RESEARCH

ARE INTRATYMPANIC STEROIDS OR HYPERBARIC OXYGEN THERAPY AS ADDITIONAL TREATMENTS TO SYSTEMIC STEROIDS EFFECTIVE IN ELDERLY PATIENTS WITH IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS?

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Abstract

Introduction: This study aimed to evaluate the efficacy of additional treatment modalities to systemic steroid regimen and to identify the prognostic factors in geriatric patients with idiopathic sudden sensorineural hearing loss.

Materials and Method: A retrospective review of clinical data was performed for elderly patients with idiopathic sudden sensorineural hearing loss at a tertiary hospital between 2014 and 2019. Among 60 patients, 22 received only systemic steroids (Group 1); 16 received systemic and intratympanic steroids (Group 2) and the remaining 22 received systemic steroids and hyperbaric oxygen therapy (Group 3). Recovery rates based on the Siegel's criteria and hearing level gains were compared among the groups. Gender, treatment modalities, types of audiogram and comorbidities such as hypertension and diabetes mellitus were evaluated in relation to prognosis.

Results: Pure-tone averages were significantly decreased after t reatment with a ll three treatment modalities; however, no superiority was observed in the three treatment regimens regarding hearing gain and recovery rate. Gender, types of audiogram, hypertension and diabetes mellitus had no significant effects on hearing gain and recovery rate.

Conclusion: Intratympanic steroids or hyperbaric oxygen therapy as an adjuvant to systemic steroids provide no better results compared with only systemic steroids in elderly patients with idiopathic sudden sensorineural hearing loss.

Keywords: Aged; Hyperbaric oxygenation; Sudden hearing loss; Prognosis.

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ARAŞTIRMA

İDİYOPATİK ANİ SENSÖRİNÖRAL İŞİTME KAYBI OLAN YAŞLI HASTALARDA SİSTEMİK STEROİDLERE EK OLARAK İNTRATİMPANİK STEROİDLER YA DA HİPERBARİK OKSİJEN TERAPİSİ ETKİLİ MİDİR?

Öz

Amaç: Çalışmanın amacı, idiyopatik ani sensörinöral işitme kaybı olan yaşı hastalarda sistemik steroid rejimine ek tedavi modalitelerinin etkinliğini ve prognostik faktörleri değerlendirmektir.

Gereç ve Yöntem: 2014 ve 2019 yılları arasında üçüncü basamak tedavi merkezinde idiyopatik ani sensörinöral işitme kaybı tanısı alan yaşlı hastaların bilgileri retrospektif olarak tarandı. 60 hastanın 22'si sadece sistemik steroid (Grup 1), 16'sı sistemik ve intratimpanik steroid (Grup 2) ve kalan 22 hasta da sistemik steroid ve hiperbarik oksijen (Grup 3) tedavileri aldığı gözlendi. Gruplar arasında iyileşme oranları, Siegel kriterleri ve işitme eşiği kazançlarına göre değerlendirildi. Cinsiyet, tedavi modaliteleri, odyogram tipleri, hipertansiyon ve diabetes mellitus gibi komorbid hastalıkların prognoz ile ilişkileri değerlendirildi.

Bulgular: Saf ses ortalamalarının her üç tedavi modalitesi ile anlamlı derecede azaldığı izlendi. Ancak üç tedavi modalitesinin de işitme kazançları ve iyileşme oranları açısından birbirlerine üstünlüğünün olmadığı gözlendi. Cinsiyet, odyogram tipi ve komorbid hastalıkların varlığının işitme kazancı ve iyileşme oranları üzerine etkilerinin olmadığı izlendi.

Sonuç: Sistemik steroidlerle birlikte uygulanabilen intratimpanik steroid ya da hiperbarik oksijen tedavisinin idiyopatik ani sensörinöral işitme kaybı olan yaşlı hastalarda sadece steroidlere göre daha iyi sonuçlarının olmadığı gözlendi.

Anahtar Sözcükler: Yaşlı; Hiperbarik oksijen; Ani işitme kaybı; Prognoz.

