

Clinical Experiences of Steroid Targeting Therapy to Inner Ear for Control of Tinnitus

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Abstract: We summarize our long-term clinical experiences with an inner-ear drug delivery system (DDS) for control of tinnitus. The inner-ear DDS consist of transtympanic perfusion of 2 or 4 mg dexamethasone to the round window via the middle ear. Therapeutic results of steroid targeting therapy to the inner ear were evaluated in 3,978 ears of 3,041 patients. Tinnitus improved in 75% of these patients immediately after treatment and in 68% after 6 months. The effects of such therapy on tinnitus varied depending on the underlying diseases. The improvement of tinnitus in the presence of labyrinthine hydrops was good, whereas the effects on noise- or drug-induced tinnitus were poor. Our results indicate that in high-tone tinnitus, the effects were poor, but they were good for low-pitched tinnitus. No correlation existed between the efficacy of management and loudness of the tinnitus.

The dangers of perforating the eardrum and of inciting the discomfort of vertigo as a result of the transtympanic injection of dexamethasone are minimal. We believe that the transtympanic infusion technique is an effective DDS for control of inner-ear diseases and symptoms. This technique may be performed by any neurotologist in an outpatient clinic.

Keywords: inner-ear drug delivery system; steroid targeting therapy; tinnitus; transtympanic perfusion technique

T*innitus aurium* is defined as a noise or ringing in the ears. It is derived from the Latin *tinnire*, to ring. The condition usually is subjective and audible only to the patient. When tinnitus is slight, the patient may not notice the ringing during most of the day. However, when tinnitus is continuous and loud, it can interfere with a person's quality of life and may be so annoying as to incite neurosis. Some patients with an inner-ear problem experience such overwhelming tinnitus that they would "cut off their ear" or "poke a hole in it with an ice pick" to try to relieve the noise. In rare instances of severe tinnitus, a patient might consider suicide.

The management of tinnitus has been the topic of many articles and special meetings of scientific societ-

ies. In this article, we describe some 15 years of clinical experience with steroid targeting therapy (STT) to the inner ear for control of tinnitus.

HISTORY OF OUR INNER-EAR DRUG DELIVERY SYSTEM

Our clinical trials of an inner-ear drug delivery system (DDS) for control of inner-ear problems began in 1974 [1]. The inner-ear DDS that we employ consists of transtympanic perfusion of medicine to the round window via the middle ear. At the beginning of our clinical trials of this system, we used 4% lidocaine hydrochloride to alleviate distressing inner-ear symptoms of tinnitus, recruitment, fullness or stiffness in the ear, and vertigo. Although the injection of 4% lidocaine hydrochloride is very effective for controlling inner-ear problems, patients complained of vertigo for several hours after the injection of medicine [2].

Consequently, in 1981, we began to use liquid dexamethasone for STT to the inner ear, to control various kinds of inner-ear diseases and symptoms [3].

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PATIENTS AND METHODS

Methods

The procedure we employed for our therapeutic modality has already been reported elsewhere [4-7]. The intratympanic injection was performed in our outpatient clinic with the patient in the sitting or the supine position. Dexamethasone, 2 or 4 mg, was introduced into the middle-ear cavity through a fine needle, just as is done in tympanic puncture. Before the procedure, the patient was asked to try to hold his or her posture steady and to avoid swallowing during the injection and for approximately 15 minutes thereafter to prevent the escape of dexamethasone through the Eustachian tube. The perfusion was repeated four times at an interval of 1-2 weeks. Depending on the clinical situation, some patients received a second course of four injections 3 months after the first course.

Patients

The investigation period spanned 63 months from January 1987 through March 1992. The subjects were 3,978 ears of 3,041 patients who received intratympanic dexamethasone perfusion for the management of vertigo, tinnitus, and the like. Patient ages ranged from 14 to 89 years, the average being 51.7 years. Most of the cases of tinnitus were assumed to be of cochlear origin. The ma-

jority of the patients could not be treated successfully by oral administration of vasodilators or mild sedatives.

