

Treatment effectiveness according to frequencies in patients with sudden sensorineural hearing loss

Eficacia del tratamiento según las frecuencias en pacientes con pérdida auditiva sensorineural súbita

Ahmet Celik^{1*} and Ferit Akil²

¹Department of Otorhinolaryngology, Silopi State Hospital, Sirmak; ²Department of Otorhinolaryngology, Memorial Diyarbakır Hospital, Diyarbakır. Turkey

Abstract

Objective: The objective of the study is to evaluate combined hyperbaric oxygen therapy (HBOT) and steroids on hearing in sudden sensorineural hearing loss (SSNHL) patients. **Method:** A total of 50 patients with sudden hearing loss that started within 1 week and who received a combination of intravenous steroid therapy and HBOT in their medical treatment were assigned to the otolaryngology department for 1 week, followed by intravenous steroid therapy at 1 mg/kg/day and then reduced doses for 1 week. They were treated once in a hyperbaric chamber where they breathed 100% oxygen at 2.5 atm pressure for 60 min, for a total of 20 sessions. **Results:** Hearing loss was observed in 54% of participants in the right ear. Significant improvements were observed in hearing thresholds across all tested frequencies after treatment with a specific intervention ($p < 0.001$ for each comparison). Combined steroid and HBOT significantly improved hearing across low and high frequencies ($p < 0.001$). Improvement in hearing at low frequencies was significantly greater than at high frequencies ($p < 0.01$). Post hoc analysis showed greater hearing improvement at lower frequencies compared to higher ones. **Conclusions:** This study demonstrated that combined steroid and HBOT significantly improves hearing thresholds in patients with idiopathic SSNHL, especially at lower frequencies.

Keywords: Sudden sensorineural hearing loss. Hyperbaric oxygen therapy. Corticosteroids.

Resumen

Objetivo: Evaluar la terapia combinada de oxígeno hiperbárico y corticosteroides en pacientes con pérdida auditiva sensorineural súbita. **Método:** Se incluyeron 50 pacientes con pérdida auditiva súbita iniciada dentro de 1 semana, quienes recibieron un tratamiento médico combinando corticosteroides intravenosos y terapia de oxígeno hiperbárico. Fueron asignados al departamento de otorrinolaringología por 1 semana, seguido de corticosteroides intravenosos a dosis de 1 mg/kg al día y luego dosis reducidas por 1 semana. Se trató a los pacientes en una cámara hiperbárica en la que respiraron oxígeno al 100% a una presión de 2.5 atm durante 60 minutos, para un total de 20 sesiones. **Resultados:** Se observó pérdida auditiva en el oído derecho en el 54% de los participantes. Se encontraron mejoras significativas en los umbrales auditivos en todas las frecuencias después del tratamiento con una intervención específica ($p < 0.001$ para cada comparación). La combinación de corticosteroides y terapia de oxígeno hiperbárico mejoró significativamente la audición en frecuencias bajas y altas ($p < 0.001$). La mejora en la audición en frecuencias bajas fue significativamente mayor que en altas ($p < 0.01$). Un análisis post hoc mostró una mayor mejora auditiva en las frecuencias bajas comparadas con las altas. **Conclusiones:** Este estudio demostró que la terapia combinada de corticosteroides y oxígeno hiperbárico mejora significativamente los umbrales auditivos en pacientes con pérdida auditiva sensorineural súbita idiopática, en especial en frecuencias bajas.

Palabras clave: Pérdida auditiva sensorineural súbita. Terapia de oxígeno hiperbárico. Corticosteroides.

*Correspondence:

Ahmet Celik

E-mail: ahmetcelikk1982@gmail.com

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Introduction

Sudden sensorineural hearing loss (SSNHL) presents a significant clinical challenge within the field of otolaryngology, representing an acute onset of hearing impairment that necessitates immediate medical attention¹⁻⁴. Characterized by a rapid reduction in hearing capacity, SSNHL is defined as a sensorineural hearing loss of 30 decibels (dB) or more across at least three contiguous audiometric frequencies occurring within a 72-h period^{5,6}. This condition is a perplexing medical emergency, not only due to its abrupt manifestation but also because its etiopathogenesis remains largely enigmatic, complicating both diagnosis and treatment strategies^{2,4,5}.