INTRODUCTION

Sudden sensorineural hearing loss is defined in the literature as a sensorineural hearing loss (SNHL) of ≥30 dB at least at three contiguous frequencies in 3 days or less (1). No identifiable cause can be detected in 84%–89% of sudden hearing loss cases, and such cases are classified as idiopathic (2). Generally, the underlying cause of idiopathic sudden sensorineural hearing loss (ISSNHL) is thought to be a viral infection or vascular disorder; however, it is obvious that there is inflammation in the inner ear (3). For this disease with many unknowns, various treatment modalities such as steroids (systemic or topical), hyperbaric oxygen therapy (HBOT), antivirals, vasoactive agents and other approaches have been tested in the literature (2). Despite the fact that several treatment protocols have been tested, there is still no consensus on the treatment of ISSNHL in the literature (2). However, the main purpose of the treatment of ISSNHL is to reduce the inflammation, increase blood flow and improve oxygenation.

Systemic steroids (SSs) have been considered as a current regimen for initial treatment of patients with ISSNHL (3). In addition to SSs, other treatment options such as intratympanic steroids (ITSs) and HBOT are being added assuming that their addition will produce a synergistic effect. ITSs and HBOT have recently become more popular in patients with ISSNHL and are used as initial or salvage treatment modalities (2, 4). Although the effects of steroids on the inner ear are not fully known, they are reportedly used because of their anti-inflammatory and anti-oedemic effects (5). Similarly, HBOT has anti-inflammatory effects and has been shown to improve tissue oxygen levels and accelerate healing (6). HBOT increases oxygen tension of perilymphatic fluids and improves the circulation (7).

Although several studies have evaluated the efficacy of steroid (systemic and/or intratympanic) and HBOT regimens, no study has investigated the efficacy of these regimens in geriatric ISSHNL patients. Therefore, in this study, we aimed to determine the additional benefits of an ITS and HBOT as adjuvant modalities in geriatric patients with ISSNHL and to compare the efficacies of a SS, combined systemic and ITSs and combined SS and HBOT. Furthermore, we aimed to evaluate the prognostic factors for ISSHNL.

MATERIALS AND METHOD

Patients aged ≥65 years and diagnosed with ISSNHL between January 2014 and January 2019 were retrospectively evaluated. The study was approved by the local ethics committee. All patients underwent pure-tone audiometric evaluation (GSI Audiostar Pro, Grason-Stadler, Minnesota, USA). Cranial and temporal magnetic resonance imaging was performed to rule out intracranial lesions, vestibular schwannoma or inner ear malformation. In the audiometry test, frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz were measured; the arithmetic mean of the thresholds at 500, 1000, 2000 and 4000 Hz was determined for the pure-tone average (PTA). Hearing loss was identified as mild (20–39 dB HL), moderate (40–54 dB HL), moderate to severe (55–69 dB HL), severe (70–89 dB HL) and profound (90 dB HL and above) according to the American Speech and Hearing Association guidelines. Audiogram types were defined as an up-sloping (>20 dB HL more severe hearing loss at 250 and 500 Hz), flat (<20 dB HL hearing loss difference at any frequency) and down-sloping (>20 dB HL more severe hearing loss at 4000 and 8000 Hz). The audiometric assessments were performed at the time of first application to the clinic (before the treatment) and 3 months after the treatment. The hearing gains for PTA and each frequency were calculated using the differences between the pre- and post-treatment thresholds. Treatment outcomes were evaluated using the Siegel's criteria. The Siegel's criteria can be categorised as follows: (1) complete recovery: final threshold of <25 dB; (2) partial recovery: gain of >15 dB, with a final hearing threshold of 25-45 dB; (3) slight recovery:

gain of >15 dB, with a final hearing threshold of >45 dB and (4) no improvement: gain of <15 dB, with a final hearing threshold of >75 dB. Prognostic factors such as gender, audiogram types, hypertension (HT) and diabetes mellitus (DM) were investigated.

Exclusion criteria were as follows: patients aged <65 years, those who received treatment 10 days after the development of hearing loss, those who had previously experienced ISSNHL, those with any surgical history that could affect the ipsilateral ear, those with any retrocochlear pathology, those with any acoustic trauma, those with any autoimmune or fluctuant hearing loss, those with any suspicious perilymph fistula and those with hearing loss with a known pathology.

