



Clinical efficacy of intratympanic steroid injection for treating idiopathic sudden sensorineural hearing loss

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Abstract

Background: Idiopathic sudden sensorineural hearing loss (ISSNHL) is an emergency that causes permanent hearing loss if timely treatment is not provided. However, the evidence supporting the effect of intratympanic steroid injection (ITSI) starting time on hearing outcome is limited.

Methods: We retrospectively enrolled 582 patients with ISSNHL who were treated with ITSIs and reviewed their clinical and audiological variables. The relationship between ITSI starting time and hearing recovery was analyzed.

Results: The mean starting time of ITSI was 13.17 ± 16.53 days. The overall hearing recovery rate was 55.15% (recovery = mean hearing level gain of ≥ 10 dB). The recovery rates were 79.2%, 67.4%, 50%, 36.6%, and 17.8% for the ITSI starting times of 1 to 3, 4 to 7, 8 to 14, 15 to 28, and ≥ 29 days, respectively. A multivariate analysis revealed that ITST starting time (odds ratio [OR] = 0.94, 95% CI, 0.92-0.96, $p < 0.001$) and salvage therapy (OR = 0.55, 95% CI, 0.35-0.86, $p = 0.009$) were independent poor prognostic factors for patients with ISSNHL.

Conclusion: Earlier ITSI treatment is associated with a higher hearing recovery rate. Comorbidities and post-ITSI complications were nonsignificant independent risk factors.

Keywords: Odds ratio; Prognostic; Salvage therapy; Sensorineural hearing loss; Sudden deafness

1. INTRODUCTION

Idiopathic sudden sensorineural hearing loss (ISSNHL) is an otologic emergency; it is defined as an acute hearing loss of ≥ 30 dB within 3 days for at least three consecutive frequencies without obvious recognizable etiology.¹ In Taiwan, the incidence rate is 8.85/100 000 for men and 7.79/100 000 for women, and it peaks in autumn.² According to the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) guidelines,¹ the main treatment for ISSNHL is the use of corticosteroids, which are either administered through systemic or intratympanic injection. Because of the various side effects of systemic steroids, especially among patients with diabetes, chronic kidney disease, glaucoma, and gastric ulcers, intratympanic steroid injections (ITSIs) are increasingly being administered as an alternative therapy or as a salvage therapy after an unsuccessful systemic steroid treatment.^{1,3,4}

Although various studies have demonstrated the efficacy of ITSI in prospective, randomized, and placebo-controlled

trials,^{5,6} the complete hearing recovery rate for ISSNHL is low, ranging from 5% to 55%.⁷ Thus, researchers are increasingly exploring methods for improving the outcome of ITSI. The AAO-HNS guideline recommends the initiation of treatment within 2 weeks of symptom onset;¹ however, timely treatment is often not provided because of delays in the diagnosis of ISSNHL. Furthermore, few studies have evaluated the effect of ITSI starting time on ITSI efficacy, and its influence on hearing prognosis also remains unclear. Therefore, the objective of our retrospective study was to investigate the clinical characteristics of patients with ISSNHL who underwent ITSI treatment in our hospital, with a focus on the related prognostic factors and the influence of ITSI starting time on hearing recovery.

2. METHODS

This is a retrospective observation study. Between January 2013 and December 2020, patients who were diagnosed as having ISSNHL and were under ITSI treatment at the Otolaryngology Department of National Cheng Kung University Hospital, Tainan, Taiwan, were retrospectively enrolled in the present study. All enrolled patients were treated with ITSI treatment as the primary or salvage therapy. Salvage therapy is defined as therapy administered to patients with incomplete hearing recovery following systemic corticosteroid treatment with the recommended dose (eg, 1 mg/kg of prednisone orally administered per day) for ≥ 7 days. We excluded patients who were lost to follow-up, those who received fewer than three ITSIs, and those with specific etiologies of sensorineural hearing loss (eg, Meniere disease or ipsilateral cerebellopontine angle tumor).