EVALUATION OF EFFECTIVENESS

To evaluate the control effects of this therapy on tinnitus, a 10-division subjective evaluation system was used. This system commonly is used for subjective evaluation of other sensory disturbances. The severity or annoyance of tinnitus before the injection was regarded as being at level 10, and the level after the injection of drug was expressed as a score from 1 to 10. A level of 0-2 for the residual symptoms represented good effects, 3-6 represented fair effects, and 7-10 represented poor effects. Overall effectiveness was defined as the sum of the good effects and fair effects.

Short-term effects on tinnitus were evaluated 2 weeks after the fourth intratympanic dexamethasone perfusion. Patients then were investigated 6 months after the injection, at which time the long-term effects on tinnitus were evaluated.

RESULTS

The short-term overall effects on tinnitus of dexamethasone perfusion into the tympanic cavity were positive in 75% of patients.

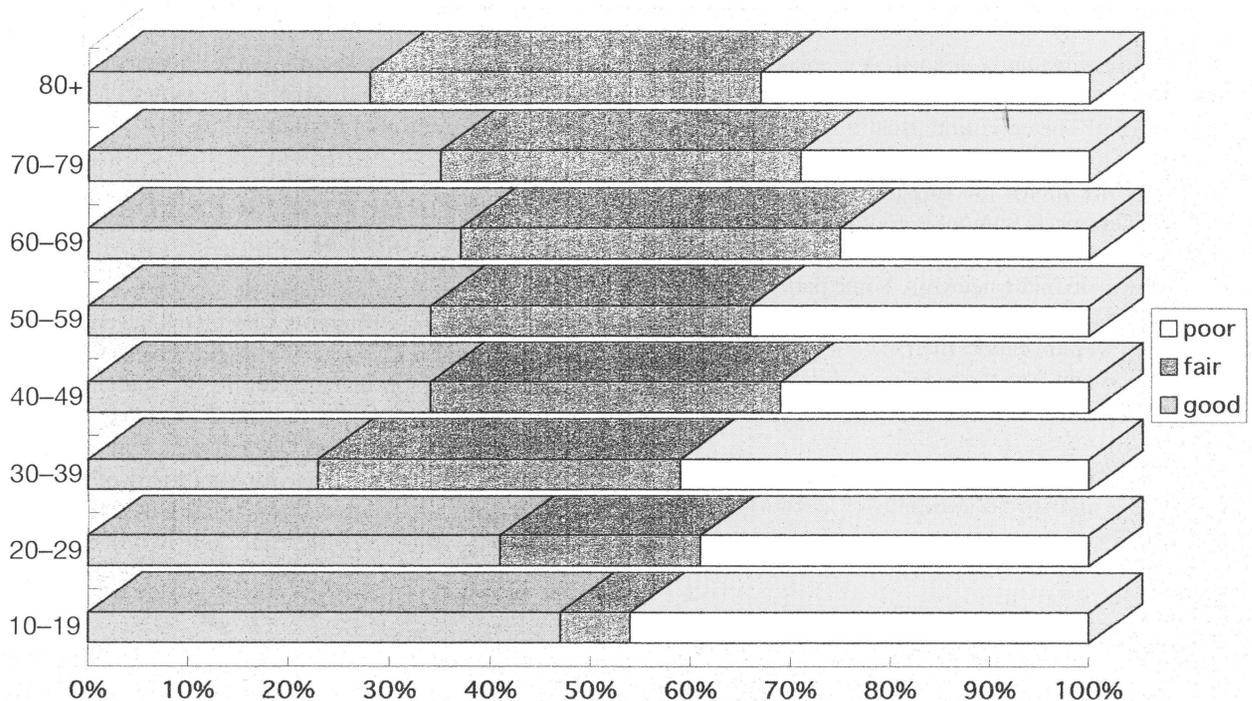


Figure 1. Effects on tinnitus of intratympanic dexamethasone perfusion in various age groups.