A SS (oral methylprednisolone 1 mg/kg, with tapering dose every day; Prednol, Mustafa Nevzat, Istanbul, Turkey) was administered to all the patients. Only the SS was administered to Group 1. An ITS (dexamethasone 8 mg/2mL, 0.5 mL injection per session, 6 sessions for 2 weeks; Dekort, Deva, Istanbul, Turkey) and the SS were administered to Group 2. The SS and HBOT (20 sessions at 2.4 ATA and 120 min/session) were administered to Group 3. Both the additional treatment modalities were administered as an initial treatment regimen.

SPSS v.20 for Mac (IBM Corp., USA) was used for the statistical analysis. A p value <0.05 was considered to be significant. Chi-square test, independent samples t-test, paired samples t-test, Mann-Whitney U test, Wilcoxon test and Kruskal-Wallis test were used for statistical analysis.

RESULTS

In total, 60 geriatric patients with ISSNHL were included in the study. Of all the patients, 36.7% (n=22; 15 females, 7 males; mean age: 70.7±5.2 years) received only the SS (Group 1); 26.7% (n=16; 10 females, 6 males; mean age: 69.8±4.5 years) received both the SS and ITS (Group 2) and 36.7% (n=22; 13 females, 9 males; mean age: 68.5±3.9 years) received both the SS and HBOT (Group 3). There were no significant differences regarding the mean age and sex ratios among all three groups.

Before treatment initiation, 2 (3.3%) patients had mild SNHL; 8 (13.3%) patients had moderate SNHL; 23 (38.3%) patients had moderate to severe SNHL; 13 (21.7%) patients had severe SNHL and 14 (23.3%) patients had profound SNHL. On the basis of the Siegel's criteria, no improvement was seen in 33 (55%) patients; slight recovery was seen in 11 (18.3%) patients; partial recovery was observed in 13 (21.7%) patients and complete recovery was observed in 3 (5%) patients (Table 1). In all patients, pre-treatment PTA (73.1±22.4 dB HL) was significantly higher than the post-treatment PTA (56.6 ± 24 dB HL)

Table 1. Hearing recovery rates according to treatment modalities. SS, systemic steroid; ITS, intratympanic steroid; HBOT, hyperbaric oxygen therapy.

	No improvement	Slight recovery	Partial recovery	Complete recovery
Group 1 (SS; n=22)	14 (63.6%)	5 (22.7%)	3 (13.6%)	-
Group 2 (SS+ITS; n=16)	9 (56.3%)	3 (18.8%)	3 (18.8%)	1 (6.3%)
Group 3 (SS+HBOT; n=22)	10 (45.5%)	3 (13.6%)	7 (31.8%)	2 (9.1%)
All patients (n=60)	33 (55%)	11 (18.3%)	13 (21.7%)	3 (5%)

Table 2. Mean hearing levels (dB HL) before and after using treatment modalities at six frequencies and for PTA (dB HL). Group 1, administered only SS; Group 2, administered SS and ITS; Group 3, administered SS and HBOT. PTA: Pure-tone average.

	250 Hz			500 Hz			1000 Hz			2000 Hz			4000 Hz			8000 Hz			PTA		
	Pretreatment	Posttreatment	p	Pretreatment	Posttreatment	p	Pretreatment	Posttreatment	p	Pretreatment	Posttreatment	p	Pretreatment	Posttreatment	p	Pretreatment	Posttreatment	p	Pretreatment	Posttreatment	p
Group 1	63.6±24	47.3±30.3	0.001	73.9±26	56.8±28.9	0.001	75±24.6	57.3±27.6	<0.001	73.4±24.6	57.1±26.3	<0.001	80.5±22.9	68.2±21.2	0.003	85±22	78.9±24.4	0.130	75.7±23	59.9±24	<0.001
Group 2	50.6±27.1	40.3±20	0.019	57.5±29.7	45±25.2	0.001	65.6±26.2	49.7±24.4	0.002	65.9±23.8	53.8±22.9	0.003	78.1±20.2	69.1±18.6	0.002	83.1±16.5	76.3±17.5	0.002	66.8±23.7	53.7±21.1	<0.001
Group 3	58.9±25.8	46.8±25.5	0.003	65±25	46.6±30.8	0.001	76.1±22.7	54.3±30.2	<0.001	77.3±23	56.8±29	<0.001	82.3±22.2	64.6±24.5	<0.001	87.1±19	74.3±24.9	0.001	75.1±20.9	55.6±26.6	<0.001
All patients	58.4±25.6	45.3±25.9	<0.001	66.3±27	49.9±28.7	<0.001	72.9±24.4	54.2±27.5	<0.001	72.8±23.8	56.1±26.1	<0.001	80.5±21.6	67.1±21.6	<0.001	85.3±19.3	76.5±22.6	<0.001	73.1±22.4	56.6±24	<0.001

(p<0.001) (Table 2). A flat audiogram was seen in 31 (51.7%) patients; down-sloping curve was seen in 25 (41.7%) patients and up-sloping curve was seen in 4 (6.7%) patients. There was no correlation of the types of audiogram with recovery rates and hearing gains (pAudiogram–RR = 0.143, pAudiogram–HG = 0.107).

