DEXAMETHASONE INJECTION INTRATYMPANIC FOR REFRACTORY SUDDEN SENSORINEURAL HEARING LOSS

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Abstract. *The purpose of this case-control study was to examine the impact of intratympanic dexamethasone injection (ITDI) as a therapeutic alternative for individuals with SSNHL who did not respond to traditional oral steroid therapy. This study comprised sixty-six SSNHL patients who had not responded to an oral steroid treatment regimen. Pure-tone average (PTA) improvement was defined as more than 10 dB. Two (6.1%) of the 33 patients in the control group and 13 (39.4%) of the 33 patients who received ITDI showed improvements in their hearing. Eleven out of twenty patients who did not exhibit any improvement in PTA by ITDI demonstrated improvement over 10 dB in certain frequencies, whereas five out of thirteen patients represented hearing improvement above 20 dB in PTA. There were no definite prognostic factors between the patients who responded to ITDI and those who did not.*

Key words: *dexamethasone, sudden sensorineural HL, tympanum, injection.*

Introduction. Sudden sensorineural hearing loss (SSNHL), typically described as an acute, one-time decline in hearing accompanied by tinnitus and vertigo, occurs in 5-20 individuals per 100,000 population according to research. The etiology of SSNHL remains idiopathic, but potential causes include viral infections, vascular disorders, cochlear membrane rupture, immunological diseases, and otological tumors. Treatment for SSNHL includes steroids, vasodilators, antiviral agents, diuretics, and low-salt diets. The spontaneous recovery rate without treatment ranges from 30% to 60%, with most cases recovering within 2 weeks after onset. It is also known that this recovery rate increases with several treatment methods, including steroids. High-dose systemic steroid therapy is currently the primary treatment for SSNHL due to its strong anti-inflammatory effects, particularly in cases of moderate and severe hearing loss. Despite the use of oral steroids for 2 weeks, either alone or in combination with other medications, the prognosis for patients with refractory hearing loss remains poor. Around 30%-50% of patients show no response to treatment. For these patients, high-dose steroid therapy over a prolonged period may sometimes be applied, but it is not easily used due to side effects such as facial flushing, edema, rash, nasal bleeding, digestive disorders, liver dysfunction, and glucose intolerance. Additionally, no alternative treatments have been reported to date. Intratympanic steroid injection involves administering steroids through the tympanic membrane, which reduces the systemic toxicity of steroids and increases the steroid concentration in the cochlear perilymph. Pärns et al. reported a recovery rate of 53% in 13 patients with SSNHL, and there are other reports showing a 38%-72% success rate with intratympanic steroid injections. However, in most of these reports, intratympanic steroid injection was used as first-line therapy for SSNHL, not as second-line therapy for refractory SSNHL. The aim of this study is to evaluate the effectiveness of intratympanic steroid injections in patients with SSNHL who poorly responded to systemic steroid treatment.

Materials and methods. A controlled study was conducted from March 2021 to January 2025, including 66 patients with idiopathic SSNHL who did not show a successful response to combined treatment, including oral steroids. We collected data on the dexamethasone intratympanic injection (ITDI) group from August 2021 to January 2025. During this period, we treated 33 patients (34 ears) with ITDI. All patients underwent medical history, physical and audiological examination, serology for syphilis, autoimmune antibody tests, and magnetic resonance imaging. We excluded patients with

SSNHL potentially caused by trauma, syphilis, Meniere's disease, tumors, or autoimmune diseases. For all 66 participants, standard treatment was provided, including oral steroid administration for 10 days, rest, smoking cessation, a low-salt diet, and other medications. The oral steroid prednisone was used for 10 days according to the following scheme: 60 mg per day for 5 days, 40 mg per day for 2 days, 20 mg per day for 2 days, and 10 mg per day for 1 day. Intravenous antiviral agent acyclovir and hydrochlorothiazide were sometimes used in combination with the oral steroid. ITDI injections were performed 4 weeks after the initial conservative treatment. After confirming the integrity of the tympanic membrane, local anesthesia was applied using 10% lidocaine spray. The procedure was performed with the patient in a supine position under a microscope. A 25-gauge spinal needle and 1 mL syringe were used to make one puncture at the upper anterior part for ventilation and another puncture at the middle anterior part for perfusion. Dexamethasone was administered through this site in a volume of 0.3-0.4 mL. The patient was instructed to avoid swallowing or movement while lying with the head tilted at a 45˚ angle towards the healthy ear for 40 minutes. ITDI injections were performed twice a week for 2 consecutive weeks. Pure-tone audiometry was conducted immediately before each injection and 1 week after the last injection. Speech discrimination testing (SDT) was also performed 1 week after the last injection. In the control group, pure-tone audiometry was performed at 4 and 8 weeks after the initial conservative treatment, and speech discrimination testing was also performed at that time. However, some patients did not undergo SDT at 8 weeks, and they were excluded from this analysis.Hearing improvement was defined as a decrease in the average pure-tone audiometric threshold at 4 frequencies (0.5, 1, 2, and 3 kHz) by 10 dB or an increase in the speech discrimination score (SDS) by 15% or more. Additionally, the difference in thresholds at each frequency on pure-tone audiometry was analyzed. Side effects and subjective symptoms were also analyzed. Statistical analysis was performed using independent t-tests, paired t-tests, and chi-square tests. Statistical significance was determined at a confidence level of $P < 0.05$.

