

Is Intratympanic Dexamethasone Injection Effective for the Treatment of Idiopathic Sudden Sensorineural Hearing Loss?

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Background and Objectives: The purpose of this study is to identify the effectiveness of intratympanic (IT) steroids when used as an initial therapy in sudden sensorineural hearing loss (SSNHL), and when it is used as a salvage therapy in a refractory SSNHL. **Subjects and Methods:** This retrospective study included 122 patients with SSNHL. First, patients were divided into three groups according to the initial treatment; IT steroid, systemic steroid and combined (systemic and IT steroid) groups. Second, patients were divided into two groups according to the salvage treatment in a refractory SSNHL; IT steroid and the control (non IT group). Fifty eight patients who did not respond to initial therapy were included in the second analysis. Hearing was assessed immediately before the treatment and 2 weeks, 4 weeks and 3 months after the treatments. Hearing recovery was defined as an improvement of >15 dB and the final hearing of 25–45 dB in the audiogram. **Results:** When we analyzed the hearing recovery in initial treatment, the comparison of audiogram among three groups did not result in significantly different outcomes. There were no differences in the recovery rate in 2 and 4 weeks throughout all the frequencies. Also, the analysis of the salvage treatment demonstrated that neither IT steroid group nor control group was significantly effective in treating the refractory SSNHL. **Conclusions:** The results suggest that initial treatment of SSNHL with IT steroid alone is as effective as systemic steroid alone or a combination therapy. Also, salvage IT steroids for refractory SSNHL did not have any additional beneficial effects.

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KEY WORDS: Sensorineural hearing loss · Intratympanic steroids · Hearing outcome.

Introduction

Sudden sensorineural hearing loss (SSNHL) is defined as a hearing loss of greater than 30 dB in at least 3 consecutive frequencies, occurring within 3 days and has a reported incidence of 5 to 20 per 100000 patients every year [1]. There has been a great deal of controversy regarding the possible therapeutic approaches of SSNHL and different treatment modalities

have been tried with no standard protocol universally accepted. At this time, systemic steroids are the only agents with proven effectiveness [2]. The recovery rate in untreated patients (within 3 weeks of onset) ranges from 32 to 65% in various studies; with systemic steroid therapy, the recovery rate increases to 49 to 89% [3].

Nevertheless, the systemic administration of steroids is associated with side effects and is contraindicated in certain pathological situations [4]. To address this problem, intratympanic (IT) steroid delivery treatment has gained its popularity for patients who do not respond to standard systemic therapy. IT delivery reduces systemic toxicity and offers significantly high drug levels to the inner ear. Pharmacokinetic animal ex-

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periments have demonstrated that much higher perilymphatic steroid concentrations are achieved with IT applications compared to oral or intravenous administrations [5-7].

IT steroids were first used as salvage therapy in refractory SSNHL. Refractory SSNHL is defined as patients who fail to respond to initial systemic steroid treatment [8,9]. Their promising results have made some clinicians promote their use as first-line therapeutic option in patients with contraindication to systemic steroids [10]. Moreover, IT steroid administration has been applied as an adjunctive treatment given concomitantly with systemic steroids. However, the efficacy of steroids in various administration methods remains controversial, and there is no settled definite protocols for IT steroids [11,12]. The aim of this study is to identify the hearing recovery results of IT steroids in the treatment of first occurred SSNHL and refractory SSNHL.

Subjects and Methods

The records and hearing test results of patients with SSNHL who visited the Department of Otorhinolaryngology in Kangnam Sacred Heart Hospital between January 2012 and April 2014 were analyzed retrospectively. Inclusion criteria for the initial treatment were the following: SSNHL of at least 30 dB or more at three or more consecutive frequencies, unilateral hearing loss, no history of previous treatment at another clinics, no identified etiologic factors to explain the hearing loss, no history of previous otologic diseases in the affected ear, start for first-line therapy within 30 days after the onset of hearing loss, the ability to complete the treatment protocol of our clinic and patients who were able to attend the clinic for at least a month. Also, the inclusion criteria for the salvage treatment were same as above, but few more things were added; no response or less than 15 dB improvement in pure tone audiometry (PTA) within 28 days of initial steroid therapy, and the patients who could attend the clinic for at least 3 months.

A total of 122 patients with SSNHL who met the inclusion criteria for initial therapy were selected to participate in the study. First, patients were divided into three groups; IT steroid only, systemic steroid only and combination (systemic and IT steroid) groups. IT steroid (dexamethasone, 5 mg/mL) were injected twice a week for 2 weeks [8]. Initial systemic steroids consisted of administration of dexamethasone (10 mg) intravenously for 5 days and followed by oral methylprednisolone (40 mg) tapering for 5 days. The combination treatment composed of both IT dexamethasone and administration of intravenous dexamethasone as same as other two groups. IT group consisted of 12 patients, the systemic ste-

roids group consisted of 26 patients and combined group 84 patients.

