectively, in the mild to moderate, severe and profound classification of initial hearing loss. This showed the highest proportion of improvement in all three initial severity of hearing loss classifications (Figure 3-2).

The two separate genders within the initial severity of hearing loss classification showed no significant difference in hearing gain. However, in male patients it can be seen that the worse initial severity of hearing loss showed greater hearing gain after HBO<sub>2</sub> treatment (Figure 4).

A total of 14 (15%) patients were 20-39 years old, 52 (56%) were between the ages of 40 and 59, and 27 (29%) were  $\geq 60$  years old (Table 1). In the 40-59 age group with the greater initial severity of hearing loss there was a major trend of hearing gain after HBO<sub>2</sub> treatment (Figure 5). However, the



**FIGURE 3-1****FIGURE 3-2****FIGURE 3-3**

three age groups in the initial severity of hearing loss showed no significant differences among them in hearing gain upon completion of HBO<sub>2</sub> therapy.

HBO<sub>2</sub> treatment with the different side affected ear in our study showed no significant difference in hearing gain (Table 2). However, it can be seen that the patients in the severe and profound categories gained more, but the mild to moderate group showed a smaller hearing gain (Figure 6).

According to data analysis of the actual recording, there was no significant difference in hearing gain among treatment effects in patients who received fewer than five sessions of HBO<sub>2</sub> therapy, five sessions, and more than five (Figure 7).

## DISCUSSION

The spontaneous recovery rate of ISSHL ranges between 32% and 65% and most commonly occurs within the first two weeks after the onset of hearing loss. Various forms of treatment have become widely accepted as being beneficial in most circumstances, and the concept of not providing such treatments to patients could conceivably be viewed as unethical [6, 10]. In our study, no patient was left untreated and all were referred from and treated at our ENT department.

Before and after HBO<sub>2</sub> treatment PTA levels were also recorded. Therefore, the spontaneous recovery rate of ISSHL and simple comparison between hyperbaric oxygen treatment with the systemic corticosteroid (SC) effect are unable to be determined from this study.

One additional study compared HBO<sub>2</sub> treatment and intratympanic (IT) steroid injection on hearing gain after attempts with primary treatment in patients with ISSHL failed [11]. The conclusion gained from this was that HBO<sub>2</sub> treatment could be successfully used as a salvage therapy in patients who experienced sudden deafness.

## LEGENDS

**Figure 3-1:** Response results of HBO<sub>2</sub> treatment ( $p = 0.002$ ).

**Figure 3-2:** Response after HBO<sub>2</sub> treatment among initial severity of hearing loss classification ( $p = 0.522$ ).

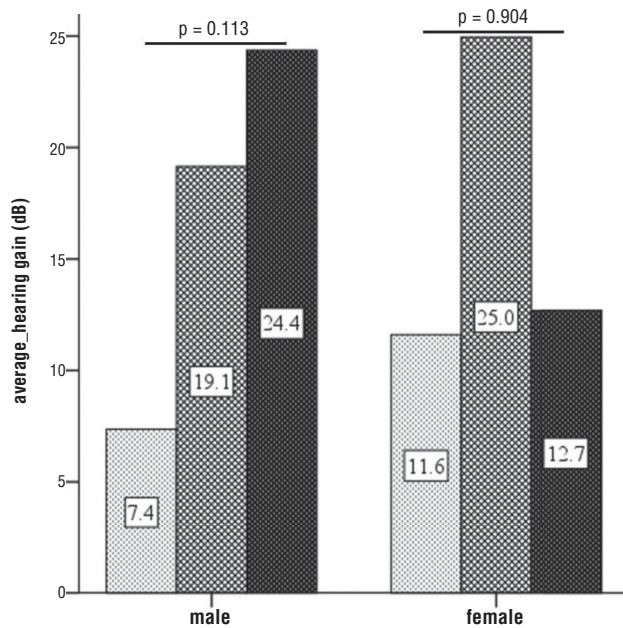
**Figure 3-3:** p-value of trend of different affected frequency effect; hearing gain (average\_difference) showed larger improvement in low frequencies.

