

Intratympanic injection of dexamethasone for treatment of tinnitus in patients with sudden sensorineural hearing loss

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Abstract

The purpose of this study is to test the effectiveness of intratympanic dexamethasone injections as a treatment for severe tinnitus in idiopathic sudden sensorineural hearing loss (SNHL). We studied 37 patients who received intratympanic dexamethasone injections and 14 control patients who did not receive it, with severe tinnitus after onset of unilateral sudden SNHL. Hearing level did not change during this study in any patient. The relationship between the duration of tinnitus and effectiveness of treatment was investigated in sudden SNHL. We used a visual analogue scale to evaluate 51 patients with severe tinnitus at the stage of stable hearing level after idiopathic sudden sensorineural hearing loss. Forty-one per cent of patients showed significant improvement after treatment. The average period between onset of sudden sensorineural hearing loss and initiation of intratympanic dexamethasone injection was significantly shorter (207 days) in the improved group than in the unchanged group (482 days) ($P < 0.001$). In control group, one of 14 patients presented significant improvement spontaneously. Intratympanic dexamethasone treatment may be effective in treatment of severe tinnitus after sudden SNHL at the stage of stable hearing level, and the shorter the period from onset of sudden deafness to the start of intratympanic dexamethasone treatment, the greater the improvement in tinnitus that can be expected.

Introduction

Systemic steroids are known to improve hearing levels in sudden sensorineural hearing loss (SNHL), Menière's disease and many other inner ear diseases. Higher steroid concentrations could be achieved in the inner ear and the systemic side effects could be avoided by using intratympanic injection. Recent clinical studies have demonstrated that gadolinium can readily diffuse through the round window membrane.^{1,2} In 1996 Sakata *et al.* treated patients with chronic otitis media (COM), labyrinthine syphilis, Menière's disease, vertigo, sudden SNHL, streptomycin intoxication, acoustic trauma, head injury, or other otological diseases by infusing a dexamethasone solution into their middle ear.³ In 2005 Araújo *et al.* in a randomized single-blind study showed no difference between intratympanic injection of dexamethasone and saline in patients with severe, disabling tinnitus.⁴ In that study, patients with COM, acoustic trauma, otosclerosis and Menière's disease were enrolled in addition to those with sudden SNHL. Although these previous studies treated a range of otological diseases with intratympanic dexamethasone, all were evaluated as a single group, and this is the first study of such treatment in a single disease, severe tinnitus after sudden SNHL.

Materials and Methods

Subjects

One ear of each of 37 patients was treated with intratympanic dexamethasone. All patients had severe tinnitus after onset of sudden SNHL. The hearing level of all patients was stable during this study. The average hearing level was expressed as the average score at three frequencies (500, 1000, and 2000 Hz). If the patients did not respond to the maximum level of sound generated by the audiometer, 5dB was added to the maximum level. The outcome of sudden SNHL was evalu-

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Table 1. Comparison of the study and control groups. Age, sex and hearing levels were not significantly different between the two groups; age, hearing levels and Improvement of VAS by t-test and sex by 2 test, respectively.

| | Study | Control | P |
|--------------------|-------|---------|-------|
| Age | 54.9 | 54.3 | 0.89 |
| Sex | | | |
| Male | 16 | 6 | 0.32 |
| Female | 21 | 8 | |
| Hearing level (dB) | 64.2 | 71.1 | 0.42 |
| Improvement of VAS | 1.54 | 0.57 | 0.068 |

Hearing level, stable hearing level after onset of sudden sensorineural hearing loss; Improvement of VAS, Average improvement of visual analog scale (severity of tinnitus).

ated using the criteria of the Ministry of Health, Labor and Welfare in Japan.⁵ The average hearing level on these criteria was calculated as the mean of the hearing levels measured at 250, 500, 1000, 2000, and 4000 Hz. Recovery was ranked as follows:⁶ no change (improvement in hearing of less than 10 dB on average); slight improvement (improvement in hearing of 10 dB or more but less than 30 dB on average); remarkable improvement (improvement in hearing of 30 dB or more on average); and complete recovery (all 5 frequencies on the final audiogram were 20 dB or less or improvement to the same degree of hearing as in the contralateral ear). In our study, all the patients have no change or slight improvement with regard to hearing improvement after onset of sudden SNHL. As a control, 14 patients had severe tinnitus at the stage of stable hearing level. They did not receive intratym-

panic dexamethasone injection. Table 1 gives the comparison of the study and control groups.