Also, a total of 58 patients were who met the inclusion criteria were selected to participate in the analysis of the effect of the salvage treatment in a refractory SSNHL. Patients were divided into two groups; IT steroid group and the control (non IT group). IT steroid (dexamethasone, 5 mg/mL) were injected twice a week for 2 weeks. IT group consisted of 14 patients, and control group 44 patients.

Auditory function was determined by PTA, and mean hearing levels were expressed as the average of hearing thresholds at 500, 1000, 2000, 4000 Hz. To analyze the initial effect of steroids, PTA examinations before the treatment and 14 days, 28 days after the treatment were collected. For the assessment of salvage effect of IT steroids, the PTA on day 28 after start of initial steroid therapy was accepted as the initial audiometric value, and the PTA evaluated at two month after that salvage therapy was used as the final audiometric value.

According to Siegel [13] criteria for hearing improvement, "good recovery" was defined as more than 15 dB gain and final hearing better than 45 dB, and "poor recovery" was defined as less than 15 dB gain and final hearing poorer than 45 dB.

Statistical analysis

All values are expressed as mean \pm SD, and significant differences between groups were determined using Fisher's exact test for categorical variables. For continuous variables, one-way ANOVA was done to identify the differences in three groups and Kruskal-Wallis test was conducted to compare between each two groups. $p < 0.05$ was defined as the cutoff for statistical significance.

Results

Initial steroid treatment for SSNHL

The mean age of the 122 patients included in the study of initial treatment was 52.48 ± 12.85 years (range 11–85 years). Of the participants, 44.3% (n=54) were men and 55.7% (n=68) were women. Twelve patients received only IT steroids, 26 patients received systemic steroids, and 84 patients received both IT and systemic steroids for the initial treatment. The descriptive characteristics of the three groups are given in Table 1. The three groups did not differ significantly except for the interval from onset of symptoms to initiation of therapy. The intervals were 15.83, 9.27, and 7.20 days, respectively, which were statistically significantly different between the groups ($p=0.004$).

The initial mean PTA values were 47.50 ± 12.65 dB, $61.65 \pm$

Table 1. Characteristics of three groups in initial treatment

	Initial IT dexta	Initial systemic	Initial combined	p value
Number	12	26	84	
Age (mean±SD)	57.33±17.08	49.96±12.85	52.57±12.11	0.259
Gender, n (%)				0.250
Male	7 (58.3)	14 (53.8)	33 (39.3)	
Female	5 (41.7)	12 (46.25)	51 (60.7)	
Ear, n (%)				0.737
Right	7 (58.3)	10 (38.5)	41 (48.8)	
Left	5 (41.7)	16 (61.5)	43 (51.2)	
Occurred days (mean±SD)	15.83±11.53	9.27±8.87	7.20±7.705	0.004
Initial PTA (mean±SD)	47.50±12.65	61.65±28.22	62.84±26.94	0.17

PTA: pure tone audiometry, IT: intratympanic

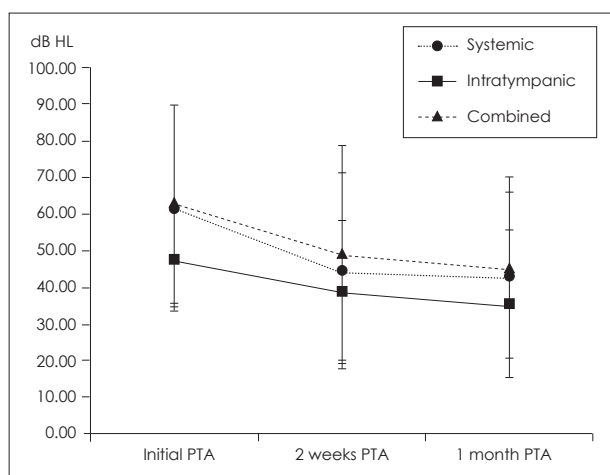


Fig. 1. Hearing thresholds of three groups in initial treatment. The PTA values of patients who received intratympanic steroids were 47.50±12.65 dB at first, 39.17±19.09 dB in 2 weeks, and 35.56±20.18 dB in 4 weeks. The PTA values of patients who received systemic steroids were 61.65±28.22 dB at first, 44.68±26.66 dB in 2 weeks and 43.18±22.66 dB in 4 weeks. The PTA values of combination group were 62.84±26.94 at first, 49.12±29.62 dB in 2 weeks, and 45.51±24.66 dB in 4 weeks. The PTA values of each group at same time spot were not different significantly ($p>0.05$). PTA: pure tone audiometry.