Of all the patients, 28 (46.7%) had HT and 9 (15%) had DM. A comparison of the presence and absence of these two conditions did not show a significant difference in terms of hearing gain for PTA (pHG–HT = 0.114, pHG–DM = 0.597). Furthermore, the presence of HT and DM was not correlated with recovery rates (pRR–HT = 0.330, pRR–DM = 0.080). In addition, gender was not related and correlated with hearing gain and recovery rates (p_{gender}–HG = 0.634, p_{gender}–RR = 0.524)

One (4.5%) patient with mild SNHL, two (9.1%) patients with moderate SNHL, seven (31.8%) patients with moderate to severe SNHL, seven (31.8%) patients with severe SNHL and five (22.7%) patients with profound SNHL were observed in group 1 (which received only SS). In this group, 10 (45.5%) patients exhibited a flat audiogram; 8 (36.4%) patients exhibited a down-sloping curve and four (18.2%) patients exhibited an up-sloping curve. HT was seen in nine cases (40.9%) and DM in five (22.7%) cases. Although complete recovery was not observed after SS treatment, partial recovery was observed in three (13.6%), slight recovery in five (22.7%) and no improvement in 14 (63.6%) patients. A significant decrease in PTA values was observed before and after treatment (PTA_{Pre}=75.7±23 dB HL, PTA_{Post}=59.9±24 dB HL; p<0.001). In addition, when all frequencies were examined separately, a significant decrease was observed in all the frequencies except for 8000 Hz, as shown in Table 2.

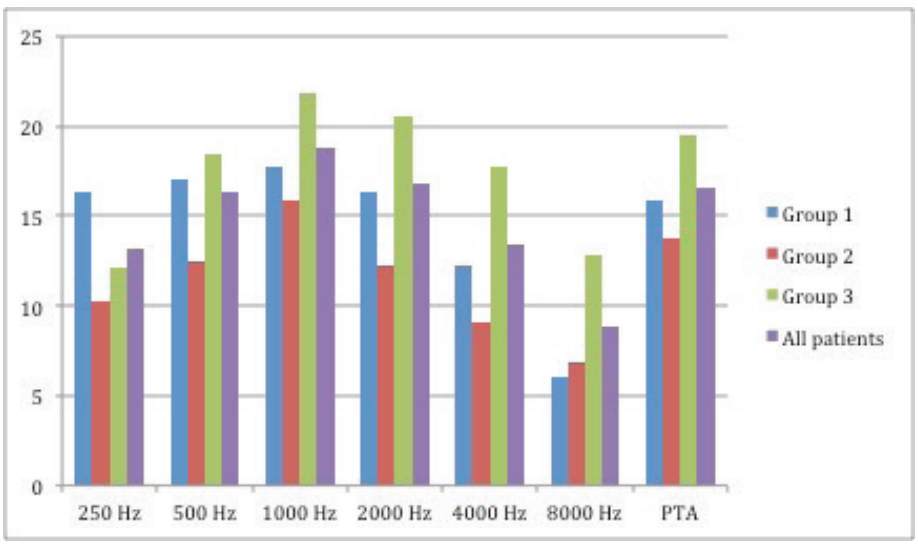
One (6.3%) patient with mild SNHL, four (25%) patients with moderate SNHL, seven (43.8%) patients with moderate to severe SNHL, one (6.3%) patient with severe SNHL and three (18.8%)

patients with profound SNHL were observed in group 2 (which received both the SS and ITS). In this group, nine (56.3%) patients exhibited a flat audiogram; seven (43.8%) exhibited a down-sloping curve and none of the patients exhibited an up-sloping curve. HT was seen in eight (50%) and DM in two (12.5%) cases. Although complete recovery was seen only in one (6.3%) patient after the SS and ITS treatment, partial recovery was observed in three (18.8%), slight recovery in three (18.8%) and no improvement in nine (56.3%) patients. A significant decrease in PTA values was observed before and after treatment (PTA_{Pre}=66.8±23.7 dB HL, PTA_{Post}=53.7±21.1 dB HL; p<0.001). In addition, when all frequencies were examined separately, a significant decrease was observed in all the frequencies, as shown in Table 2.