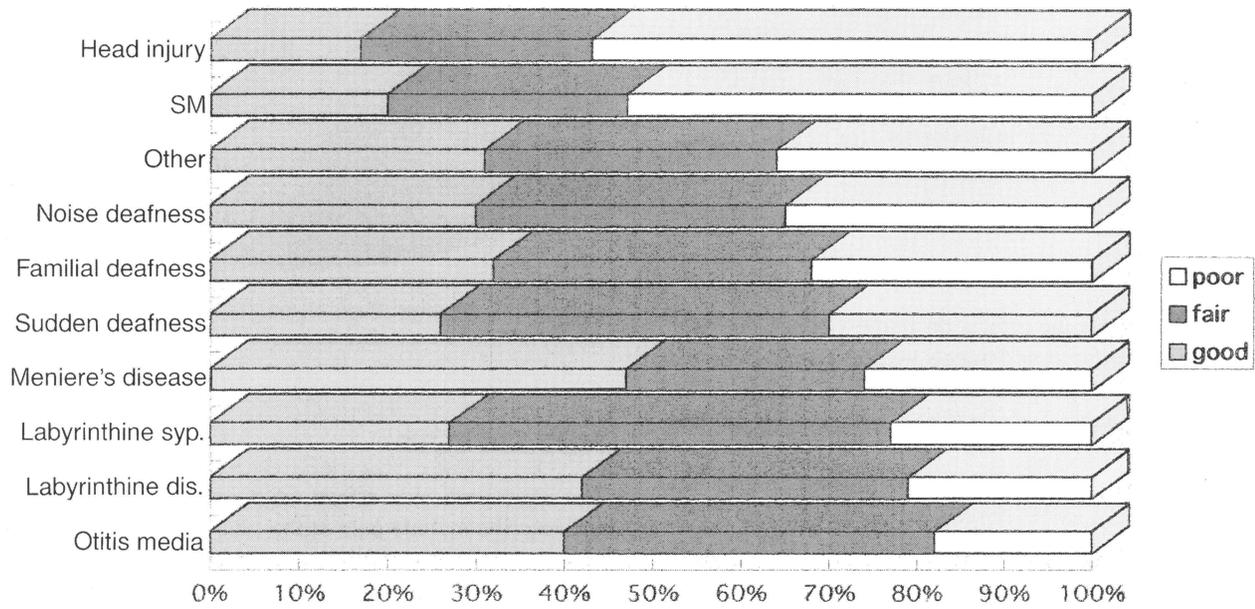


Figure 2. Effects on tinnitus of intratympanic dexamethasone perfusion in the presence of various underlying diseases.

Age and Effects

Figure 1 shows the effects on tinnitus in various age groups. The effects ranged from 54% to 73%. No correlation could be demonstrated between patients' ages and improvement of tinnitus.

Diseases and Effects

Figure 2 depicts the effectiveness of drug management of tinnitus in the presence of various underlying diseases. Of patients with Meniere's disease, 74% experienced improvement of tinnitus. In contrast, the effec-

