Original Article

The outcome of intratympanic steroid therapy as a salvage treatment for sudden sensorineural hearing loss

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ABSTRACT

Objectives: The aim of this study is to evaluate the outcomes of intratympanic steroid (ITS) treatment for idiopathic sudden sensorineural hearing loss (SSNHL).

Patients and Methods: Between January 2014 and November 2016, medical charts of a total of 63 patients (47 males, 16 females; mean age: 44.2±17.5 years; range, 18 to 77 years) who were hospitalized due to SSNHL were retrospectively analyzed. The patients were divided into two groups as those who received standard treatment (Group 1, n=32) and those who received ITS treatment as a salvage treatment (Group 2, n=31). Treatment modalities and the results of pure tone audiometry tests were recorded. Recovery was assessed according to the Furuhashi criteria.

Results: There was no significant difference in the hearing recovery rates between Group 1 and Group 2. In the patients receiving standard treatment, the recovery rate was significant (78%), while it was only 35.4% in the patients receiving ITS treatment (p=0.361).

Conclusion: Although recent guidelines strongly recommend ITS treatment, in our study, ITS, which was started on Day 5 of admission, was not found to be superior to standard systemic treatment.

Keywords: Intratympanic injection, salvage treatment, sudden sensorineural hearing loss.

Sudden sensorineural hearing loss (SSNHL) is still an undiscovered clinical entity with a non-standardized treatment and requires clinical evidence. Multidrug therapy is the most common treatment of choice in SSNHL. In the primary treatment of SSNHL, many reports in the literature have demonstrated that intratympanic steroid (ITS) treatment and systemic steroid combination provides improved hearing gain than systemic steroid alone.[1-4] On the other hand, there are some reports showing no significant difference in the improvement of hearing recovery between the patients treated with ITS+systemic steroid combination and those treated with systemic steroids alone.[5,6] Therefore, the necessity of the ITS treatment is still controversial due to various recovery rates in the literature and there is no consensus on the use of salvage treatments.[7,8]

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In the present study, we aimed to evaluate the outcomes of ITS treatment for idiopathic SSNHL.

PATIENTS AND METHODS

Between January 2014 and November 2016, medical charts of a total of 63 patients (47 males, 16 females; mean age: 44.2±17.5 years; range, 18 to 77 years) who were hospitalized in a tertiary referral center due to SSNHL were retrospectively analyzed. Sudden sensorineural hearing loss was defined as at least of 30 dB hearing loss at three sequential frequencies over days or less with no identifiable etiology.[9] Refractory SSNHL was defined as unresponsiveness or an improvement in pure-tone averages (PTAs) of less than 20 dB at the end of the fifth day of standard treatment protocol. A written informed consent was obtained from each patient. The study protocol was approved by the Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A detailed history of demographic features, side of hearing loss, previous history of ear surgery, recent history of upper respiratory tract infection, duration of hearing loss before admission, presence of comorbid diseases, such as diabetes mellitus and hypertension, audiogram pattern, and audiological data at baseline and at the end of the treatment were recorded. All patients with SSNHL who completed a full course of standard treatment protocol and attended regular follow-up visits were included in the study. Those without audiological follow-up data and patients who were under 18 years old were excluded. Also, those with a known otologic disease of the external/middle/inner ear or history of ear surgery and patients who had bilateral SSNHL were also excluded. Patients who had uncontrolled diabetes mellitus, decompensated ischemic heart disease, hyperlipidemia, and chronic renal failure were consulted to the Internal Medicine Department and those who had contraindications to systemic steroid administration were excluded from the study.

All patients were informed about the benefits and complications of the ITS treatment and were divided into two groups as those who received standard treatment (Group 1, n=32) and those who received ITS treatment as a salvage treatment (Group 2, n=31).