All ITSI procedures were performed on an outpatient basis. The patients received intratympanic dexamethasone (5 mg/1 mL/amp) injections (two to four 0.4-0.6-mL injections

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administered over a 2-week period). The patients were placed in a supine position, with their heads tilted at 40° to 45° on the healthy side. Topical anesthesia was achieved using 20% lidocaine spray that was applied to the external auditory canal for 10 minutes to fill it. The lidocaine was then sucked out before the injection was administered. Under microscopy, each injection was administered using a 22-G spinal needle through the anteroinferior quadrante of the eardrum and into the middle ear cavity. After the injection was administered, patients were instructed to avoid moving their head, speaking, or swallowing for 30 minutes.

Data on clinical variables including age, sex, side of hearing impairment, smoking, and comorbid disease (ie, hypertension, diabetes mellitus, chronic kidney disease, coronary artery disease, cerebrovascular accident, and liver cirrhosis) were collected. We also collected data pertaining to the patients' ITSI starting time (the time from the onset of symptoms of hearing loss to the initiation of first-time ITSI) and post-ITSI complications (including persisted eardrum perforation within 3 months after ITSI, vertigo, and any other forms of discomfort that occurred immediately after ITSI and persisted such that a transfer to the emergency room was required).

Hearing was evaluated using standardized methods for pure-tone threshold audiometry before ITSI treatment and at 3 months after the final ITSI. Mean hearing level was defined as the average hearing threshold at four frequencies (500 Hz, 1 kHz, 2 kHz, and 4 kHz). Hearing improvement was defined as a mean hearing gain of ≥ 10 dB.⁸⁻¹⁰ We chose this definition to assess main outcome and further analysis due to its frequent utilization in previous research,¹ allowing for meaningful comparisons with the outcomes presented in our study. Due to the absence of standardized format, coupled with limitations in each measurement, we also applied Siegel¹¹ criteria as a second method for evaluating hearing recovery to mitigate the limitations in outcome measurement; under these criteria, recovery was classified as complete recovery (final hearing threshold of < 25 dB), partial recovery (hearing gain of > 15 dB and final hearing threshold of

25-45 dB), slight improvement (hearing gain of > 15 dB and final hearing threshold of > 45 dB) and no improvement (hearing gain of < 15 dB and final hearing threshold of > 75 dB).

Data are summarized as means and ranges for continuous variables and as numbers and percentages for categorical variables. The chi-square and Mann-Whitney *U* tests were conducted to compare categorical and continuous variables, respectively. We also performed univariate and multivariate logistic regression analyses to assess the odds ratios (ORs) of treatment in association with various potential prognostic factors. The Cochran-Armitage test was applied to determine whether improvement rate and ITSI starting time are negatively correlated. A $p < 0.05$ was regarded as statistically significant in all hypothesis's tests. All analyses were performed using the statistical software SAS 9.4 (version 9.4; SAS Institute, Cary, NC) and R (version 4.2.1; R Core Team, www.r-project.org).

The present study was approved by the National Cheng Kung University Hospital Institutional Review Board (NCKUH IRB; approval no. A-ER-111-21).

3. RESULTS

In total, 582 ISSNHL patients (302 men [51.89%] and 280 women [48.11%]) who received 2267 ITSIs (average of 3.89 injections per patient) were included in the present study. Their mean age was 56.7 ± 14.05 years, and 274 (47.1%) and 308 (52.9%) patients were affected in the right and left ears, respectively. A total of 165 (28.35%) patients were given ITSIs as salvage treatment after an unsuccessful standard systemic steroid treatment. With respect to the patients' comorbid diseases, 239 (41.07%) had hypertension, 228 (39.18%) had diabetes mellitus, 83 (14.26%) had chronic kidney disease, 52 (8.93%) had coronary artery disease, 24 (4.12%) had cerebrovascular accidents, and 10 (1.72%) had liver cirrhosis. The mean starting time of ITSI from the onset of hearing loss symptoms was 13.17 ± 16.53 days. These data are summarized in Table 1.