28.22 dB, and 62.84±26.94 dB, in the IT, systemic and combined group respectively, and did not differ significantly ($p>0.05$) (Table 1, Fig. 1). The PTA of patients who received IT steroids improved by 10.78±16.33 dB, and final PTA after a month was 35.56±20.18 dB. The PTA of patients who received systemic therapy only improved by 18.23±17.47 dB, and final PTA after a month was 43.18±22.66 dB. And the PTA of patients who received both IT and systemic steroids improved by 16.88±22.15 dB, and final PTA was 45.51±24.66 dB. The degree of hearing recovery and the final PTA were not different significantly among three groups (Fig. 1, 2). Also, hearing recovery rate among three groups did not differ significantly (Table 2).

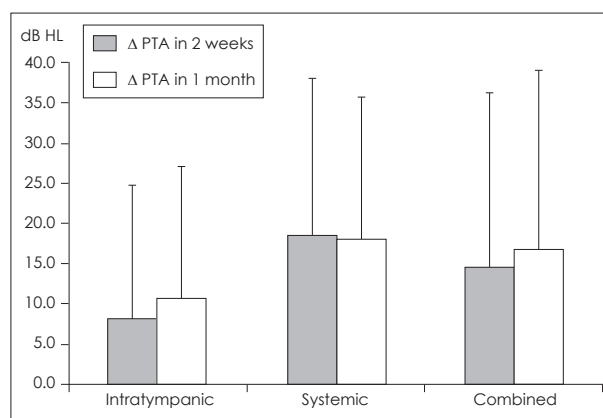


Fig. 2. Hearing gains of three groups in initial treatment. The PTA of patients who received IT steroids improved by 8.33±16.43 dB in 2 weeks and 10.78±16.33 dB in a month. Patients who received systemic therapy improved by 18.69±19.36 in 2 weeks and 18.23±17.47 dB in a month. Finally, patients who received combined therapy improved by 14.73±21.48 dB in 2 weeks and 16.88±22.15 dB in a month. The degree of hearing recovery and the final PTA were not different significantly ($p>0.05$). PTA: pure tone audiometry, IT: intratympanic.

Salvage IT steroid treatment for refractory ISSNHL

The mean age of the 58 patients included in the study of salvage treatment was 54.29±11.90 years (range 21–81 years). Of the participants, 46.6% (n=27) were men and 53.4% (n=31) were women. Fourteen patients received salvage intratympanic steroids, and 44 patients did not receive salvage treatment (control). The descriptive characteristics of two groups are given in Table 3. The initial hearing level and the hearing level after a month of initial treatment did not differ significantly in two groups. The audiogram at three month which was the final hearing level after the salvage therapy was 60.44±17.68 dB in control group, 59.50±16.39 dB in IT group and was not different significantly in both groups (Fig. 3). Also, hearing recovery rate in IT group was 35.7% and 20.5% in control group but did not differ significantly (Table 4).

Table 2. Recovery rate of SSNHL with different initial treatments

	Initial IT dexa (n=12)	Initial systemic (n=26)	Initial combined (n=84)	p value
Recovery rate				0.476
Good recovery (n, %)	7 (58.3)	14 (53.8)	42 (50.0)	
Poor recovery (n, %)	5 (41.7)	12 (46.2)	42 (50.0)	

SSNHL: sudden sensorineural hearing loss, IT: intratympanic

Table 3. Characteristics of two groups in salvage treatment

	IT steroid	Control	p value
Numbers	14	44	
Age (mean±SD)	55.36±8.76	53.95±12.81	0.647
Gender, n (%)			0.063
Male	10 (71.43)	17 (38.64)	
Female	4 (28.57)	27 (61.36)	
Ear, n (%)			0.543
Right	5 (35.71)	21 (47.73)	
Left	9 (64.29)	23 (52.27)	
Initial PTA (mean±SD)	76.64±28.56	71.34±25.15	0.541
1 month PTA (mean±SD)	59.57±17.43	62.07±17.43	0.646