Results. The average age of patients in the ITDI group was 39.4 years, while in the control group, it was 42.8 years. The male-to-female ratio in the ITDI group was 13:20, and in the control group, it was 14:19. The average time from the onset of the disease to the start of treatment in the ITDI group was 5.2 days, and in the control group, it was 6.5 days. The baseline hearing level in the ITDI group was 72.0 ± 23.4 dB PTA, while in the control group, it was 76.5 ± 28.7 dB. There were no statistically significant differences between the two groups in terms of age ($P = 0.096$), sex ratio ($P = 0.977$), time from disease onset to treatment ($P = 0.831$), and baseline hearing level ($P = 0.221$) (Table I).

Table I.

Comparison of the Characteristics between the Group Receiving Intratympanic Dexamethasone Injection (ITDI) and the Control Group

Variable	Itdi group* (n = 33; 34 ears)	Control group (n = 33)	P value
Age (years)	39.3	42.8	.096
Sex (male: female)	13:20	14:19	.977
Duration from onset to initial treatment (days)	5.2	6.5	.831
Pure-tone average (db)	72.0 ± 23.4	76.5 ± 28.7	.221

** Patients who were treated with a course of ITDI therapy. χ^2 test and independent t-test.*

Objective Hearing Improvement. When comparing clinical outcomes between the two groups, improvement of 10 dB or more in PTA was observed in 13 (38.2%) of the 34 ears in the ITDI group, while no improvement was noted in the remaining 21 ears. In the control group, hearing improvement was recorded in only two ears (6.1%), while no changes in hearing thresholds were observed in 29 ears (87.8%), and two ears (6.1%) showed worsening.

In the ITDI group, the average PTA before and after ITDI treatment was 72.0 ± 23.4 dB and 62.9 ± 22.5 dB, respectively, resulting in an improvement of 9.1 dB in average PTA, which was statistically significant (P = 0.001). In the control group, the average PTA at 4 and 8 weeks after treatment was 76.5 ± 28.7 dB and 74.1 ± 25.7 dB, respectively, resulting in an improvement of 2.4 dB. This difference was not statistically significant.

In the ITDI group, five ears showed hearing improvement of more than 20 dB, eight ears showed improvement of 10-20 dB, and eleven ears showed improvement of more than 10 dB at certain frequencies without a significant change in PTA.

Table II shows hearing improvement in patients treated with ITDI, depending on their response to initial treatment, including oral steroids. No statistically significant differences (P = 0.127) were found between seven patients (43.8%) who showed a partial response and six patients (33.3%) who showed no response. Additionally, Table III shows hearing improvement in ITDI-treated patients based on PTA prior to ITDI treatment.

When analyzing hearing improvement by frequency in the ITDI group (34 ears), improvement of 10 dB or more was observed at low frequencies (0.25, 0.5, and 1 kHz) in 17 ears (50.0%), at mid frequencies (2, 3 kHz) in 12 ears (35.3%), and at high frequencies (4, 6, and 8 kHz) in 13 ears (38.2%). These results showed that hearing improvement most commonly occurred at low frequencies.

In the ITDI group, the number of patients showing improvement in hearing after each injection was as follows: 12 ears (35.3%) after the first injection, 5 ears (14.7%) after the second injection, 4 ears (11.8%) after the third injection, and 7 ears (20.6%) after the fourth injection. The average number of injections needed for hearing improvement was 2.2.

Subjective Hearing Improvement. Among 20 patients in the ITDI group who did not show hearing changes after ITDI, three patients experienced subjective hearing improvement, and 10 patients reported a reduction in tinnitus. Additionally, three patients reported that the sound became clearer. In the control group, only three of the 31 patients who showed no hearing improvement reported a reduction in tinnitus.