Table 1
Clinical characteristics of 582 patients with ISSNHL

Variables	Total (N = 582)	Subgroup	
		Primary (N = 417)	Salvage (N = 165)
Age, years \pm SD	56.7 \pm 14.0	58.89 \pm 14.0	51.2 \pm 14.1
Gender			
Female, N (%)	280 (48.11)	195 (46.76)	85 (51.51)
Male, N (%)	302 (51.89)	222 (53.23)	80 (48.48)
Side			
Right, N (%)	274 (47.1)	190 (45.56)	84 (50.90)
Left, N (%)	308 (52.9)	227 (54.43)	81 (49.09)
Comorbid disease			
Smoking, N (%)	76 (13.06)	49 (11.75)	27 (16.36)
Hypertension, N (%)	239 (41.07)	199 (47.72)	40 (24.24)
Diabetes mellitus, N (%)	228 (39.18)	199 (47.72)	29 (17.57)
Chronic kidney disease, N (%)	83 (14.26)	76 (18.23)	7 (4.24)
Coronary artery disease, N (%)	52 (8.93)	44 (10.55)	8 (4.84)
Cerebrovascular accident, N (%)	24 (4.12)	24 (5.75)	0 (0)
Liver cirrhosis, N (%)	10 (1.72)	10 (2.39)	0 (0)
ITSI starting time, days \pm SD	13.17 \pm 16.53	10.61 \pm 16.53	19.64 \pm 16.53
Complication, N (%)	9 (1.55)	6 (1.44)	3 (1.82)
Pre-ITSI mean hearing level (of affected ear), dBHL \pm SD	75.3 \pm 25.87	76.53 \pm 25.87	72.18 \pm 25.87
Post-ITSI mean hearing level (of affected ear), dBHL \pm SD	56.87 \pm 27.26	55.67 \pm 27.26	59.89 \pm 27.26
Mean hearing level gain, dBHL \pm SD	18.43 \pm 20.00	20.86 \pm 20.00	12.29 \pm 20.01

ISSNHL = idiopathic sudden sensorineural hearing loss; ITSI = intratympanic steroid injection; Mean hearing level = average PTA at 500, 1 k, 2 k, 4 k Hz; N = numbers; PTA = pure-tone audiometry.

Before the patients underwent ITSI treatment, the mean hearing level of their affected ear was 75.3 ± 25.87 dB. After they underwent the treatment, the mean hearing level of their affected ear was 56.87 ± 27.26 dB. That is, their mean hearing level gain was 18.43 ± 20 dB. Table 2 presents the patients' hearing outcomes after they underwent ITSI treatment. Overall, after undergoing ITSI treatment, 321 (55.15%) patients experienced hearing recovery, which was defined as a mean hearing level gain of ≥ 10 dB. In accordance with Siegel criteria, 81 (13.92%), 76 (13.06%), 141 (24.23%), and 284 (48.8%) patients experienced complete, partial, slight, and no recovery, respectively. That is, their Siegel recovery rate (complete recovery and partial recovery) was 26.98%.

The patients with ISSNHL were further stratified into five groups on the basis of the following ITSI starting time ranges: 1 to 3 days ($n = 144$), 4 to 7 days ($n = 138$), 8 to 14 days ($n = 134$), 15 to 28 days ($n = 93$), and ≥ 29 days ($n = 73$). The post-ITSI-treatment hearing improvement rates (defined as a mean hearing level gain of ≥ 10 dB) for the five groups were 79.2% (1-3 days, $n = 114$), 67.4% (4-7 days, $n = 93$), 50% (8-14 days, $n = 67$), 36.6% (15-28 days, $n = 34$), and 17.8% (≥ 29 days, $n = 13$). In accordance with Siegel criteria, the recovery rates (Siegel complete recovery and partial recovery) for the five groups were 72.2% (1-3 days, $n = 104$), 63.8% (4-7 days, $n = 88$), 46.3% (8-14 days, $n = 62$), 35.5% (15-28 days, $n = 33$), and 15.1%

(≥ 29 days, $n = 11$). Notably, the improvement rates decreased when ITSIs were started later ($p < 0.001$). The results are presented in Fig. 1.