**TABLE 3: Hearing gain**

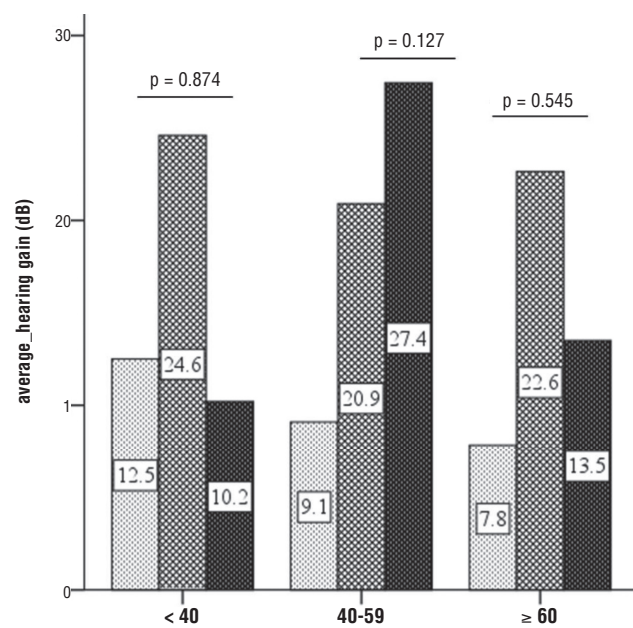
	initial (dB)	after HBO <sub>2</sub> treatment (dB)	hearing gain (dB)	p#	≥ 30dB: N (%)		p <sup>○</sup>
					initial	after HBO <sub>2</sub> treatment	
250 Hz	67.7± 25.7	49.2± 29.9	18.4± 24.7	0.000*	84 (90.3)	61 (65.6)	0.000*
500 Hz	73.5± 26.6	53.9± 30.7	19.6± 24.4	0.000*	88 (94.6)	66 (71.0)	0.000*
1K Hz	76.9± 25.4	59.2± 31.1	17.6± 23.2	0.000*	91(97.8)	75 (80.6)	0.000*
2K Hz	73.1± 24.9	57.1± 30.6	16.0± 22.3	0.000*	91 (97.8)	76 (81.7)	0.001*
4K Hz	75.0± 24.4	62.5± 29.8	12.5± 19.9	0.002*	91 (97.8)	79 (84.9)	0.004*
8K Hz	82.7± 19.8	72.4± 29.6	10.4± 20.5	0.006*	92 (98.9)	80 (86.0)	0.002*

# : independent t test; °: chi-square test; \* : p< 0.05

Hearing gain showed significant difference in different affected frequencies. Patients with hearing loss ≥30dB before and after HBO<sub>2</sub> treatment showed significant changes in different frequencies.

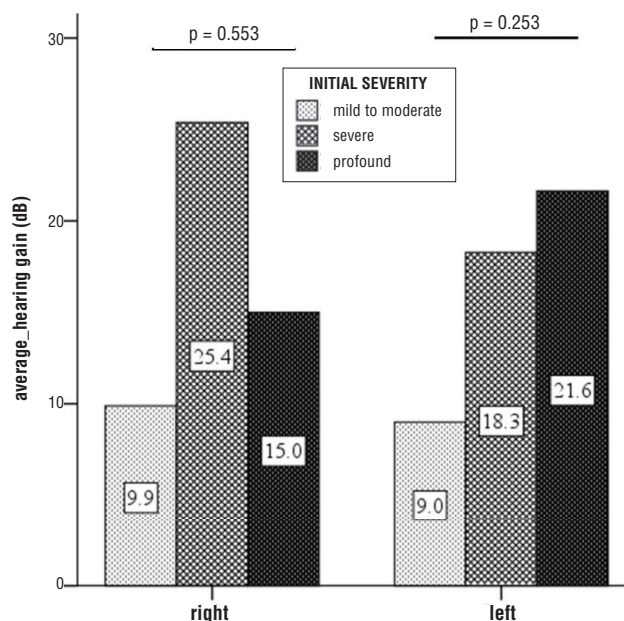
**FIGURES 4 and 5: Trend analysis of hearing gain**

**Figure 4:** Trend analysis of hearing gain among initial severity of hearing loss classification with gender. P-value of male and female was 0.113 and 0.904, respectively.



