ORIGINAL ARTICLE

Intratympanic Dexamethasone Injections as a Treatment for Severe, Disabling Tinnitus

Does It Work?

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Objective: To test the effectiveness of intratympanic dexamethasone injections as a treatment for severe disabling cochlear tinnitus.

Design: Randomized, prospective, single-blind study.

Setting: Academic tertiary referral hospital.

Patients: Thirty-six patients with severe disabling tinnitus predominantly of cochlear origin were randomly assigned to receive intratympanic injections of a dexamethasone solution or isotonic sodium chloride (saline) solution.

Interventions: Under topical anesthesia and after randomization, 36 patients received 0.5-mL intratympanic injections once per week for 4 weeks of either a 4-mg/mL dexamethasone solution or saline solution. Five patients were excluded from analysis because they did not complete the treatment or did not return for follow-up.

Main Outcome Measure: Improvement of tinnitus measured with a visual analog scale.

Results: The 2 groups were similar in age, sex, tinnitus laterality, measurement of tinnitus intensity on the visual analog scale, and main otologic diagnosis. We considered a 2-point improvement on the visual analog scale to be significant. Twenty-nine percent of the ears in the saline group and 33% of the ears in the dexamethasone group showed significant improvement immediately after completion of treatment. These measurements were not significantly different from each other. Follow-up varied from 13 to 31 months, and the patients with improved tinnitus returned to the initial measurements over time.

Conclusions: There was no advantage in intratympanic injections of dexamethasone over saline solution in the treatment of severe, disabling tinnitus. Both solutions produced a placebolike improvement.

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In 1982 Sakata et al[1] treated patients who had "cochlear tinnitus" by infusing a dexamethasone solution into their middle ear. In 1996 the same group[2] treated 1214 patients (1466 ears) with tinnitus of presumed cochlear origin with intratympanic dexamethasone injections. These patients had chronic otitis media (COM), labyrinthine syphilis, Ménière's disease, vertigo, sudden deafness, genetic deafness, streptomycin intoxication, acoustic trauma, head injury, or other otological diseases. The authors reported good overall results in 77% of the ears immediately after the treatment and in 68% after 6 months. Ears with COM, Ménière's disease, and labyrinthine syphilis had the best results.

In 2000 Shulman and Goldstein[3] treated 10 patients with intratympanic dexamethasone injections. These patients were selected as having predominantly cochlear tinnitus, and the intensity of the symptoms was characterized as severe and disabling. Five patients experienced tinnitus control for at least 1 year and 2 had tinnitus control for only a few hours. Three patients experienced no improvement.

In 2002 Cesarani et al[4] described 54 patients treated with intratympanic dexamethasone injections. They used chemical tests (furosemide, caraverine, and carbamazepine) to establish a cochlear origin for the tinnitus. Of these patients, 34% experienced complete resolution of tinnitus, 40% experienced significant improvement, and 26% experienced no change. At the 6-week follow-up examination, complete resolution was present in only 13.5% of the patients. At the 1-year follow-up examination, only 2 patients continued reporting complete resolution of the symptoms.

In 1999 Oliveira et al[5] described the tinnitus program at the Department of Otolaryngology of Brasília University Medi-

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cal School. They administered a questionnaire about the presence and clinical characteristics of tinnitus to all new patients at the Otology Clinic of the University Hospital, and, during a 6-month period, the authors were able to identify 500 patients with the symptom. Presbycusis, COM, otosclerosis, Ménière's disease, noise-induced hearing loss (NIHL), ototoxicity, and acoustic neuroma, in decreasing order of frequency, were the diagnoses for these patients. However, tinnitus was mild in 81%, moderate in 18%, and severe in only 1% of the patients. Patients with mild tinnitus did not need treatment, and when symptoms were moderate, they were easily controlled with drugs such as vestibular suppressants, calcium channel blockers, and/or gingko biloba; only 1% needed further treatment.

Subjective idiopathic tinnitus refers to noise that is heard only by the patient. Severe disabling tinnitus (SDT) refers to a symptom whose intensity and level of annoyance disrupts the patient's daily life. Subjective idiopathic tinnitus can be cochlear or central, ie, have a retrocochlear origin; subjective idiopathic tinnitus, however, always seems to have a central component.