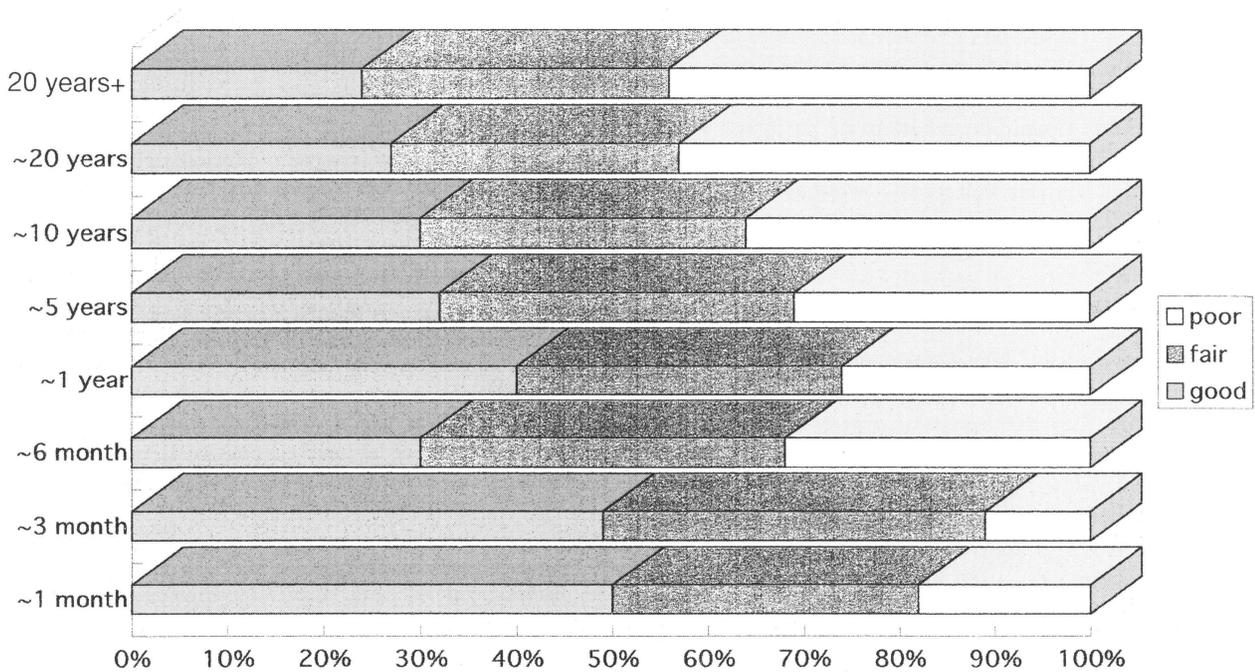


Figure 3. Effects on tinnitus of intratympanic dexamethasone perfusion in relation to disease duration.

tiveness of our therapeutic regimen on tinnitus accompanied by streptomycin deafness was 48% and, in the presence of head injury, this figure dropped to 42%. The improvement of tinnitus with labyrinthine hydrops was good, but effectiveness for noise- or drug-induced tinnitus was poor.

Duration and Effects

Figure 3 displays the effects on tinnitus control in relation to disease duration. Patients treated within 3 months of the onset of tinnitus had very good results. The effectiveness tended to decrease with longer disease duration.

The effects of our DDS trials on tinnitus control and average hearing levels ranged between 64% and 72%. A good result was seen in patients with mild hearing disturbances.

Evaluation of the effects on various pitches of tinnitus indicates that high-tone tinnitus was less improved than was low-pitched tinnitus. Efficacy of our regimen in high-tone tinnitus was poor.

No correlation was confirmed between efficacy of management and loudness of the tinnitus.

Overall Long-Term Effects

The long-term effects on tinnitus of dexamethasone perfusion into the tympanic cavity were evaluated at approximately 6 months after the last injection. The same 10-division subjective evaluation was used as was applied for the short-term evaluation. Overall positive effects on tinnitus were seen in 75% of cases immediately after intratympanic dexamethasone perfusion and in 68% after 6 months. It appears that, to some degree, tinnitus control via our therapeutic regimen remained constant.

MECHANISM OF ACTION

In this intratympanic dexamethasone perfusion technique, it is assumed that the medicine that was introduced directly into the tympanic cavity acts on the plexus tympanicus, is absorbed through the round window, and acts on the inner ear [8–13]. The mechanism of action of this therapeutic modality is multifactorial, including sedative effects, a metabolic improving effect, and an edema-relieving effect, which may eliminate abnormal excitation of auditory hair cells, which are believed to cause tinnitus. In Meniere's disease, steroid injection to the middle ear might improve endolymphatic hydrops.

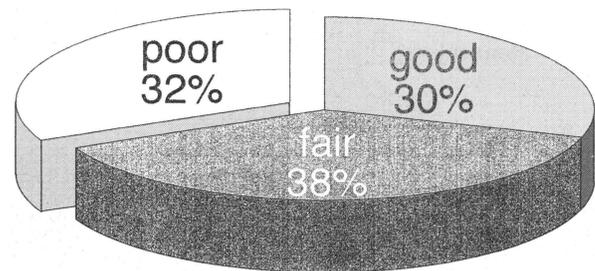


Figure 4. Long-term effects on tinnitus of intratympanic dexamethasone perfusion (after 6 months).

SIDE EFFECTS

The short-term side effects of the inner-ear DDS that we describe include pain at the time of tympanic puncture and temporary vertigo immediately after the injection. The temporary vertigo probably is caused by caloric stimulation. This effect might be avoided by infusing the drug solution at body temperature. Acute otitis media was seen in 0.1% of 3,978 ears. Persistent side effects were rare; tympanic perforation in 0.2% lasted 15 years. No patients experienced rapid hearing reduction after the injection.

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