**Figure 5:** Trend analysis of hearing gain among initial severity of hearing loss classification with age. P-value of ages <40, 40-59 and ≥60 was 0.874, 0.127 and 0.545, respectively.

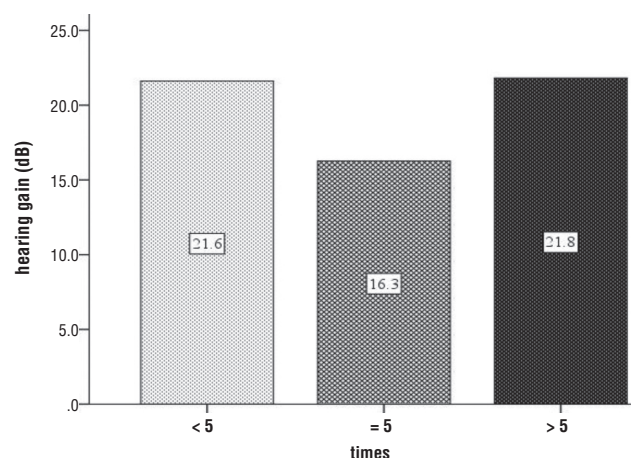
**INITIAL SEVERITY**  
 mild to moderate  
 severe  
 profound

**FIGURE 6: Trend analysis of hearing gain**

**Figure 6:** Trend analysis of hearing gain among initial severity of hearing loss classification with different side affected ear. P-value of the right and left side was 0.553 and 0.253, respectively.

An additional study was also performed in order to compare the efficacy of IT steroid injection, HBO<sub>2</sub>, and combination therapy as salvage treatments in patients with ISSHL [13]. The conclusion here was that the IT steroid injection, HBO<sub>2</sub>, and combined therapy offered some benefits toward hearing improvement. Some studies showed that a delay in treatment was a negative prognostic factor [1, 5, 12]. The results of one study showed that the best and most consistent results were obtained when HBO<sub>2</sub> treatment was initiated within two weeks of symptoms onset and combined with corticosteroid treatment [14]. In general, adjunctive HBO<sub>2</sub> treatment and SC at our ENT department were provided simultaneously. There was no delay in offering HBO<sub>2</sub> therapy. Our HBO<sub>2</sub> treatment is initiated within two weeks of symptom onset and combined with SC.

The treatment of ISSHL remains a most challenging subject. Due to the fact that the etiology is unclear, many treatment options are attempted using various protocols.

**FIGURE 7: Hearing gain comparison**

**Figure 7:** HBO<sub>2</sub> treatment sessions showed no significant difference in hearing gain ( $p=0.628$ ) with the Kruskal-Wallis test: < 5 sessions,  $n=13$ ; 5 sessions,  $n=64$ ; > 5 sessions,  $n=16$

Systemic corticosteroid continues to be widely used. Additional treatment modalities, including HBO<sub>2</sub>, have been studied with conflicting results [5, 10]. In our study, we included adjunctive HBO<sub>2</sub> treatment for ISSHL patients and set the definition of improvement at ( $\geq 10$  dB), steady (between 0 and 10 dB), and deterioration ( $\leq 0$  dB) to evaluate the therapeutic effect. A total of 46 (50%) patients showed improvement ( $p=0.002$ ) in hearing gain after HBO<sub>2</sub> treatment. For more patients with affected high frequency, the treatment response is good, but even better in affected low frequency. Further research is needed to understand these results.

To define “recovery” is a matter of debate when both reporting and comparing the results of ISSHL cases. Criteria may include either absolute decibel (dB) gain or relative dB gain (percentage of improvement), or it may use the contralateral ear as a reference [10]. Studies performed by Pezzoli M, et al. and Bennett MH, et al. recorded in the Cochrane database [3, 12] showed results of absolute improvement in average PTA (15.6 dB) after HBO<sub>2</sub> treatment. In our study, we used the absolute dB gain as the evaluation for the effect of HBO<sub>2</sub> treatment. Our study showed a total average hearing gain of 17.9 dB after HBO<sub>2</sub> treatment ( $p=0.001$ ).