Of the 500 patients whom Oliveira et al[5] identified as having tinnitus, 1% had SDT. Because compelling evidence points to central mechanisms in patients with SDT even when it originates in the cochlea,[6] we reasoned that intratympanic dexamethasone injections should not be effective to treat SDT.

Taking into consideration that (1) previous studies did not use a control group and placebo effect is very high with tinnitus; (2) Sakata et al[1,2] did not characterize their patients as having SDT and their patients were very much like our 500 patients—of whom only 1% had SDT; and (3) even though Shulman and Goldstein[3] characterized their patients as having SDT, they treated only 10 of them and did not use a control group (nor did Cesarani et al,[4]) we decided to undertake a prospective, randomized, single-blind trial to investigate intratympanic dexamethasone injections as a treatment for SDT. We report the results of this trial.

METHODS

Starting in June 1997, we developed a protocol to identify patients with SDT of probable cochlear origin for whom treatment with drugs had failed. During a 2-year period we selected 36 patients who met the requirements stated in the protocol.

To ensure that the tinnitus was of cochlear origin, detailed anamnesis of the symptom was requested from the patients from its inception up to the time of their first visit; otomicroscopic examination and audiologic testing were also performed to identify the presence of otological diseases associated with the symptom of tinnitus (NIHL, ototoxicity, COM, otosclerosis, sudden deafness, and Ménière's disease) and hearing loss.

A complete head and neck examination was performed in all patients. Laboratory evaluations included complete blood cell count; serum electrolyte concentrations; serum glucose, cholesterol, and triglyceride levels; and venereal disease research laboratory slide testing. A thyroid hormone test was performed when there was reason to suspect thyroid malfunction. Impedance testing was done in all patients, and brainstem-evoked response audiometry was also performed when there was a suspicion of retrocochlear involvement. Vectoelectronystagmography was performed when vestibular symptoms were present.

The patients selected to enter the study then responded to a specific tinnitus questionnaire regarding the following: tinnitus duration (<1 year, 1-2 years, 2-5 years, and >5 years), ear affected (left, right, or both), subjective hearing loss, description of the sound heard (rain, waterfall, whistle, pulsating noise, click, or other), and known otologic diseases and previous treatments. The patients were then asked to indicate the intensity of tinnitus on a visual analog scale graded from 1 to 10 (1 was low and 10 was an unbearable level of intensity).

Informed consent was obtained from all patients and the Ethics Committee for Research Involving Human Individuals of the Brasília University Medical School gave formal approval of the study protocol. The patients were then randomly assigned to receive 0.5-mL intratympanic injections of either a 4-mg/mL dexamethasone solution or isotonic sodium chloride (saline) solution (control group). The patients were placed in a supine position on the table with their heads turned about 45° away from the surgeon. Topical anesthesia of the tympanic membrane was administered using a gel containing 2.5% lidocaine hydrochloride and 2.5% prilocaine (EMLA; Astra Medical, São Paulo, Brazil). Using a tuberculin syringe and a 25-gauge needle, the assigned solution was injected under direct vision through an operating microscope at the junction of the posterosuperior and posteroinferior quadrants of the tympanic membrane. Each patient remained for about 20 minutes in the described position. Four injections were performed with the dexamethasone or the saline solution, 1 per week for 4 weeks. The solutions were warmed to body temperature before injection to avoid vertigo. If the patient felt partial improvement of the tinnitus and was willing to have another series of injections, another series was done. When there was no improvement at all or when there was a good response the treatment was interrupted.

After finishing the treatment, the patients answered a questionnaire about the status of their tinnitus (worse, unaltered, slightly improved, greatly improved, and in remission). They also indicated, on the visual analog scale, the level of tinnitus intensity following the treatment. We considered that improvement was significant when a lowering of at least 2 gradations on the visual analog scale was reported.

RESULTS

Five patients who started treatment were excluded from analysis (2 from the study group and 3 from the control group) because they did not complete treatment or failed to return for follow-up. Of the 31 patients who remained, 4 had both ears treated. Thus, a total of 35 ears were treated and evaluated.