The prevalence and incidence rates of SSNHL underscore its significance within the general population, with estimates suggesting that it accounts for approximately 1% of all sensorineural hearing loss cases^{1-3,7}. Epidemiological studies report an incidence ranging from 5 to 20 cases/100,000 individuals annually, highlighting the condition's relatively uncommon yet impactful presence in clinical practice^{2,8,9}. Despite its rarity, the potential for spontaneous recovery – reported in various studies to range between 32% and 65% – further complicates the clinical approach to management and underscores the urgency for efficacious treatment modalities^{4,8,9}.

The etiology of SSNHL is multifactorial, with numerous proposed mechanisms including viral infections, vascular occlusions, autoimmune diseases, and more^{2,10}. However, a significant proportion of cases remains idiopathic, with no discernible cause, which has led to challenges in developing targeted treatment strategies. In the absence of clear etiological pathways, the management of SSNHL often adopts a broad-spectrum approach aimed at mitigating the effects of potential underlying causes¹⁰.

Corticosteroids have long been the cornerstone of SSNHL treatment, favored for their anti-inflammatory and immunosuppressive properties¹¹⁻¹³. Administered either systemically or locally (intratympanically), corticosteroids aim to reduce cochlear inflammation and edema, thereby potentially salvaging hearing. The choice between systemic and local administration often depends on the severity of hearing loss, patient comorbidities, and potential side effects, making treatment personalization a critical aspect of management^{11,13}.

Beyond corticosteroids, hyperbaric oxygen therapy (HBOT) has emerged as a supplementary treatment

modality for SSNHL, especially in idiopathic cases¹⁴. First introduced in 1979, HBOT increases the amount of dissolved oxygen in the blood, enhancing oxygen delivery to the cochlea and potentially reducing hypoxia-induced damage^{14,15}. While not universally accepted as a standard treatment due to variable efficacy across studies, HBOT has shown promise, particularly when used in conjunction with corticosteroids¹⁶. The synergistic effects of HBOT and corticosteroids have been documented in several clinical trials, suggesting improvements in both high and low-frequency hearing thresholds in patients with idiopathic SSNHL¹⁷.

In this study, we investigated the impact of combined HBOT and intravenous steroid treatments on hearing recovery across high and low-frequency ranges in patients with idiopathic SSNHL.

Method

Patients and design

In this study, a meticulously selected cohort of 50 individuals presenting with SSNHL was examined. These participants were recruited from the patient population at the Department of Otorhinolaryngology, a leading institution renowned for its specialized care and innovative treatment approaches in the realm of ear, nose, and throat disorders.

The sample size, comprising 54 patients, was determined based on a 95% confidence level, utilizing the Jamovi J power software for calculations. To confidently (with a probability > 0.95) we identify an effect size of $\delta \geq 0.5$, required a sample size of 54, assuming a two-sided detection criterion. This criterion accommodates a maximum Type I error rate of $\alpha = 0.05$ (Fig. 1).

Eligibility criteria

The eligibility for participation was confined to patients who experienced the onset of sudden hearing loss within a 1-week timeframe. This criterion was essential to differentiate the acute phase of SSNHL from more prolonged or progressive hearing impairments, thereby focusing on those most likely to benefit from immediate intervention. In addition, only those who had commenced a combined treatment regimen consisting of intravenous steroid therapy and HBOT were considered for inclusion.

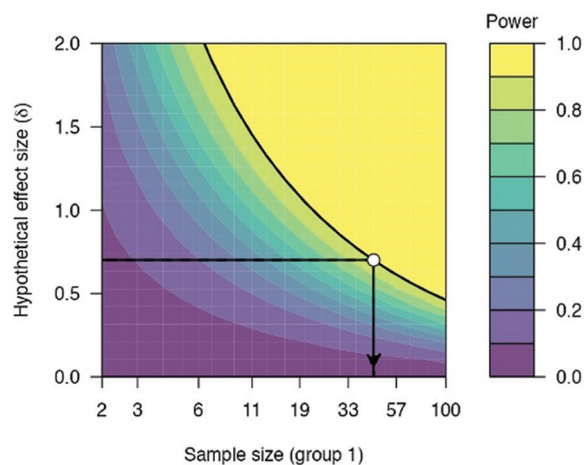


Figure 1. Power contour.

Ethical approval

The research protocol received formal approval from the local Ethical Committee. This endorsement, signified by approval number 121, was officially granted on May 22, 2017.