ISSHL occurs throughout a wide range of ages. It is more common for those between 30 and 50 years of age. In our study, most of the patients – 52 (56%) – were between 40 and 59 years of age. Additional studies have found that younger patients were reported to have a better prognosis [5, 11]. In our study, HBO<sub>2</sub> treatment had the better effect in the worse initial severity of hearing loss category for patients aged 40–59. Patients aged 20–39 and ≥60 years showed a poor response to HBO<sub>2</sub> in both the mild to moderate and profound severity of hearing loss classification. Throughout all age groups, the severe initial severity of hearing loss patients showed solid hearing improvement after HBO<sub>2</sub> treatment (Figure 5). However, the three age groups in the initial severity of hearing loss classification showed no significant difference in hearing improvement after HBO<sub>2</sub> treatment.

The correlation between the initial severity of hearing loss and recovery (hearing gain after HBO<sub>2</sub> treatment) has been established [5-6, 11-12], but the results are conflicting. Three studies showed more effective results in mild initial hearing loss [5-6, 11]. One study showed that patients with worse hearing loss had the greater degree of improvement [12]. In our present study, hearing gain after HBO<sub>2</sub> treatment during the initial severity of hearing loss before treatment implied no statistical significance. However, the initial severity of hearing loss classification recorded the highest percentage of improvement (Figure 3-2). Initial severity of mild to moderate, severe, and profound hearing loss showed 9.4 dB, 21.7 dB and 18.0 dB of hearing gain, respectively, after HBO<sub>2</sub> treatment. Regardless of the initial severity of hearing loss classification, close to 50 percent of patients were treated effectively.

A study performed by Ceylan AI, et al. [15] showed that poor prognostic factors in the outcome of sudden hearing loss were female gender, presence of vertigo, initiation of treatment more than seven days after onset of hearing loss, and >40 dB hearing loss on admission. In our study, hearing gain showed a significant good response within the worse initial severity of hearing loss in males (Figure 4). However, it showed no significant difference in hearing gain.

A study for a general population has found that the left ear was on an average slightly but significantly poorer than the right ear at high frequencies, while at low frequencies the right ear was on average poorer than the left ear. It seems that handedness cannot be responsible for hearing threshold asymmetry [16]. HBO<sub>2</sub> treatment hearing gain was analyzed using the different side affected ear hearing loss in our study. The effect of hearing gain was noted in the right side affected ear (19.3 dB) and the left side affected ear (16.7 dB). There was no significant difference ( $p=0.600$ ) in hearing gain between two sides.

A study by Körpınar S, et al. [17] demonstrated that hearing gain was statistically significant after a higher number of HBO<sub>2</sub> treatment sessions (twice a day, mean sessions 18, range 5-31 sessions, the decision to terminate HBO<sub>2</sub> treatment by the referral clinic by evaluating the audiometric follow-ups). In our study, the number of treatment sessions was determined by the patient. Patients elected receive more treatment sessions to enhance the efficacy, or they chose to give up treatment to save money. Hence, HBO<sub>2</sub> therapy hearing gain with the number of treatment sessions showed no significant difference in our study.

## CONCLUSION

This study found that adjunctive HBO<sub>2</sub> treatment and systemic corticosteroid at our ENT department are efficacious. A total of 46 (49.46%) patients showed hearing improvement ( $p=0.002$ ), with total average hearing gain of 17.9 dB after HBO<sub>2</sub> treatment ( $p=0.001$ ). For patients age 40-59 and male gender, the HBO<sub>2</sub> treatment had the better effect regardless of the initial severity of hearing loss. Further studies with an increasing sample size are required to construct a more comprehensive understanding of variables in this research study. ■

## Conflict of interest statement

*Authors declare no conflicts of interest exist with this submission.*



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