Because only 4 patients had tinnitus in both ears, we refer to the number of ears rather than the number of patients. **Table 1** gives the otologic diagnosis for the 35 ears, with the number and percentage of ears with each diagnosis. Presbycusis was the most prevalent diagnosis, followed by NIHL, COM, otosclerosis, Ménière's disease, idiopathic tinnitus (no cause for the symptom was found), sudden deafness, and ototoxicity.

Duration of tinnitus was greater than 5 years in 57% and less than 1 year in only 4% of the ears. Patients graded tinnitus intensity from 5 to 7 on the visual analog scale for 48% of the ears and higher than 7 for 51% of the ears. These results reflect patient selection, as they experienced only SDT.

Of the patients who completed both treatment and evaluation, 13 (14 ears) received injections of a normal saline solution and 18 (21 ears) received injections of a dexamethasone solution. Follow-up varied from 3 to 31 months, with an average of 13.4 months.

STUDY GROUP

Table 2 gives the otologic diagnoses in the 21 ears of the study group. They were similar to the diagnoses for the entire group (35 ears) (Table 1).

Tinnitus intensity as measured on the visual analog scale was from 5 to 7 for 43% of ears and above 7 for 57% of the ears in the study group. These results were similar to those obtained for the entire group. Duration of tinnitus was greater than 5 years in 57%, between 2 and 5 years in 19% and less than one year in 14%. Hearing loss in the high frequencies (4 to 8 kHz) was present in 72% of the ears, 2 ears were anacusic (11%), and 3 ears had normal hearing (17%). The age of the patients in the study group varied between 30 and 80 years, averaging 55 years of age.

Table 2 presents the results of the treatment with intratympanic injections of dexamethasone in 21 ears. The average score on the visual analog scale was 8.04 before treatment and 6.90 after treatment, with an average improvement of 1.14.

Seven ears in 6 patients had significant improvement (at least 2 gradations on the visual analog scale) (Table 2). Three had COM, 2 had NIHL, 1 had otosclerosis, and 1 had Ménière's disease. Tinnitus intensity was greater than 7 on the visual analog scale in 3 ears (43%) and 5, 6, or 7 in 4 ears (57%). One ear had mild hearing loss, in the median frequencies, 5 had high frequency hearing loss and 1 was anacusic. Tinnitus improvement was moderate in 5 ears and marked in both ears of the same patient (Table 2).

Fourteen ears in 14 patients did not show any improvement either on the visual analog scale or in patients' answers to the questionnaire that they completed after treatment. The otologic diagnoses were much like those found in the 7 ears that had some improvement, except that there were 3 ears with idiopathic tinnitus in the no-improvement group. Nine ears (62%) in the no-improvement group had tinnitus intensity greater than 7, and 5 ears (36%) had a tinnitus intensity of 5, 6, or 7 on the visual analog scale. Symptom duration was greater than 5 years in 8 patients (57%), from 2 to 5 years in 1 (7%), between 1 and 2 years in 2 (14%), and less than 1 year in 3 (21%).

CONTROL GROUP

Table 3 gives the otologic diagnoses in the 14 ears of the control group. They were similar to those for the entire group (Table 1) and for the study group (Table 2).

Tinnitus intensity on the visual analog scale was 5, 6, or 7 in 8 ears (53%) and greater than 7 in 6 ears (47%). Tinnitus duration was greater than 5 years in 57%, between 2 and 5 years in 21%, and less than 2 years in 21%. High-frequency hearing loss was present in 60% of the ears, mid-frequency hearing loss was present in 27%, and low-frequency hearing loss in 13%. Age in this group varied from 20 to 80 years with a mean age of 55 years, which was similar to the age of the patients in the study group.

Table 1. Otologic Diagnosis in 35 Ears Selected for Treatment

Diagnosis	Ears, No. (%)
Presbycusis	7 (20)
Chronic otitis media	6 (17)
Noise-induced hearing loss	6 (17)
Otosclerosis	5 (14)
Ménière's disease	4 (11)
Idiopathic tinnitus	4 (11)
Sudden deafness	2 (6)
Ototoxicity	1 (3)

Table 3 presents the overall results of saline intratympanic injections regarding tinnitus intensity in the 14 ears of the control group. The average score on the visual analog scale was 7.57 before the injections and 6.21 after the injections, with an average improvement of 1.36.