Treatment protocol

All participants in this study underwent a meticulously designed treatment regimen within a hyperbaric chamber, a specialized medical environment designed to significantly increase atmospheric pressure. Within this chamber, patients inhaled pure 100% oxygen at a pressure of 2.5 atmospheres (atm) for a duration of 60 min. This elevated pressure, significantly above sea-level atmospheric conditions, facilitates the dissolution of greater amounts of oxygen in the bloodstream, potentially enhancing the repair of damaged auditory cells and tissues. The HBOT was administered across a series of 20 sessions, conducted daily, to ensure a consistent and cumulative therapeutic effect aimed at optimizing hearing recovery outcomes. Concurrently, patients received a concomitant treatment regimen of intravenous steroid therapy, initiated at a dosage of 1 mg/kg/day.

Statistical analysis

IBM SPSS 25.0 for the Windows statistical package program was used for the statistical evaluation of the research data. Measured variables were expressed as mean $\pm$ standard deviation and categorical variables

as numbers and percentages (%). It was checked whether the data conformed to the normal distribution. Normally distributed dependent t-test was used to compare the previous and next groupings. The one-way analysis of variance (ANOVA) test technique was used to compare more than two independent groups. When a significant difference was observed in the ANOVA test, the *post hoc* LSD test was used to determine the source of the difference between the groups. Wilcoxon signed-rank test was used to compare before and after groupings that did not show normal distribution. χ^2 test was used to compare qualitative variables. The hypotheses were taken bilateral and $p \leq 0.05$ was accepted as a statistically significant result.

Results

A total of 50 patients were included in this study. The study presents a demographic breakdown with an average age of 51 ± 15.1 years, comprising 62% males and 38% females. Hearing loss was observed in 54% of participants in the right ear and 46% in the left. Upper respiratory tract infections were reported in 38% of the subjects, whereas 62% were unaffected. Smoking habits were noted, with 42% of participants being smokers and 58% non-smokers. Vertigo and vascular pathology were each reported in 22% of the subjects, significantly lower than those without these conditions (78%). Effort-related issues were rare, affecting only 2% of participants (Table 1).

Significant improvements were observed in hearing thresholds across all tested frequencies after treatment with a specific intervention. For the frequency of 250 Hz, the median hearing threshold improved from 65.00 dB before treatment to 22.50 dB after treatment, with a mean reduction from 62.00 ± 28.61 dB to 32.00 ± 27.79 dB ($p < 0.001$). At 500 Hz, the median threshold decreased from 72.50 dB to 27.50 dB, and the mean values improved from 66.60 ± 31.16 dB to 35.70 ± 29.15 dB ($p < 0.001$). For 1000 Hz, the median threshold went from 72.50 dB to 27.50 dB, with mean values changing from 68.00 ± 33.58 dB to 38.40 ± 31.29 dB ($p < 0.001$). At 2000 Hz, the median threshold improvement was from 72.50 dB to 37.50 dB, with mean values improving from 69.00 ± 32.13 dB to 43.40 ± 32.57 dB ($p < 0.001$). The 4000 Hz frequency showed a median threshold decrease from 72.50 dB to 55.00 dB, and mean values decreased from 73.90 ± 30.26 dB to 53.20 ± 33.12 dB ($p < 0.001$). At 8000 Hz, both median and mean thresholds showed improvement from

Table 1. Demographic data

Frequencies	Mean $\pm$ SD or n (%)
Age	51 $\pm$ 15.1
Gender	
Male	31 (62)
Female	19 (38)
Hearing loss	
Right ear	27 (54)
Left ear	23 (46)
Upper respiratory tract infection	
Yes	19 (38)
No	31 (62)
Smoking	
Yes	21 (42)
No	29 (58)
Vertigo	
Yes	11 (22)
No	39 (78)
Vascular pathology	
Yes	11 (22)
No	39 (78)
Related to efforts	
Yes	1 (2)
No	49 (98)

SD: standard deviation.

75.00 dB and 71.90 $\pm$ 31.25 dB before treatment to 55.00 dB and 54.20 $\pm$ 33.63 dB after treatment, respectively ($p < 0.001$). The data for each frequency and the statistical results are presented in table 2, and their graphical representation is displayed in figure 2.

The study also examined the impacts of combined steroids and HBOT on hearing loss, focusing on both low (250 Hz, 500 Hz, and 1000 Hz) and high (2000 Hz, 4000 Hz, and 8000 Hz) frequency ranges. The results indicated a significant enhancement in hearing thresholds across these frequencies. Notably, statistical analysis revealed that the improvements were highly significant ($p < 0.001$) across all comparisons, as visually represented in figure 3.