The results of the univariate and multivariate analyses of the prognostic factors for the patients with ISSNHL are presented in Table 3. An improvement was defined as a mean hearing level gain of ≥ 10 dB after ITSI treatment. The results reveal that ITSI starting time (OR = 0.93, 95% CI, 0.91-0.95, $p < 0.001$) and salvage ITSI (OR = 0.41, 95% CI, 0.28-0.59, $p < 0.001$) were significant negative risk factors for the hearing improvement of patients with ISSNHL. These factors were further evaluated in a multivariate logistic regression model, which revealed that ITSI starting time (OR = 0.94, 95% CI, 0.92-0.96, $p < 0.001$) and salvage ITSI (OR = 0.55, 95% CI, 0.35-0.86, $p = 0.009$) were both verified as significant independent risk factors. Through the univariate logistic regression model, diabetes mellitus (OR = 1.94, 95% CI, 1.37-2.73, $p < 0.001$) and mean hearing level of the affected ear (OR = 1.02, 95% CI, 1.01-1.02, $p < 0.001$) were revealed to be protective factors for the hearing improvement of patients with ISSNHL; however, diabetes mellitus was revealed to be a nonsignificant factor in multivariate analysis.

A total of nine patients developed complications after undergoing ITSI treatment. Six patients experienced persistent vertigo and were transferred to the emergency room for intravenous

Table 2
Treatment outcomes of 582 patients with ISSNHL after ITSI treatment

Definition of recovery	Total	Subgroup	
		Primary	Salvage
Mean hearing level gain ≥ 10 dB, N (%)	321 (55.15)	256 (61.39)	65 (39.40)
Siegel criteria, N (%)			
I (complete recovery)	81 (13.92)	64 (15.35)	17 (10.30)
II (partial recovery)	76 (13.06)	65 (15.59)	11 (6.67)
III (slight recovery)	141 (24.23)	107 (25.66)	34 (20.60)
IV (no recovery)	284 (48.80)	181 (43.40)	103 (62.42)

Complete recovery = final hearing threshold < 25 dB; ISSNHL = idiopathic sudden sensorineural hearing loss; ITSI = intratympanic steroid injection; N = numbers; No improvement = hearing gain < 15 dB and final hearing threshold > 75 dB; Partial recovery = hearing gain > 15 dB and final hearing threshold 25-45 dB; Slight improvement = hearing gain > 15 dB and final hearing threshold > 45 dB.