Four of the 14 ears showed significant improvement (Table 3); NIHL was the otologic diagnosis in 2, COM in 1, and presbycusis in 1. Age in the control patients with significant improvement varied between 40 and 60 years. Tinnitus intensity was from 5 to 7 in 2 ears and greater than 7 in 2. Tinnitus duration was from 2 to 5 years in 3 ears and less than 2 years in 1 for these patients. Three ears that showed tinnitus improvement had high-frequency hearing loss and 1 had mid-frequency hearing loss.

Ten ears in the control group had no improvement. The otologic diagnoses for these ears are displayed in Table 3 and are not different from the diagnoses for the 4 ears that showed improvement, except that there was 1 patient with ototoxicity, 1 with Ménière's disease, and 1 with otosclerosis; 1 patient was considered to have idiopathic tinnitus. The age of the patients in the control group who had no improvement varied from 30 to 80 years, with a mean age of 52 years. Tinnitus intensity was 5, 6, or 7 in 60% of the ears and was greater than 7 in 40%. High-frequency sensorineural hearing loss was present in 6 ears, 2 ears had mid-frequency hearing loss, and 1 ear had low-frequency hearing loss. Over time, the study and control groups both experienced a return to pretreatment tinnitus intensity.

COMPARISON OF THE 2 GROUPS

The χ^2 test (with a significance level of .05) showed no significant difference between the groups regarding sex, age, tinnitus intensity, and laterality of the tinnitus. There was no significant difference between the results of treatment with a dexamethasone solution and treatment with a saline solution (there was a 33% and a 29% improvement, respectively).

Two patients in the study group had light vertigo following the intratympanic injection. Two patients in the control group had light vertigo, and 1 complained of otalgia following the injections. These complaints were mild and resolved spontaneously soon after the injections. No

Table 2. Otologic Diagnoses in 21 Ears in the Study Group

Patient No.	Sex	Side of Symptom	VAS Score*		Complication	Diagnosis
			Pretreatment†	Posttreatment‡		
1	M	R	6	5		Otosclerosis
2	M	L	8	8		Presbycusis
3	M	L	7	6		NIHL
4	M	L	7	4§		NIHL
5	M	R	7	6		Otosclerosis
6	F	L	10	9	Vertigo	Sudden deafness
7	F	R	9	9		Ménière's disease
8	F	R	7	6		Idiopathic tinnitus
9	F	R	9	9		Presbycusis
10	F	L	7	6		Idiopathic tinnitus
11	F	R	10	10	Vertigo	Sudden deafness
12	M	R	10	8§		NIHL
13	F	L	10	8§		Ménière's disease
14	F	R	8	8		Ménière's disease
15	M	L	8	8		Otosclerosis
16	M	R	7	5§		Otosclerosis
17	M	R	6	2§		COM
18	M	L	5	2§		COM
19	M	R	8	8		Idiopathic tinnitus
20	F	R	10	10		COM
21	F	L	10	8§		COM

Abbreviations: COM, chronic otitis media; NIHL, noise-induced hearing loss; VAS, visual analog scale.
*Mean score improvement, 1.14.
†Mean pretreatment score, 8.04.
‡Mean posttreatment score, 6.90.
§Improvement was significant (defined as a lowering of tinnitus by at least 2 gradations on the VAS).

Table 3. Otologic Diagnoses in 14 Ears in the Control Group

Patient No.	Sex	Side of Symptom	VAS Score*		Complication	Diagnosis
			Pretreatment†	Posttreatment‡		
1	F	L	10	10	Vertigo	Ototoxicity
2	F	L	10	9	Otalgia	Ménière's disease
3	M	L	7	4§		NIHL
4	M	R	6	4§		NIHL
5	F	R	5	5	Vertigo	Presbycusis
6	F	R	9	9		Presbycusis
7	M	R	8	6§		COM
8	M	R	8	8		Presbycusis
9	M	R	7	6		Otosclerosis
10	M	R	7	6		Presbycusis
11	F	L	9	1§		Presbycusis
12	F	L	7	7		Idiopathic tinnitus
13	M	L	6	6		NIHL
14	F	R	7	6		COM

Abbreviations: COM, chronic otitis media; NIHL, noise-induced hearing loss; VAS, visual analog scale.
*Mean score improvement, 1.36.
†Mean pretreatment score, 7.57.
‡Mean posttreatment score, 6.21.
§Improvement was significant (defined as a lowering of tinnitus by at least 2 gradations on the VAS).

changes in hearing level were noted in either group after treatment.