In the analysis conducted to identify the frequencies at which the treatment was most effective, it was found that the improvement in hearing at low frequencies was significantly greater than at high frequencies, with a t -value of 3.780 and a $p < 0.001$, as detailed in table 3. Furthermore, the calculated Cohen's d value of 0.53 for this difference indicates a medium effect size, suggesting a moderate but significant disparity in treatment effectiveness between low and high frequencies.

Table 2. Evaluation of the effects of combined steroid and hyperbaric oxygen therapy on (sudden) sensorineural hearing loss separately by each frequency pathway

Mean $\pm$ SD	Median (dB)	Mean $\pm$ SD (dB)	p
250 Hz			< 0.001
Before treatment	65.00	62.00 $\pm$ 28.61	
After treatment	22.50	32.00 $\pm$ 27.79	
500 Hz			< 0.001
Before treatment	72.50	66.60 $\pm$ 31.16	
After treatment	27.50	35.70 $\pm$ 29.15	
1000 Hz			< 0.001
Before treatment	72.50	68.00 $\pm$ 33.58	
After treatment	27.50	38.40 $\pm$ 31.29	
2000 Hz			< 0.001
Before treatment	72.50	69.00 $\pm$ 32.13	
After treatment	37.50	43.40 $\pm$ 32.57	
4000 Hz			< 0.001
Before treatment	72.50	73.90 $\pm$ 30.26	
After treatment	55.00	53.20 $\pm$ 33.12	
8000 Hz			< 0.001
Before treatment	75.00	71.90 $\pm$ 31.25	
After treatment	55.00	54.20 $\pm$ 33.63	

SD: standard deviation.

To ascertain at which frequency the combined steroid and HBOT yielded the most significant improvement, average hearing gains at frequencies 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz were analyzed using a one-way ANOVA. The ANOVA results revealed a significant variance in the average hearing gains across the measured frequencies, with an F value of 2.467 and a $p = 0.033$, as detailed in table 4.

The *post hoc* analysis, conducted to pinpoint the specific frequencies where these differences in hearing gain were observed, revealed that the improvement in hearing at 250 Hz was significantly greater than at 8000 Hz. Similarly, hearing gains at 500 Hz and 1000 Hz were also found to be significantly higher than those at 4000 Hz and 8000 Hz, indicating a notable variation in the effectiveness of the treatment across these frequencies (Table 5).

A Venn diagram involving gender, upper respiratory infection, smoking, and vertigo is given in figure 4.

Discussion

In this study involving 50 patients, we observed significant improvements in hearing thresholds across all frequencies after combined steroid and HBOT,

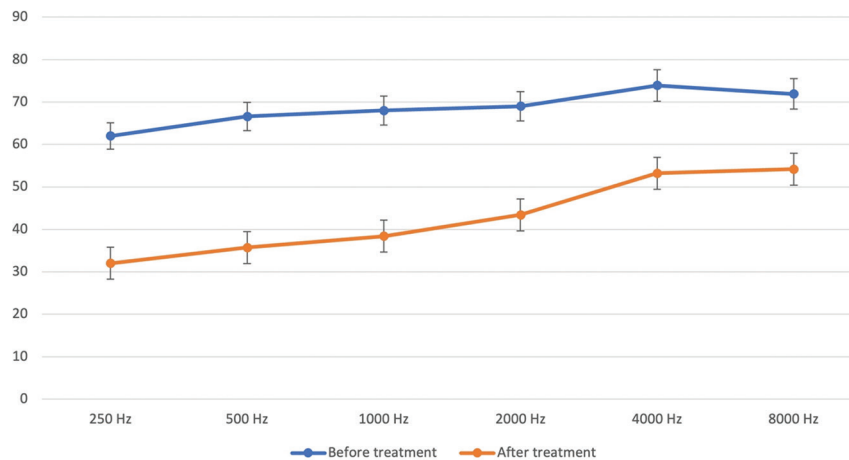


Figure 2. Illustration of the effects of combined steroid and hyperbaric oxygen therapy on (sudden) sensorineural hearing loss separately by each frequency pathway.