PTA: pure tone audiometry, IT: intratympanic

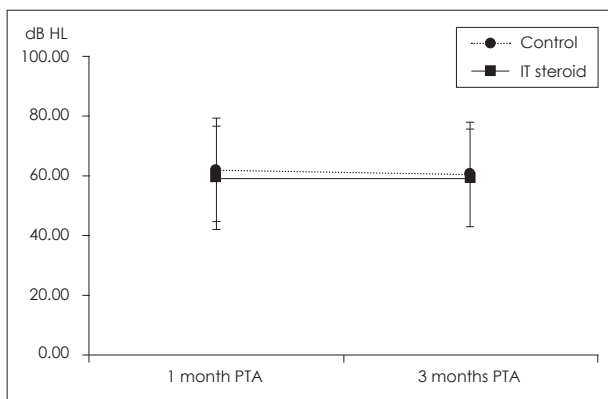


Fig. 3. Hearing thresholds of two groups in salvage treatment. The PTA values of patients who received IT steroids were 59.57 ± 17.31 dB at 1 month (beginning of the salvage treatment), and 59.50 ± 16.39 dB at 3 months. The PTA values of control group were 62.07 ± 17.43 dB at 1 month and 60.44 ± 17.68 dB at 3 months. The final hearing level after the salvage treatment was not different significantly in both groups ($p>0.05$). PTA: pure tone audiometry, IT: intratympanic.

Discussion

There is a continuous controversy regarding the efficacy of IT steroid therapy in ISSNHL. IT steroids are reported to have effect on refractory ISSNHL [8,9,14], and additional IT steroids with systemic therapy also are known to provide effectiveness [11,12,15]. However, their reported potency is variable probably due to the different types of steroids used, concentrations, frequencies, injection intervals, and so on.

Ahn, et al. [12] used 5 mg dexamethasone for IT procedure with systemic 48 mg methylprednisolone for initial

Table 4. Recovery rate of ISSNHL with two groups with salvage treatment

	Salvage IT steroids (n=14)	Control (n=44)	p value
Recovery rate			0.208
Good recovery (n, %)	5 (35.7)	9 (20.5)	
Poor recovery (n, %)	9 (64.3)	35 (79.5)	

SSNHL: sudden sensorineural hearing loss

combination therapy and reported that combination therapy didn't have additional benefits compared with systemic steroids alone but increased hearing recovery in a lower frequency (250 Hz). Choi, et al. [16] conducted the investigation with frequent IT dexamethasone administration (0.3 mL of 5 mg/mL dexamethasone, 5 times per day through the ventilation tube for 5 consecutive days) in addition to intravenous administration of dexamethasone for initial combination therapy and reported that combination therapy didn't have additional benefits compared with systemic steroids. However, Koltsidopoulos, et al. [15] carried out the investigation with 4 mg IT dexamethasone with systemic intravenous prednisolone and identified that the combination therapy was effective in mild to severe SSNHL than systemic steroids alone. Our study was conducted with 5 mg IT dexamethasone with intravenous prednisolone, but combination therapy didn't have beneficial effect over systemic steroids. The hearing outcomes achieved by three different protocols that is IT dexamethasone alone, systemic therapy and combination therapy, were not different after 1 month of treatment. However, IT dexamethasone alone had same therapeutic potency with other protocols.

Filipo, et al. [17] proposed that IT treatment as a sole initial treatment. A systematic review assumed that IT steroids can be an important solution for patients with SSNHL who cannot tolerate systemic steroid therapy, such as patients with diabetes [18]. IT steroids are usually administered as either dexamethasone or solumedrol, with wide range of concentrations; most studies on IT corticosteroids refer to dexamethasone 10 to 24 mg/mL and higher [5]. Although our study was conducted with 5 mg/mL of dexamethasone, timely injection of steroid had therapeutic effect.

According to the clinical guideline of sudden hearing loss,

salvage therapy with IT steroid is recommended [8]. Yang, et al. [9] also observed that 5 mg IT dexamethasone induced larger hearing gain (especially at lower frequencies), good recovery rate, and better word recognition score than the control in the treatment of refractory ISSNHL. But in the current study, IT steroid was not effective in the management of refractory SSNHL. IT dexamethasone (5 mg/mL) was administered within 28 days of start of initial therapy and injected at the anterior superior part of tympanic membrane with a 23 gauge needle, twice a week for 2 week. However, the hearing recovery was not significantly different from the control. Considering the injection protocols were similar to that of initial treatment, the onset of salvage treatment initiation is assumed to be as important as the concentration of the agent.

Our study has some limitations. Because the data were analyzed retrospectively, the subjects could not be randomized to reduce selection bias. In addition, the numbers of patients in each group are not even or large enough to obtain statistically significant differences between the groups. A randomized prospective study with a larger sample is needed to more thoroughly analyze the efficacies IT steroid therapy in the treatment of SSNHL.

Conclusion

The results of this study suggest that initial treatment of ISSNHL with IT dexamethasone (5 mg/mL) alone is as effective as systemic steroid or a combination therapy. Also, salvage IT steroids treatment did not have any additional beneficial effects.

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