COMMENT

Our results clearly show that there is no difference between dexamethasone and normal saline intratympanic injections in relation to treatment of SDT. Twenty-nine percent of the ears in the control group and 33% of those in the study group had significant improvement of the symptom (at least 2 gradations on the visual analog scale).

These findings are not significantly different from each other, and both are similar to the known placebo effect of any tinnitus treatment (30%-40%).

If we compare our study with the study by Sakata et al,[2] the differences are very clear, as they treated 1466 ears without selecting those presenting with SDT. In 1999 Oliveira et al[5] determined that of 500 patients with the symptom of tinnitus, and with otologic diagnoses very similar to those present in the sample of Sakata et al,[2] only 1% had SDT. In 81% of the patients, tinnitus was mild and did not really bother the patients. In 18% it was moderate, perfectly tolerable, and easily controlled with routine medication.

Severe disabling tinnitus is different from the more common form of tinnitus in several ways. The symptom is intense, with a high annoyance level and an affective component that alters the patient's routine and makes him or her unable to perform daily tasks efficiently.

Some facts must be considered to understand why SDT is different. In 1989, House[6] severed the cochlear nerves of patients with Ménière's disease who were undergoing vestibular nerve section and who also had severe tinnitus. Considering that tinnitus in Ménière's disease certainly has a cochlear origin, it was surprising to learn that a large percentage of these patients continued to experience the unaltered symptom after the cochlear nerve was severed. Somehow, central auditory pathways kept the symptom of tinnitus alive after cochlear deafferentation. A lack of central suppression of spontaneous auditory pathways could explain the noise permanence.

In 1995 Shulman et al[7] reported 2 carefully studied cases of SDT who had regional cerebral blood flow abnormalities detected by single photon emission computed tomography with technetium Tc 99m hexamethyl propyleneamine oxide. These abnormalities were present in the medial temporal lobe region (temporal, parietal, and hippocampal amygdala). Since the patients had no neurological diseases or symptoms, they concluded that these changes in blood flow were from SDT and hypothesized the development of a paradoxical memory for SDT in this area of the brain. In addition, the affective component of tinnitus would be related to this paradoxical memory for the symptom, so that a final common pathway for the sensorial and affective components of SDT would be established.

Even though these hypotheses are still unproven, one fact seems clear: SDT always has a central component even when of cochlear origin. It is not surprising, then, that intratympanic injections of dexamethasone or saline solutions are equally inefficient in the treatment of SDT. Drug therapies directed to the central nervous system (GABAergics, benzodiazepine, and calcium channel blockers), retraining therapy, and masking strategies should be more promising avenues in this regard.

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REFERENCES

1. Sakata E, Itoh A, Ohtsu K, Nakasawa H, Iwashita N. Pathology and treatment of cochlear tinnitus by blocking with 4% lidocaine and decadron infusion. *Pract Otol (Japan)*. 1982;75:2525-2535.
2. Sakata E, Itoh A, Itoh Y. Treatment of cochlear tinnitus with dexamethasone infusion into the tympanic cavity. *Int Tinnitus J*. 1996;2:129-135.
3. Shulman A, Goldstein B. Intratympanic drug therapy with steroids for tinnitus control. *Int Tinnitus J*. 2000;6:10-20.
4. Cesarani A, Capobianco S, Soi D, Giuliano DA, Alpini D. Intratympanic dexamethasone treatment for control of subjective idiophatic tinnitus: our clinical experience. *Int Tinnitus J*. 2002;8:11-113.
5. Oliveira CA, Venosa A, Araújo MF. Tinnitus program at Brasília University Medical School. *Int Tinnitus J*. 1999;5:141-143.
6. House JW. Therapies for tinnitus. *Am J Otol*. 1989;10:163-165.
7. Shulman A, Strashun AM, Afryie M, Aronson F, Abel W, Goldstein B. SPECT imaging of brain and tinnitus: neurotologic/neurologic implications. *Int Tinnitus J*. 1995;1:13-29.