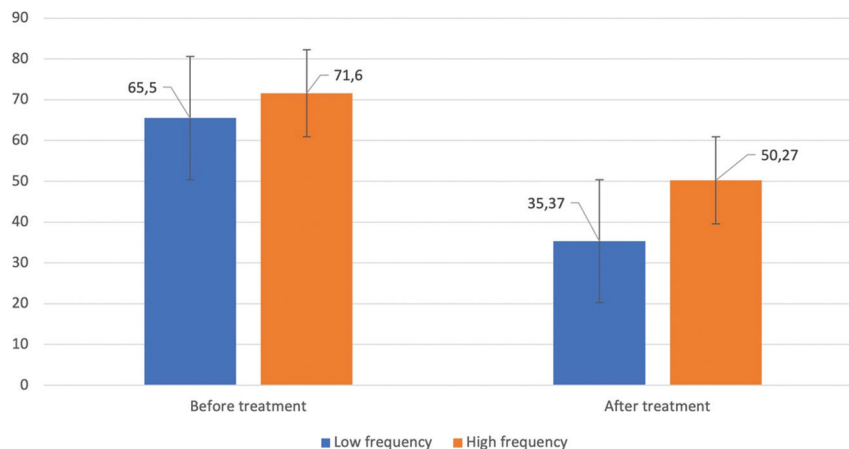


Figure 3. Effect of hyperbaric oxygen and steroid therapy on low and high frequencies in patients with sudden hearing loss.

Table 3. Evaluation of the efficacy of combined steroid and hyperbaric oxygen therapy in terms of average hearing gains at high and low frequencies

Frequencies	Mean $\pm$ SD (dB)	T	p
Hf_Lf	30.17 $\pm$ 25.5	3.780	< 0.001
Lf_Lf	21.33 $\pm$ 20.5		

Hf_Lf: improvement difference at high frequencies; Lf_Lf: improvement difference at low frequencies; N: number; $\bar{X} \pm SD$: mean $\pm$ standard deviation; t: dependent t-test value; p: dependent t-test statistical significance value; Effect size (Cohen d) value, d = 0.53.

particularly at lower frequencies. Analysis highlighted a notable enhancement in hearing at 250 Hz, 500 Hz, and 1000 Hz compared to higher frequencies, with statistical significance ($p < 0.001$). The effectiveness

varied across frequencies, showing greater improvements at lower frequencies.

SSNHL is considered an urgent otologic condition with an unclear cause. It is characterized by a rapid hearing decline of more than 30 dB across three consecutive pure tone frequencies within 3 days^{13,18,19}. While improvements in hearing can occur later, they are uncommon, with most recovery happening within the initial 2 weeks. Consequently, initiating corticosteroid treatment within the first 2-4 weeks following symptom onset is advised, as its effectiveness diminishes significantly after 4-6 weeks^{11,14,17,19}. This study included cases of SSNHL diagnosed within the last week.

The recommended treatment approach is to administer oral prednisolone at a dosage of 1 mg/kg/day in