The patients filled a specific tinnitus questionnaire, based on the proposals of a tinnitus research conference in Japan, that asked about tinnitus duration, affected ear (left, right, or both), subjective hearing loss, description of the sound heard (rain, waterfall, whistle, pulsating noise, click, or other), and previous treatments.⁷ The patients were then asked to indicate the severity of tinnitus on a visual analogue scale (VAS) graded from 0-10 (0 was none and 10 was an intolerable level of severity) based on that used in a previous report.⁴ We defined severe tinnitus as patients had to stop daily chores by the symptom. The protocol of the study was approved by the Ethics Review Committee of Nagoya University School of Medicine (approval numbers 369, 369-

Table 2. Patient characteristics of the study group.

| Patient No. | Sex | Age | Side of symptom | VAS score | | Period to injection (day) | Hearing level (dB) | |
|-------------|-----|-----|-----------------|--------------|---------------|---------------------------|--------------------|-----|
| | | | | Pretreatment | Posttreatment | | | |
| 1 | F | 67 | R | 6 | 4 | * | 44 | 68 |
| 2 | F | 77 | L | 7 | 2 | * | 1403 | 53 |
| 3 | F | 73 | L | 8 | 5 | * | 147 | 57 |
| 4 | M | 36 | R | 8 | 6 | * | 71 | 70 |
| 5 | F | 61 | R | 10 | 10 | | 449 | 75 |
| 6 | M | 46 | R | 8 | 8 | | 456 | 98 |
| 7 | M | 18 | L | 5 | 5 | | 46 | 67 |
| 8 | M | 28 | R | 7 | 7 | | 49 | 68 |
| 9 | F | 62 | R | 5 | 5 | | 870 | 113 |
| 10 | M | 47 | R | 8 | 5 | * | 28 | 22 |
| 11 | M | 58 | L | 3 | 1 | * | 21 | 113 |
| 12 | F | 58 | L | 6 | 6 | | 83 | 35 |
| 13 | F | 69 | L | 8 | 8 | | 2490 | 43 |
| 14 | F | 62 | L | 5 | 5 | | 435 | 58 |
| 15 | M | 52 | R | 6 | 5 | | 23 | 55 |
| 16 | F | 74 | R | 6 | 5 | | 243 | 100 |
| 17 | F | 70 | L | 4 | 4 | | 973 | 58 |
| 18 | M | 64 | R | 6 | 5 | | 1948 | 107 |
| 19 | M | 76 | L | 9 | 2 | * | 153 | 25 |
| 20 | F | 51 | R | 5 | 5 | | 424 | 70 |
| 21 | F | 41 | R | 4 | 1 | * | 39 | 50 |
| 22 | F | 56 | L | 6 | 6 | | 1473 | 19 |
| 23 | M | 53 | L | 9 | 3 | * | 34 | 45 |
| 24 | M | 68 | R | 6 | 3 | * | 23 | 113 |
| 25 | M | 63 | R | 7 | 4 | * | 600 | 80 |
| 26 | M | 28 | R | 3 | 2 | | 33 | 82 |
| 27 | F | 84 | L | 8 | 4 | * | 171 | 90 |
| 28 | M | 19 | L | 5 | 5 | | 47 | 32 |
| 29 | F | 44 | L | 7 | 3 | * | 45 | 37 |
| 30 | F | 67 | L | 8 | 8 | | 59 | 42 |
| 31 | F | 69 | R | 7 | 7 | | 67 | 60 |
| 32 | F | 53 | L | 6 | 6 | | 112 | 8 |
| 33 | M | 37 | R | 7 | 7 | | 49 | 112 |
| 34 | F | 44 | R | 8 | 6 | * | 275 | 45 |
| 35 | F | 56 | L | 4 | 3 | | 257 | 15 |
| 36 | F | 46 | L | 7 | 4 | * | 46 | 77 |
| 37 | M | 56 | R | 5 | 5 | | 22 | 113 |

VAS, visual analog scale; Period to injection, period from onset of tinnitus to intratympanic steroid injection; Hearing Level, average hearing level was expressed as the average score at three frequencies (500, 1000, and 2000 Hz). *Improvement was significant (defined as a decrease of at least two graduations on the VAS).

2). All patients gave their informed consent to participate in this study.