Standard treatment protocol included intravenous 5 mg/kg low-molecular-weight dextran (Rheomacrodex®, Eczacıbaşı, Baxter; Istanbul, Turkey), 24 mg oral betahistine tablet (Betaserc®, Abbott Healthcare SAS, Chalarone, France) twice a day, and 800 mg oral piracetam tablet (Nootropil®, UCB Pharma, Istanbul, Turkey) three times a day. In addition, if there were no contraindications, 1 mg/kg oral prednisolone (Prednol®, Mustafa Nevzat, Istanbul, Turkey) which was tapered by 10 mg was administered every three days with lansoprazole (Lansor®, Sanovel, Istanbul, Turkey). Standard treatment protocol was applied to Group 1, while Group 2 received intratympanic dexamethasone on Day 5 of admission combined with the standard protocol. Before the ITS application, 10% lidocaine local anesthetic spray (Vemcaine®, Vem Pharmaceuticals, Istanbul, Turkey) was applied to the external ear canal. Then, approximately 1 mL dexamethasone (Dekort®, Deva Co., Istanbul, Turkey) was injected into the middle ear through the posteroinferior quadrant of the tympanic membrane using a 27-Gauge needle. The head of the patient was, then, tilted about 45° toward the healthy side and the patient was instructed to remain in the same position for 30 min and to avoid swallowing, coughing, or moving. Injections were repeated on Days 7 and 9 and, thus, patients received injection a total of three times on alternate days.

Audiological examination results were recorded and the treatment protocol was evaluated to determine whether ITS was administered. Audiological evaluation was performed using the Madsen Astera (Otometrics, Taasturp, Denmark). Initial audiological configurations were classified as the ascending sloping type (hearing loss more severe in low frequencies), descending sloping type (hearing loss more severe in high frequencies), and flat type (mean threshold differences at 250/500 Hz, 1,000/2,000 Hz and 4,000/8,000 Hz were <15 dB).

The PTA values were calculated by taking the mean hearing thresholds at 0.5, 1, and 2 kHz (average of three tones). In addition,

Table 1. Furuhashi criteria for the assessment of the audiological hearing outcomes

	Criteria
Complete recovery	PTA <25 dB or identical to contralateral nonaffected ear
Marked recovery	PTA improvement >30 dB
Slight recovery	PTA improvement between 10 and 30 dB
No recovery	PTA improvement <10 dB

PTA: Pure-tone average (500, 1000, 2000 4000 Hz).

pre- and post-treatment audiometric PTA values were evaluated and classified according to the Furuhashi criteria which categorize the outcome as complete recovery, marked recovery, slight recovery, and no recovery (Table 1).[10] Accordingly, complete recovery was defined as the thresholds improving to the same level as the non-affected ear or improving at a rate of ≥25 dB on average. Marked recovery was defined as a PTA improvement more than 30 dB. Slight recovery was defined as a hearing improvement between 10 and 30 dB on average. Hearing recovery less than 10 dB was accepted as no recovery.

Statistical analysis

Statistical analysis was performed using the PASW for Windows version 17.0 software

Table 2. Demographic and clinical characteristics of patients

	Group 1 (n=32)		Group 2 (n=31)		
	n	Mean±SD	n	Mean±SD	*p*
Age (year)		45.8±19.5		42.5±14.7	0.592
Gender					0.579
Male	25		22		
Female	7		9		
Side					0.359
Right	12		14		
Left	20		17		
Presence of vertigo					0.113
Yes	6		11		
No	26		20		
Presence of tinnitus					0.185
Yes	24		19		
No	8		12		
Presence of diabetes mellitus					0.372
Yes	5		3		
No	27		28		
Presence of hypertension					0.585
Yes	8		8		
No	24		23		
Presence of upper respiratory tract infection					0.125
Yes	2		0		
No	30		31		
Time interval between the onset of symptom and therapy (days)		4.5±4.5		5.9±6.7	0.125

SD: Standard deviation.

(SPSS Inc., Chicago, IL, USA). Continuous variables were expressed in mean ± standard deviation (SD), median (min-max), number, and frequency. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to analyze the distribution patterns of variables. The chi-square test was used to compare categorical variables between the groups. The t-test was done to compare continuous variables between the groups. A p value of <0.05 was considered statistically significant.

RESULTS

Of a total of 63 patients included in the study, 32 patients in Group 1 received standard treatment, while 31 patients in Group 2 received ITS treatment. There was no significant difference in the baseline demographic and clinical characteristics between the patient groups. The patients were predominantly male with a mean age of 45.81±19.45 years in Group 1 and 42.45±14.71 years in Group 2 (p=0.592). The mean time from the onset of hearing loss to the initiation of the treatment was 4.50±4.52) days in Group 1 and 5.86±6.70 days in Group 2, indicating no statistically significant difference (t-test, p=0.146) (Table 2). Most of the patients had tinnitus, while some others had vertigo as an accompanying symptom. There were only two patients in Group 1 with a history of a recent upper respiratory infection. The number of patients with diabetes mellitus and hypertension was similar between the groups (chi-square test, p=0.372 and p=0.585, respectively). In addition, there were no significant differences between the two groups regarding the thresholds during the interval between the onset of hearing loss and pre-treatment hearing thresholds, which could have affected the hearing gain outcomes. Audiological configurations were homogenously distributed between the groups (chi-square test, p=0.609) (Table 3). The degree of recovery was measured in terms of the PTA improvement. The mean degree of recovery was 26.6±17.1 dB and 27.4±22.1 dB in Group 1 and