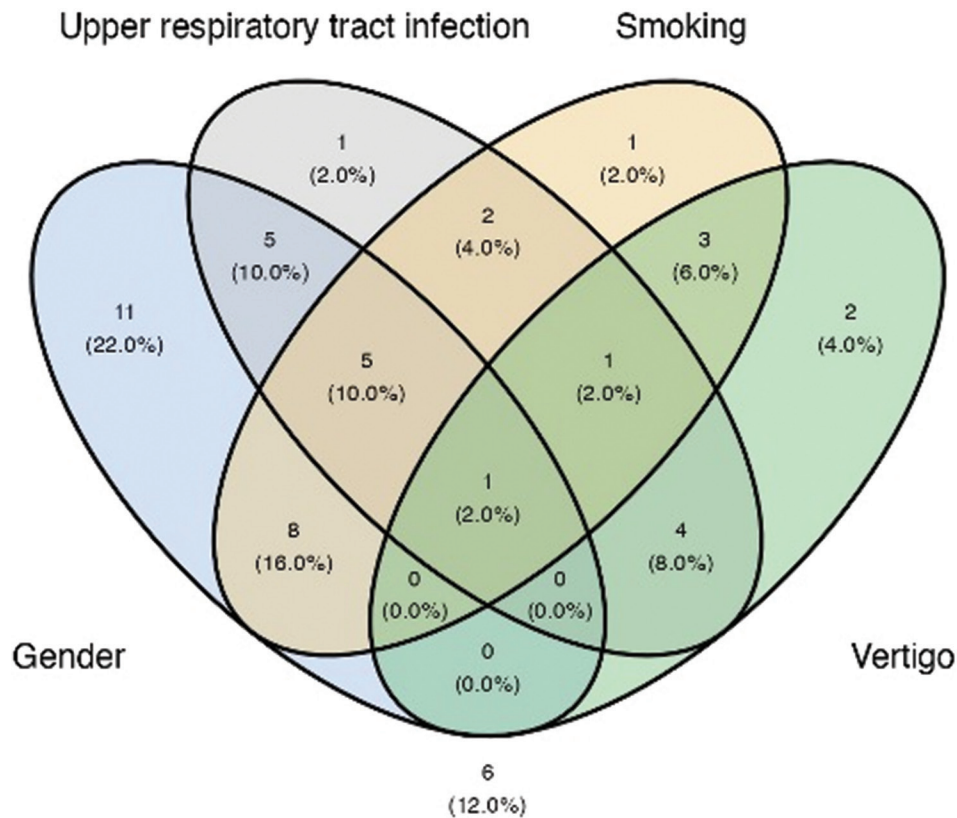


Figure 4. Venn diagram of demographic data.

Table 4. Evaluation of the efficacy of combined steroid and hyperbaric oxygen therapy with mean hearing gains at 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz

Source of variance	Sum of squares	DF	Mean of squares	F	p
Between groups	7489.750	5	197.350	2.467	0.033
Within groups	178419.500	294	606.869		

DF: degrees of freedom, F: one-way analysis of variance (ANOVA) test value, p: one-way analysis of variance (ANOVA) test statistical significance value.

a single daily dose, continuing for 10-14 days. In this study, participants received a full dosage of 1 mg/kg/day for the 1st week, followed by tapered doses of prednisolone^{20,21}. Steroids play a multifaceted role in the treatment of SSNHL, enhancing micro-vascular flow which is often reduced, dampening immune responses, lowering endolymphatic pressure, and exerting mineralocorticoid effects^{14,17,18}. However, the precise mechanisms through which steroids aid in SSNHL treatment remain partially understood.

Systemic corticosteroids are typically the first line of treatment for SSNHL^{22,23}. HBOT is suggested as

either a primary treatment or a secondary option if the initial treatment does not lead to satisfactory recovery¹⁴⁻¹⁶. In this research, all participants underwent HBOT, breathing 100% oxygen at a pressure of 2.5 atmospheres for 60 min per session, across a total of 20 daily sessions, in conjunction with their prednisolone treatment.

HBOT as a treatment method for sudden hearing loss was first considered in the 1970s¹⁵. While the perilymphatic oxygen pressure decreases in SSNHL patients, the oxygen pressure in the perilymphatic fluid increases by 450% under hyperbaric conditions^{24,25}. In today's conditions, oxygenation under hyperbaric conditions is the only known method of increasing the oxygen level in the endolymph. In the treatment of SSNHL, HBOT aims to increase the partial pressure of oxygen in the blood and then increase the partial pressure of oxygen in the endolymph, which feeds the sensory and neural elements of the cochlea through diffusion^{17,26}.

At present, HBOT is utilized either as a primary treatment or as a supplementary rescue therapy for SNHL. It is now advised to incorporate HBOT into the

Table 5. Evaluation of the efficacy of combined steroid and hyperbaric oxygen therapy for differences in mean hearing gains at 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz

Frequencies	Mean $\pm$ SD (dB)	8000 Hz	4000 Hz	2000 Hz	1000 Hz	500 Hz
250 Hz	26.59 $\pm$ 3.76	p = 0.013	p = 0.060	p = 0.373	p = 0.935	p = 0.855
500 Hz	26.92 $\pm$ 3.80	p = 0.008	p = 0.039	p = 0.283	p = 0.792	
1000 Hz	25.75 $\pm$ 3.64	p = 0.016	p = 0.418	p = 0.418		
2000 Hz	25.24 $\pm$ 3.57	p = 0.110	p = 0.321			
4000 Hz	21.82 $\pm$ 3.08	p = 0.543				
8000 Hz	20.78 $\pm$ 2.93					

N: number; Mean $\pm$ SD: mean $\pm$ standard deviation; p: statistical significance value of one-way analysis of variance (ANOVA) test.