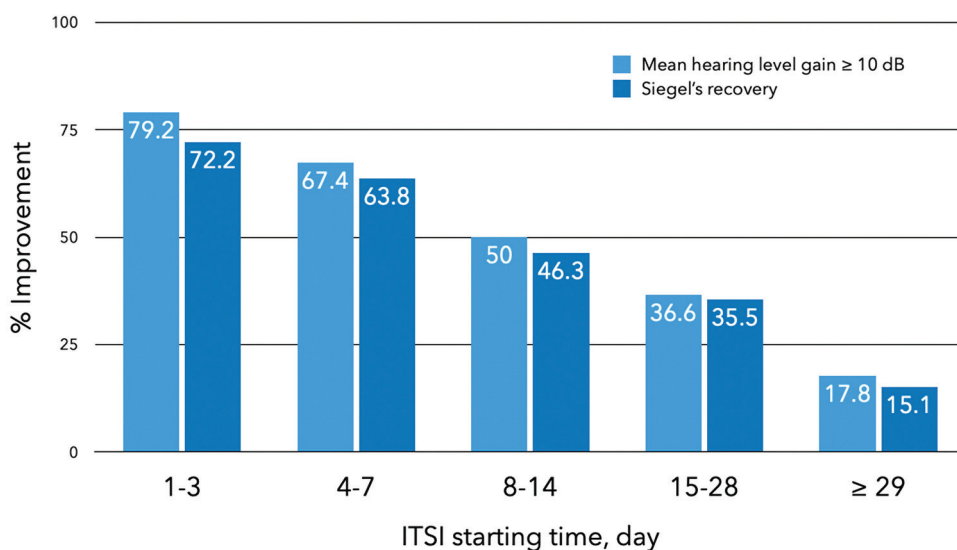


Fig. 1 Relationship between ITSI starting time and hearing improvement rate. Two different definitions of hearing improvement are listed (mean hearing level gain of ≥ 10 dB and Siegel criteria for recovery). ITSI = intratympanic steroid injection; Siegel recovery = complete recovery (final hearing threshold of < 25 dB) and partial recovery (hearing gain of > 15 dB and final hearing threshold of 25-45 dB).

Table 3
Univariate and multivariate analyses of prognostic factors for patients with ISSNHL

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Age, y	1.00	(0.99-1.02)	0.543	0.99	(0.97-1.00)	0.110
Male	0.81	(0.58-1.12)	0.207	0.70	(0.48-1.03)	0.069
Smoking	1.07	(0.66-1.74)	0.789	1.10	(0.62-1.95)	0.739
Hypertension	1.27	(0.91-1.77)	0.166	0.93	(0.60-1.42)	0.720
Diabetes mellitus	1.94	(1.37-2.73)	<0.001*	1.45	(0.95-2.22)	0.084
Chronic kidney disease	1.35	(0.84-2.18)	0.214	0.90	(0.50-1.63)	0.736
Coronary artery disease	1.60	(0.88-2.90)	0.123	1.18	(0.58-2.41)	0.646
Cerebrovascular accident	0.81	(0.36-1.82)	0.605	0.46	(0.19-1.11)	0.083
Liver cirrhosis	0.34	(0.09-1.34)	0.123	0.23	(0.06-0.97)	0.046
Mean hearing level of affect ear	1.02	(1.01-1.02)	<0.001*	1.02	(1.01-1.02)	<0.001*
ITSI starting time	0.93	(0.91-0.95)	<0.001*	0.94	(0.92-0.96)	<0.001*
Salvage ITSI	0.41	(0.28-0.59)	<0.001*	0.55	(0.35-0.86)	0.009*
Complication (%)	0.65	(0.17-2.43)	0.518	0.63	(0.15-2.56)	0.516

Significant differences are shown in bold.

ISSNHL = idiopathic sudden sensorineural hearing loss; ITSI = intratympanic steroid injection; Mean hearing level = average PTA at 500, 1 k, 2 k, 4 k Hz; OR = odds ratio; PTA = pure-tone audiometry. **p* < 0.05.

medical treatment. During the 3-month outpatient follow-up period, two patients reported post-ITSI eardrum perforation that did not spontaneously heal. A patient who had underlying hypertension and a previous cerebrovascular accident experienced chest pain immediately after undergoing ITSI treatment and was referred to the emergency room. The patient's blood test results for two sets of high-sensitivity troponin were within the normal limits. The patient's electrocardiogram revealed a sinus rhythm without ST-T changes. He was subsequently discharged from the hospital and did not exhibit any symptoms. The characteristics of patients who experienced complications are listed in Table 4.

4. DISCUSSION

Since the introduction of ITSIs in 1986,¹² numerous clinicians and researchers have used ITSIs to treat ISSNHL. However, few studies have evaluated the effect of ITSI starting time on hearing outcomes. To the best of our knowledge, this single center-based study has the largest patient population for this research area in East Asia. We analyzed 582 patients with ISSNHL who received ITSI treatment. A total of 321 (55.15%) patients reported clinically significant improvements in their 3-month follow-up.