Factors Affecting Hearing Improvement in the Intratympanic Dexamethasone Injection Group. We analyzed several prognostic factors between 13 patients (positive response group) who experienced hearing improvement after ITDI and 20 patients (non-response group) who showed no improvement. The average age in the positive response group was 41.5 years, while in the non-response group, it was 37.7 years. The male-to-female ratio in the positive response group was 2:10 and in the non-response group, it was 10:11. The period from the onset of hearing loss to the start of initial treatment was 6.5 days in the positive response group and 4.7 days in the non-response group. The period from disease onset to the start of dexamethasone injections was 31.8 days in the positive response group and 35.1 days in the non-response group. No statistically significant differences were found.

Discussion. Sudden sensorineural hearing loss (SSNHL) is typically characterized by a rapid onset of hearing loss, usually within 3 days, with a hearing loss greater than 30 dB at three consecutive frequencies. The etiology of SSNHL remains undetermined in otolaryngology, although various causes have been proposed, such as vascular lesions, membrane ruptures, and viral infections. Therefore, treatment for SSNHL may aim to eliminate these etiological factors or create conditions in the middle ear that promote hearing restoration.

Table II.

Hearing Improvement in Patients Treated with Intratympanic Dexamethasone Injection (ITDI) According to the Response to Initial Treatment Including Oral Steroids

Initial response	>20 db hearing gain	10–20 db hearing gain	No gain
Partial response* (n = 16)	1 (6.3%)	6 (37.5%)	9 (56.3%)
No response (n = 18)	4 (22.2%)	2 (11.1%)	12 (66.7%)

** Patients who showed hearing improvement of 10 dB or more at initial treatment, including oral steroids, and were subsequently treated with a course of ITDI therapy.*

Steroid therapy has long been considered the primary treatment for SSNHL.

Table III.

Hearing Improvement in Patients Treated with Intratympanic Dexamethasone Injection (ITDI) According to Pure-Tone Averages Before ITDI

Pta range before itdi (db)	>20 db hearing gain	10–20 db hearing gain	No gain
26–40 (N = 2)	2	–	–
41–55 (N = 10)	2	1	7
56–70 (N = 3)	3	–	–
71–90 (N = 11)	1	6	4
91–110 (N = 8)	2	1	5

On the other hand, 10 patients showed hearing improvement of more than 10 dB at certain frequencies among the 20 patients whose average pure-tone threshold (PTA) values did not improve. These 20 patients reported changes in subjective symptoms, such as improved hearing, reduced tinnitus, or clearer sound perception. These subjective symptoms may be associated with hearing improvement at specific frequencies, despite the lack of improvement in overall PTA. In conclusion, the ITDI group demonstrated significantly greater hearing improvement (9.1 dB) compared to the control group (2.4 dB), as well as a greater improvement in subjective symptoms. This effect is most likely due to ITDI rather than the natural course of the disease.

Since steroids administered through the tympanic membrane penetrate the perilymph of the cochlea via the round window, the steroid may have a greater effect on the basal turn than the apical turn. Therefore, we expected hearing improvement to be more pronounced at high frequencies (basal turn) than at low frequencies (apical turn). However, in this study, 50% of hearing improvements (average 11.0 dB) occurred at low frequencies, whereas 34%–38% of improvements (average 5.2–7.5 dB) occurred at mid and high frequencies. These results suggest that ITDI may be more effective in patients with low-frequency hearing loss. It is hypothesized that once a certain concentration of steroid is achieved in the cochlea, hearing recovery may occur more easily at low frequencies than at high frequencies. This phenomenon may be explained by differences in the damage threshold or reversibility of hair cell recovery depending on their location. Some support for this hypothesis can be found in the fact that hearing loss caused by noise, ototoxic drugs, or trauma more frequently affects the high-frequency (basal) region of the cochlea than the apical region.

ITDI is a procedure performed under microscopic visualization with local anesthesia, requiring the patient to remain in a specific position for 40 minutes. It demands space and additional time for the procedure. Therefore, determining the optimal number of injections and the interval between them is essential, although such data have not yet been published. We also evaluated hearing changes by performing pure-tone audiometry immediately before each injection. In the ITDI group, the number of ears showing hearing improvement was as follows: 12 ears (35.3%) after the first injection, 5 ears

(14.7%) after the second injection, 4 ears (11.8%) after the third injection, and 7 ears (20.6%) after the fourth injection. Based on these results, we cannot definitively determine the optimal number of injections, but we believe that at least four may be required.

Known disadvantages of intratympanic steroid injections include temporary dizziness, tympanic membrane perforation, and otitis media caused by stimulation of the middle ear mucosa. In this study, only three patients experienced temporary dizziness, which appeared to result from the caloric effect of the medication and may be preventable by warming the dexamethasone solution.

Conclusion. ITDI may be a simple and effective treatment method for patients with SSNHL who do not respond to initial treatment, including systemic steroid therapy.

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