Table 3. Pre-treatment audiological results

	Group 1 (n=32)		Group 2 (n=31)		
	n	Mean±SD	n	Mean±SD	p
Audiogram shape (number of patients)					
Ascending	11		13		
Flat or deaf	18		15		0.609
Descending	3		3		
Pretreatment PTA treshold (dB)		57.0±30.2		56.0±27.6	0.335
Pre-treatment SDS		78.3±33.0		87.5±24.7	0.051
Recovery degree (dB)		26.6±17.1		27.4±22.1	0.151

PTA: Pure tone average: Threshold of 500, 1000, 2000 and 4000 Hz; dB: Decibels; SDS: Speech Discrimination Score.

Table 4. Post-treatment results according to Furuhashi criteria

	Group 1	Group 2	
Recovery classification	n	n	p
Complete recovery (number of patients)	19	5	0.523
Marked improvement (number of patients)	6	6	0.221
Slight improvement (number of patients)	2	3	0.253
No recovery (number of patients)	5	17	0.546
Total (number of patients)	32	31	

Table 5. Recovery results

	Group 1		Group 2		
Treatment result	n	%	n	%	*p*
Successful	25	78.1	11	35.5	0.361
Unsuccessful	7	21.9	20	64.5	
Total	32		31		

Group 2, respectively. There were no significant differences between the two groups in terms of the degree of recovery (t-test, p=0.151).

In Group 1, 19 patients (59.4%) had complete, six patients (18.8%) had marked, and two patients (6.3%) had slight recovery. In Group 2, five patients (16.1%) had complete, six patients (19.4%) had marked, and three patients (9.7%) had slight recovery. Steroid administration had no statistically significant effect in either complete, marked, slight recovery or no recovery groups (p=0.523, p=0.221, p=0.253, and p=0.546, respectively) (Table 4). Five patients (15.6%) in Group 1 and 17 patients (54.8%) in Group 2 had no recovery. There was no statistically significant difference between the recovery rates of both groups (chi-square test, p=0.546). Treatments which yielded marked or complete recovery were defined as successful, while those resulting in slight or no recovery were accepted as unsuccessful. The successful treatment rate was 78% (n=25) in Group 1 and 35.4% (n=11) in Group 2 (chi-Square test, p=0.361) (Table 5).

DISCUSSION

Sudden sensorineural hearing loss is a complex entity with multiple possible etiologies and treatment modalities. Currently, steroids (systemic or intratympanic), rheological agents, vasodilators, antiviral agents, vitamin electrolyte complexes, anticoagulants, and hyperbaric oxygen therapy have been the most commonly used treatment modalities for SSNHL in different combinations.[11,12] To date, none of the treatment options has shown superiority to one another in randomized clinical trials.[13]

Although there are numerous studies showing significantly higher rates of hearing improvement with the use of oral steroids;[11,14] the efficacy of salvage treatment options still remains unclear. Intratympanic steroid injection is an effective, safe, and well-tolerated office-based procedure for the treatment of SSNHL as the primary treatment or salvage treatment which can avoid the potential adverse effects of systemic steroids.[14] As ITS has been considered a promising therapeutic strategy, since high concentrations of drug directly passes to cochlea without any systemic adverse effect, it has become a salvage treatment option after the failure of systemic treatment or for the patients with systemic steroid contraindication. In addition, ITS has been thought to reach higher perilymph concentrations compared to systemic administration and, thus, it provides some additional hearing recovery.[15]

The greatest spontaneous improvement in hearing usually occurs during the first two weeks, while late recovery is rare. Similarly, treatment with corticosteroids appears to offer the greatest recovery within the first two weeks.[16] In the SSNHL Clinical Practice Guideline of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) (2012), ITS is recommended as a salvage treatment in patients with insufficient recovery after the initial treatment including oral steroids.[16] In the guideline, 'immediate treatment is defined as the use of oral corticosteroids ideally within the first 14 days.[16] Salvage treatment is defined as the use of ITS administration after systemic treatment fails. Instead of the term salvage, second-line treatment can be preferred by some authors.