Steroids can reduce inflammation and edema, increase microcirculation in the inner ear, and produce antioxidant and immune-modulation effects. Studies have demonstrated that steroids can help protect hair cells against noise and other adverse factors.¹³ Compared with systemic steroids, ITSIs can deliver a higher drug concentration to the inner ear, thereby avoiding most of the side effects of oral steroids.¹⁴ The literature findings on the therapeutic effect of ITSIs are inconsistent; various definitions of hearing recovery have been proposed, and various demographics have been examined.¹⁵ Koltsidopoulos et al⁸ reported significant hearing recovery in 31 (67.39%) of 46 patients who underwent ITSI treatment. Siegel¹¹ used the final pure-tone audiometry (PTA) of the affected ear as a measure of recovery. Ghanie et al³ retrospectively reviewed all patients with ISSNHL who received six injections of intratympanic steroid within 6 weeks from onset, and reported that 17.7% and 34.4% of the patients they examined experienced complete and partial recovery, respectively, following ITSI as primary treatment. In a study conducted by Chen et al¹⁶, 4.76% and 41.91% of a group of older patients who underwent ITSI as primary treatment with mean onset of treatment of 2.22 days, achieved complete and partial recovery, respectively. In our study, 81 (13.92%) and 76 (13.06%) patients met Siegel criteria for complete and partial recovery, respectively. However, because of the

Table 4
Characteristics of patients with post-ITSI complications (n = 9)

	Age	Gender	Comorbid disease	ITSI starting time, d	Pre-ITSI MHL, dB	Post-ITSI MHL, dB	Mean hearing level gain, dB	Siegel criteria
Post-ITSI vertigo								
No. 1	62	Male	DM	1	53	26	27	II
No. 2	53	Female	No	2	117.5	71	46.5	III
No. 3	73	Male	No	4	61	43	18	II
No. 4	58	Female	No	3	71	65	6	IV
No. 5	62	Female	DM	10	70	55	15	IV
No. 6	40	Female	No	30	73	79	-6	IV
Post-ITSI eardrum perforation								
No. 1	65	Male	HTN, DM, CKD	5	65	63	2	IV
No. 2	65	Male	No	19	66	77	-11	IV
Chest pain								
No. 1	76	Male	HTN, CVA	10	93	93	0	IV

CKD = chronic kidney disease; CVA = cerebrovascular accident; DM = diabetes mellitus; HTN = hypertension; ITSI = intratympanic steroid injection; MHL = mean hearing level.

different clinical characteristics of the cases included in these studies, direct comparison of the results between studies may not be suitable.

Although ISSNHL is commonly regarded as an otologic emergency, few studies have evidenced the necessity of providing urgent medical care for ISSNHL. According to the updated clinical practice guideline released by the AAO-HNS in 2019, clinicians may offer corticosteroids as the initial treatment within 2 weeks of symptom onset;¹ however, the specific effects of ITSI starting time on ITSI efficacy requires further clarification. Studies have asserted that the optimal time for treating ISSNHL is <7 days after symptom onset.^{4,17} Our study revealed that the earlier an ITSI treatment is started, the more favorable is the hearing outcome; this also applies to the group with an ITSI starting time of 1 to 3 days and that with an ITSI starting time of 4 to 7 days. If ITSI treatment is not provided within 7 days of symptoms onset, the recovery rate for ISSNHL decreases to <50% (Fig. 1). Attanasio et al also reported that each additional day of ITSI treatment delay following the onset of hearing loss reduces the possibility of recovery by an average of 2% to 3%.^{5,18} From another perspective, our study also revealed that ITSIs can still be beneficial even if they are delayed by more than 4 weeks after symptom onset, as evidenced by the 17.8% hearing improvement rate achieved by patients who underwent ITSI treatment more than 4 weeks after symptom onset. The results for delayed treatment group were comparable with previous studies: Haynes et al¹⁹ reported 15.79% of cases improved hearing after the delayed salvage ITSIs (time to injection >1 month), using the criteria of 20-dB gain in PTA. As the primary but delayed ITSIs treatment and using AAO-HNS reporting criteria, Osafo et al¹⁵ published the recovery rate after ITSIs was slightly more than 20%. Our results, with a larger sample size, offer more robust evidence for this matter.