treatment regimen for SSNHL unless there are clear reasons not to. In a study by Liu et al., 465 patients were categorized into three groups: the first group of 76 patients received only steroid treatment; the second group of 277 patients were treated with systemic steroids and dextran; and the third group, consisting of 112 patients, received a combination of steroids, dextran, and HBOT²⁷. The findings indicated that adding HBOT to the treatment protocol resulted in an additional improvement of 10 dB in hearing gain compared to the other treatments²⁷. Alimoglu et al. analyzed 58 patients (26.5%) who received only oral steroids (Group A), 61 patients (27.9%) who received oral steroids plus HBOT (Group B), 43 patients (19.6%) who were given intratympanic steroids (Group C), and 57 patients (26%) who underwent solely HBOT (Group D). The outcomes showed treatment success rates of 63%, 86%, 46%, and 43%, respectively, with the group receiving both steroids and HBOT showing the highest rates of complete recovery and response²⁸. A 2007 study by Fujimura et al. found that combining steroids with HBOT had a more favorable impact on recovery in SSNHL compared to using steroids alone²⁹. Similarly, Satar et al. found significant recovery in patients treated with medical therapy alone and those who received additional HBOT; however, no substantial difference was observed between the two groups³⁰. Fattori et al. demonstrated that HBOT alone was less effective than a combined therapy of systemic steroids and HBOT³¹. In research conducted by Waldemar et al., when comparing patients who received a combination of high-dose steroids, betahistine, and HBOT (Group A) against those treated with steroids and betahistine alone (Group B), Group A exhibited superior hearing gain across all frequencies, with the differences being statistically significant³².

Overall, when assessing the impact of combining steroid treatment with HBOT on hearing loss in patients with SSNHL, a significant improvement in the average hearing threshold post-treatment compared to before treatment was observed.

Research indicates that HBOT can be used not only as a primary form of treatment but also as a secondary, or salvage therapy, according to various studies^{27,33,34}. Evidence from some studies suggests that HBOT significantly improves hearing thresholds when used as a rescue treatment^{27,34}. In addition, it has been noted that HBOT tends to be more effective in cases of severe hearing loss²⁷. In a 2017 retrospective study by Ajduk et al., on HBOT as a rescue treatment, findings indicated that patient age did not influence the effectiveness of the treatment. However, patients with hearing losses of 61 dB or greater showed a more significant response to HBOT compared to those with hearing losses under 60 dB³⁵. Conversely, in a 2015 study conducted by Pezzoli et al. involving 135 patients undergoing HBOT as a rescue treatment, results demonstrated no significant difference in terms of initial hearing loss severity and recovery outcomes after HBOT³⁶. In our study, all patients received both steroid therapy and HBOT within the 1st week of treatment.

Topuz et al. showed that the efficacy of HBOT is higher in younger patients (under 50 years of age) where it is significant to add HBOT to steroid treatment, especially at low frequencies (losses up to 60 dB)³⁷. Hara et al. showed in their study that HBOT improves hearing, especially at low frequencies in the treatment of SSNHL³⁸. In our study, when the effects of combined steroid and HBOT on hearing thresholds before and after treatment were examined separately for each frequency, it was observed that there was a significant improvement in the thresholds of each

frequency (250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz). It was observed that the hearing gain of the treatment, especially at low frequencies, was higher than at high frequencies. In our study, unlike other studies, the specific response of combined therapy on frequencies was evaluated for the 1st time. In our study, a significant difference was found between the average hearing gains of the frequencies. The hearing gain at 250 Hz was significantly higher than the hearing gain at 8000 Hz, the hearing gain at 500 Hz compared to the hearing gain at 4000 Hz and 8000 Hz, and the hearing gain at 1000 Hz compared to the hearing gain at 8000 Hz.

One limitation of this study is its relatively small sample size of 50 patients, which may affect the generalizability of the findings to the broader population with SSNHL. In addition, its retrospective design may introduce selection biases, impacting the robustness of the conclusions drawn. The research focuses exclusively on idiopathic SSNHL, potentially overlooking the nuances of hearing loss stemming from identifiable causes. Furthermore, the study's reliance on immediate post-treatment outcomes without long-term follow-up might not fully capture the durability of therapeutic effects. Future investigations should consider larger, more diverse populations and longitudinal designs to enhance the generalizability and depth of understanding of SSNHL treatment efficacy.

Conclusions

This study demonstrated that combined steroid and HBOT significantly improves hearing thresholds in patients with idiopathic SSNHL, especially at lower frequencies.

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The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical

research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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