In a recent meta-analysis of Qiang et al.,[17] initial ITS treatment was found to be superior to systemic treatment in terms of PTA improvement. However, salvage treatment with ITS was not

evaluated in the aforementioned study. In the present study, however, our main objective was to investigate the efficacy of salvage ITS in patients which did not benefit from systemic steroid treatment. The number of patients who benefited from ITS was only 11 (35.5%) in our study and systemic treatment was more successful (78.1%) in terms of successful recovery based on the Furuhashi criteria. Although these figures significantly differed, the statistical analysis showed no significant difference, probably due to the limited sample size. Interestingly, the success rate was lower in the patients treated with ITS. This can be explained by the fact that ITS treatment was administered to the already failed cases following systemic steroid treatment. In present study, we analyzed patients with refractory hearing loss and ITS treatment was initiated on Day 5 of admission. This five-day delay of ITS treatment might have yielded lower success rates in the patients treated with ITS group. The efficacy of steroids showed no significant difference in terms of the administration procedure.

A recent study of Hong et al.[18] concluded that salvage ITS treatment following oral steroid treatment for patients with SSNHL did not yield an additional therapeutic effect. The authors investigated 68 patients in three groups receiving three alternative treatment methods: oral prednisolone, intratympanic dexamethasone injection, or a combination of oral prednisolone and intratympanic dexamethasone injection. In profound SSNHL cases, they found no significant difference in complete recovery, partial recovery, and slight improvement rates among the three treatment methods, similar to our study. In our study, the therapeutic outcome of the ITS treatment applied on Day 5 of admission and repeated two times on alternate days was evaluated. When hearing recovery was compared between Group 1 and Group 2, the ITS administration had no statistically significant effect on recovery according to the Furuhashi criteria.

There are certain reports in the literature showing that the recovery from SSNHL is lower among patients with diabetes and hypertension.[19] Among our patients, there were five diabetic patients in the systemic steroid group and three patients in the ITS salvage treatment group. In each group, eight patients had hypertension. However, we found no significant correlation between the recovery rate and diabetes and/or hypertension.

In their study, Yang et al.[20] classified the patients according to the level of initial hearing loss and audiogram configuration as ascending, flat, and descending and evaluated the additional effects of ITS to provide guidelines for ITS indications. The authors found that additional ITS was beneficial to the patients with an ascending type audiogram or patients with an initial hearing loss of 60 to 90 dB. Concomitant ITS, however, resulted in a negative effect on hearing in the patients with an initial hearing loss of <60 dB. Interestingly, ITS was only effective in profound or severe hearing losses in their study. In our study, however, we were unable to obtain a statistically significant result according to the audiogram types, probably due to the small sample size in our study (only three patients had descending type audiogram). The majority of the patients had flat and ascending type audiograms, although there was no significant difference between these two configurations in terms of the recovery rates. Therefore, additional ITS was not found to be effective in most of our patients, irrespective of the configuration of audiogram.

The most common complication of ITS treatment is persistent tympanic membrane perforation.[21] Among our patients, none had tympanic membrane perforation. In addition, other possible complications such as vertigo, otitis media, and intolerable pain were not observed in our patients.

The present study found that salvage ITS is not superior to systemic steroids in patients with SSNHL and, thus, it should be considered as the first-line treatment combined with systemic treatment, even if it appears more invasive. Nonetheless, there are some limitations to this study. The number of patients in each group was not large enough to obtain a statistically significant difference between the groups. In addition, the data were analyzed in a retrospective design which lacks randomization and the vast majority of the patients were unable to be included,

due to missing follow-up data. Based on these findings, we cannot draw a definite conclusion and provide a strong recommendation for clinical practice. Therefore, further randomized-controlled studies are needed to establish a standardized treatment protocol for SSNHL.

In conclusion, although recent guidelines strongly recommend ITS treatment, in our study, ITS, which was started on Day 5 of admission, was not found to be superior to standard systemic treatment in patients with SSNHL. Nevertheless, these results should be cautiously interpreted considering the limitations of our study. We believe that, with the increasing use of ITS in clinical practice, more evidence would emerge and contribute to the literature.

Declaration of conflicting interests

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