The patients were placed in a supine position on the table with their heads turned about 30 degrees away from the surgeon. Using a 1 mL syringe and a 23-gauge needle, 0.4-0.6 ml dexamethasone (4 mg/mL) was injected into the anteroinferior quadrant of the tympanic membrane under direct visualisation through an operating microscope. The solution was warmed to body temperature before injection to avoid vertigo. Each patient remained in the described position for about 30 min after injection. Intratympanic injections were performed once a week for three weeks. Before commencing treatment and one week after finishing treatment the patients answered a questionnaire about the status of their tinnitus (worse, unchanged, slightly improved, greatly improved, and in remission). They also indicated on the VAS the intensity of tinnitus following treatment. The period between the onset of sudden SNHL and first VAS evaluation was not significantly different between the treated and untreated groups of patients. Based on a previous report,⁴ we judged that improvement was significant when a decrease of at least two graduations on the VAS was reported by the patient. Patients with such improvement were classified as the *improved group* and the remaining patients as the *unchanged group*. All statistical analyses were performed using the t-test and χ^2 test with level of significance set at $P < 0.05$.

Results

Table 2 gives the age, sex, side of the affected ear, VAS score and the time between the onset of sudden SNHL and the first intratympanic dexamethasone injection for the 37 patients. Tinnitus severity before treatment as measured by the VAS score ranged between 3 and 10 with an average of 6.4. It scored between 5 and 7 for 57% of patients and above 7 for 30% of patients in the study group. Fifteen of the 37 patients showed significant improvement with treatment. There was no correlation between the age of the patients and impact of treatment. Seven of the 15 patients who have good response acquired satisfaction after a month, and 5 patients were relieved from severe tinnitus after a year.

Table 3 showed patient characteristics of the control group. Tinnitus severity before treatment as measured by the VAS score ranged between 3 and 7 with an average of 4.1. It scored between 5 and 7 for 35.7% of patients in the control group. The average hearing level was 64.1 dB in treatment group and 71.1 dB in control group. No significant difference was observed between the two groups. No significant difference was observed between the two groups concerning the affected side of the ear: 19 on the right side and 18 on the left side in the study group and 7 on the right side and 18 on the left side in the control group.

From the tinnitus questionnaire, we have 4 cases with high-pitch tinnitus and 1 case with low pitch in control group. On the other hand, there were 16 with high-pitch tinnitus and 3 with low pitch in study group. The others were unclassified type of tinnitus. There was no relationship between improvement of VAS and tinnitus pitch.

Comparison of the two groups with treatment

The χ^2 test showed a significant difference between the improved group and the unchanged group with respect to the duration of tinnitus before intratympanic treatment ($P < 0.001$) but no significant difference with respect to age, sex or the side of the affected ear (Figure 1).

Furthermore, there were no significant differences between the groups in hearing level (all frequencies), configuration of audiogram, or tone and variety of tinnitus. No patient had vertigo following the

intratympanic injection. No changes in hearing level were noted in either group after treatment.

Discussion

This is the first report to evaluate the effectiveness of intratympanic steroid injection in severe tinnitus of sudden idiopathic SNHL patients. Our results showed that the shorter the period from onset of sudden deafness to the start of intratympanic treatment of dexametha-

Table 3. Patient characteristics of control group.

| Patient No. | Sex | Age | VAS score | | Hearing level (dB) | |
|-------------|-----|-----|-----------------|----------|--------------------|-----|
| | | | Side of symptom | Pre Post | | |
| 1 | M | 72 | L | 4 | 2 * | 81 |
| 2 | M | 70 | L | 3 | 2 | 39 |
| 3 | M | 57 | R | 5 | 5 | 56 |
| 4 | F | 54 | L | 4 | 3 | 63 |
| 5 | F | 55 | R | 5 | 5 | 78 |
| 6 | F | 59 | L | 5 | 5 | 70 |
| 7 | M | 43 | L | 3 | 3 | 111 |
| 8 | F | 43 | R | 6 | 6 | 88 |
| 9 | F | 35 | L | 4 | 3 | 84 |
| 10 | M | 43 | R | 4 | 3 | 73 |
| 11 | F | 62 | L | 7 | 7 | 55 |
| 12 | M | 28 | R | 3 | 3 | 62 |
| 13 | F | 57 | R | 3 | 2 | 71 |
| 14 | F | 82 | R | 2 | 1 | 65 |

VAS, visual analog scale; Pre, at the point of stable hearing level after sudden sensorineural hearing loss; Post, one year later from Pre point; Hearing Level, average hearing level was expressed as the average score at three frequencies (500, 1000, and 2000 Hz). *Improvement was significant (defined as a decrease of at least two graduations on the VAS).