No patient with mild SNHL, two (9.1%) patients with moderate SNHL, nine (40.9%) patients with moderate to severe SNHL, five (22.7%) patients with severe SNHL and six (27.3%) patients with profound SNHL were observed in group 3 (which received the SS and HBOT). In this group, 12 (54.5%) patients exhibited a flat audiogram; ten (45.5%) exhibited a down-sloping curve and none of the patients exhibited an up-sloping curve. HT was seen in 11 (50%) and DM in two (9.1%) cases. Although complete recovery was seen in only two (9.1%) patients after the SS and HBOT treatments, partial recovery was observed in seven (31.8%), slight recovery in three (13.6%) and no improvement in 10 (45.5%) patients. A significant decrease in PTA values was observed before and after the treatment (PTA_{Pre}=75.1±20.9 dB HL, PTA_{Post}=55.6±26.6 dB HL; p<0.001). In addition, when all frequencies were examined separately, a significant decrease was observed in all the frequencies, as shown in Table 2.

There was no difference between the three treatment modalities in terms of hearing gain for PTA ($GainPTA_{SS}$=15.9±18.2 dB HL, $GainPTA_{SS+ITS}$=13.8±10.6 dB HL, $GainPTA_{SS+HBOT}$=19.5±15.4 dB HL; $p_{SSvsSS+ITS}$=0.625; $p_{SSvsSS+HBOT}$=0.290; $p_{SS+ITSvsSS+HBOT}$=0.209) (Figure 1). There was no significant difference regarding hearing gain at all frequencies and with all treatment modalities. In addition, there was no relation and no correlation between recovery rates and treatment modalities (p = 0.568).

Figure 1. Hearing gain (dB HL) at each frequency and PTA gain (dB HL). Group 1, administered only SS; Group 2, administered SS and ITS; Group 3, administered SS and HBOT. PTA: Pure-tone average.



DISCUSSION

ISSNHL is a condition with uncertain aetiology and an increasing incidence with age (11/100,000 for people aged <18 years to 77/100,000 for geriatric population) (8). However, several factors including age and comorbidities such as HT and DM affect the course of ISSNHL. The hearing recovery rate in the geriatric population has been reported to be lower (odds ratio 3.25) than that in the younger population, with age being an independent prognostic risk factor for hearing recovery (9). This may be due to the ageing-related impairment of microvascular circulation. The inner ear is highly affected by microangiopathic situations that arise with ageing or other comorbidities because it is one of the important organs with high mass-specific oxygen consumption (9). This shows that the decrease in hearing recovery with age is due to the conditions such as HT, DM, dyslipidaemia and thromboembolic risk that disrupt microcirculation; the prevalence of these conditions increases with age (10). However, some studies showed that hearing recovery did not correlate with age, and some comorbid conditions were not found to be the risk factors for recovery rates (11, 12). ISSNHL studies have been generally performed in all age populations in the literature, but these studies are quite limited in the geriatric population. Considering that disease response to standard treatments becomes low with age, additional treatment modalities may provide superior outcomes. With this in mind, the goal of this study was to evaluate the correlation between possible comorbid conditions and ISSNHL and to determine the efficacy of popular treatment modalities in elderly patients with ISSNHL.