Several factors have been reported to have a prognostic effect on ISSNHL. Kang et al²⁰ retrospectively investigated 494 patients with ISSNHL and discovered that the time from onset to treatment and the severity of initial hearing loss are significant prognostic factors for hearing improvement. Studies have also proposed advanced age, hypertension, dyslipidemia, diabetes, initial speech discrimination, and vertigo as poor prognostic factors.^{3,5,16,19} However, a general consensus on the effects of these factors on recovery has yet to be reached. In the present study, univariate and multivariate analyses revealed that ITSI starting time and salvage ITSI were independent negative prognostic factors for patients with ISSNHL. Age, sex, smoking, comorbidities (including hypertension, chronic kidney disease, coronary artery disease, cerebrovascular disease, and liver cirrhosis), and post-ITSI complications were nonsignificant independent risk factors. The paradoxical finding that the pre-ITSI mean hearing level of the affected ear is a protective factor is attributable to the definition of hearing improvement and the statistical method applied in the present study. Specifically, because hearing recovery was defined as a mean hearing level gain of ≥ 10 dB, the patients with severe initial hearing loss were more likely to meet the applied criteria. Furthermore, most studies that reported profound hearing loss as a poor prognostic factor have discussed hearing thresholds as a categorical variable;^{3,8,11,15,16} by contrast, our study analyzed continuous variables. Although diabetes was revealed to be a protective factor in our univariate analysis, it was nonsignificant in our multivariate analysis. This finding may be related to the selection of first-line treatment for ISSNHL. Large-scale systemic reviews and meta-analyses have demonstrated that systemic steroid and ITSIs provide comparable efficacy when they are used as the initial treatment for patients with ISSNHL;^{4,21} however, systemic steroids are still more commonly used as the initial treatment worldwide and in Taiwan,

and ITSIs are usually reserved as an alternative treatment for patients who contraindicate for systemic steroids.^{22,23} Thus, patients with diabetes mellitus are usually given ITSI treatment as the initial treatment. However, numerous nondiabetic people who were given systemic steroids received inadequate dosages initially, which delayed the effects of ITSIs.

An ITSI is an invasive procedure. The common complications of ITSIs include otalgia, vertigo, tongue numbness, and eardrum perforation.^{24,25} Post-ITSI otalgia is the most common side effect, but it is usually self-limited and can be controlled with oral analgesics.²⁶ The post-ITSI eardrum perforation rates reported by various studies range from 1.6% to 5.9%.^{25,27} The incidence of perforation in our study was 1.03% (six patients), which was lower than those reported by other studies. Hu et al²⁵ did not detect any significant association between the occurrence of complications and hearing outcomes; this finding aligns with that of our study.

This study has several limitations. First, the enrolled patients were from a single center and were analyzed retrospectively. Therefore, potentially valuable information could have been overlooked. However, such data would not have influenced our interpretation. Second, we defined ITSIs as a salvage treatment that is administered following an unsuccessful systemic steroid treatment with the recommended dose. The patients who were treated with underdosed systemic steroids and subsequently received ITSIs were classified as patients who underwent primary treatment. Therefore, the effect of low-dose steroid on ITSI efficacy remains unclear. Third, even though it is widely used, the absolute change in hearing threshold of just 10 dB may be excessively low for assessing recovery, and this standard could have led to an overestimation of the efficacy of IT steroids.¹⁵ Fourth, all the patients were given 0.4 to 0.6 mL of intratympanic dexamethasone that was injected three to four times; thus, whether the dose and frequency of ITSIs influence their efficacy is unclear. These topics should be addressed in future studies.

In conclusion, the present study investigated 582 patients who had ISSNHL and received ITSI treatment, with an overall recovery rate of 55.15% (recovery was defined as a mean hearing level gain of ≥ 10 dB). We demonstrated that the earlier an ITSI treatment is started, the more favorable the hearing outcomes are. This finding also applies to the group with an ITSI starting time of 1 to 3 days and that with an ITSI starting time of 4 to 7 days. Comorbidities and post-ITSI complications were not significant independent risk factors.

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