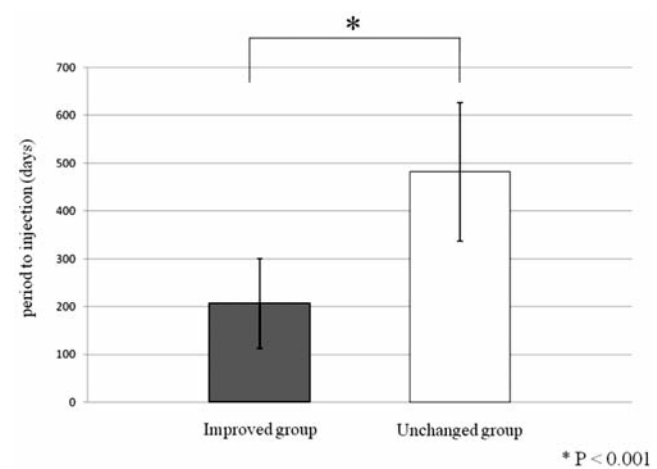


Figure 1. Comparison of the duration of tinnitus associated with sudden sensorineural hearing loss between the group whose tinnitus improved after treatment (*improved group*) and the group whose tinnitus was unchanged (*unchanged group*). In the improved group the period between onset of tinnitus and treatment was shorter (207 ± 94 days) than in the unchanged group (482 ± 145 days) ($P < 0.001$). Period to injection = period from onset of sudden sensorineural hearing loss to intratympanic dexamethasone injection; Improved group = those patients who reported a decrease of at least two graduations on the visual analogue scale of tinnitus; Unchanged group = all other patients.

son, the greater the improvement in tinnitus that could be expected after treatment. Forty-one per cent of patients had significant (at least two graduations on VAS) improvement of their symptoms. Only one patient presented significant improvement spontaneously in control group. However, we recognize weakness of this study because control cases did not include intratympanic saline injection group.

A previous study by Sakata *et al.*³ reported good overall results in 77% of patients with various diseases immediately after the intratympanic dexamethasone treatment, and Shulman and Goldstein⁸ showed that five of 10 patients who received intratympanic treatment experienced tinnitus control for at least one year after treatment. In contrast, Araújo *et al.*⁴ showed in a randomized, prospective and single blind study that 33% of patients in the dexamethasone group and 29% in the saline group had significant improvements of their symptoms. However, these previous studies included patients with tinnitus from several different causes, while our study focused on sudden SNHL. In addition, we showed a relationship between the duration of tinnitus and the effectiveness of treatment in sudden SNHL. It is possible that in the early phase of sudden SNHL, even in those patients with a stable hearing level, disorder or inflammation of the inner ear has not yet settled down. In a study using three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging, a high pre-contrast signal in the affected inner ear did not disappear until 90-150 days after the onset of sudden SNHL, although the hearing level was stable within two months. High pre-contrast signals may reflect minor haemorrhage or an increased concentration of protein in the inner ear.⁶

Our study revealed that intratympanic dexamethasone injection might be an effective treatment for tinnitus associated with sudden SNHL. Inflammation is associated with increased permeability of blood vessels. Contrast enhancement of the inner ear after intravenous gadolinium injection, which is recognized in one-third of cases with sudden SNHL, indicates increased permeability of blood vessels in the inner ear.⁶ Anti-inflammatory function of dexamethasone may be effective when there is increased permeability of blood vessels in the inner ear. In such cases, we considered a possibility of electrolyte altering and increasing cochlear blood flow effects of the corticosteroid.^{9,10}

Conclusions

There appears to be an advantage for intratympanic dexamethasone

injection in the treatment of severe tinnitus in the early phase of sudden SNHL at the stage of stable hearing levels. However long-time effect of intratympanic steroids is unclear, our preliminary study revealed that intratympanic steroid treatment might be a good treatment option for severe tinnitus in idiopathic sudden SNHL in short term. Further placebo-controlled studies are needed in order to verify the effectiveness of transtympanic dexamethasone injections for the treatment of patients with tinnitus and sudden SNHL.

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