There is still no consensus on the treatment of ISSNHL, and even spontaneous resolution of ISSNHL varies between 30% and 65% (13). SSs are the generally accepted treatment regimen for ISSNHL (2). Wilson et al. showed that a SS regimen significantly ameliorated hearing loss in 61% of patients in the treatment group compared with 32% in the placebo group (14), whereas a meta-analysis revealed that treatment with SSs did not produce better results than placebo in patients with ISSNHL (15). Despite the fact that there was no placebo group in the present study, complete recovery rates were extremely low (5%). Although the effectiveness of SSs is controversial, they are most widely used in ISSNHL. SSs can be used at different doses, but generally, it is accepted to start treatment with a 1 mg/kg/day single dose of systemic prednisone or methylprednisolone and complete the treatment in 10–14 days (2). In the present study, steroid regimen was applied for all patients according to the literature. Complete recovery was not observed in any patient, and no hearing improvement was seen in 14 (63.6%) patients in group 1. A previous study reported that complete recovery was observed only in one (2.3%) patient and that 20 out of 43 (46.5%) geriatric patients with ISSNHL exhibited no changes in hearing gain, similar to the results of the present study (16). In addition, in that study, hearing recovery rates after treatment were better in geriatric patients who received a conventional SS regimen than in those who received a low-dose SS regimen. Notably, the possible adverse effects of SSs such as HT, hyperglycaemia, myocardial infarction, gastrointestinal bleeding and even death should be considered during treatment, especially in the elderly (16).

One of the steroid applications in patients with ISSNHL is intratympanic administration. It is known to have some advantages over systemic administration-less complications and increased steroid concentration in perilymph (17). ITS has been found to have a similar efficacy as only SS application in patients with ISSNHL (4). In addition, combined therapy (SS+ITS) has been found to be superior to only SS or only ITS (18). However, in the present study, the combination of SS+ITS was not found to be superior to only SS application in geriatric patients with ISSNHL. The difference between our study results and

those reported in the literature may be due to the fact that we included patients from a geriatric population with lower recovery rates.

HBOT has been used in the treatment of systemic or local vascular diseases for more than half a century. HBOT is an option for patients with ISSNHL, and it mainly acts by increasing oxygen pressure of blood and the inner ear (7). In a Cochrane review, HBOT was found to improve the mean PTA by 25% in patients with ISSNHL (19). Co-administration of HBOT and SS may have a synergistic effect on hearing recovery in ISSNHL patients. A combination of SS+HBOT reportedly provided better results than only SS administration for hearing gain in patients with ISSNHL > 61 dB HL (20). In addition, a combination of SS+HBOT showed a better effect than ITS+HBOT in patients with profound ISSNHL (21). However, we did not find any difference in terms of recovery rates and hearing gains among SS+HBOT, SS+ITS or only SS modalities. The discrepancy with the results reported in the literature may be due to the fact that the patients in the literature were selected from all ages because a combination of SS+HBOT was found to be significantly less effective for hearing gain in elderly ISSNHL patients (20). In addition, HBOT is generally preferred as a salvage treatment option for SS-failed ISSNHL cases due to its unclear benefit and high costs (22).

In the literature, complete recovery was observed in 5.9% (2/34), partial recovery in 8.8% (3/34), slight improvement in 29.4% (10/34) and no hearing improvement in 55.9% (19/34) of patients aged >60 years according to the Siegel's criteria (23). In the present study, no improvement was seen in 33 (55%), slight improvement in 11 (18.3%), partial recovery 13 (21.7%) and complete recovery in 3 (5%) of 60 patients. When both studies were compared, it was noteworthy that although some treatment modalities were different, the recovery rates were similar. The impact of the type of audiogram on the results is not well known. It is stated that the type of audiogram might be a prognostic factor for hearing recovery rates, with up-sloping audiogram curve related to a better prognosis and down-sloping curve related to a worse prognosis (24). However, in the literature, the type of audiogram reportedly had no effect on recovery rates (23). Similarly, in the present study, there was no correlation between audiogram types and hearing gain and recovery rates in elderly patients with ISSNHL. Comorbidities such as HT and DM were evaluated as prognostic factors for recovery rates; this issue is controversial in the literature (11, 25). In the present study, these two comorbidities were not found to be correlated with recovery rates and hearing gains. In the literature, delayed treatment has been reported to be related to poor recovery rates, especially if treatment was started 10 days after onset (23). In order to eliminate the delayed treatment effect, patients who were treated after 10 days were excluded from the study. Limitations of the present study were its retrospective nature and the absence of a placebo group.

In conclusion, the present study showed that ITS or HBOT as additional initial therapies to SS have no effect on recovery rates and hearing gain in elderly patients with ISSNHL. However, ITS or HBOT should be considered as a treatment regimen for salvage treatment or in cases where SS cannot be used.

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CONFLICT OF INTEREST

The authors declare that no conflict of interest regarding the publication of this manuscript.

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