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Intratympanic and Round-Window Drug Therapy: Effect on Cochlear Tinnitus

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Abstract: Tinnitus is a common symptom for which few existing therapeutic approaches can produce reliable reduction or elimination. Chemical perfusion involves the delivery of medication directly into the inner ear via the round-window membrane. This report discusses the use of dexamethasone or gentamicin in 20 individuals who had inner ear diseases in which disturbing cochlear tinnitus was one of the symptoms. Preliminary results indicate that chemical perfusion is a promising option for the treatment of cochlear tinnitus.

Tinnitus is a symptom affecting 50 million Americans. It is primarily a subjective complaint for which objective indicators usually are sparse and lack a proven animal model. Though tinnitus often is associated with other symptoms, the degree of suffering it produces ranges from an occasional awareness to the contemplation of suicide [1]. Approximately 20% of individuals with tinnitus have what is described as a severe or extreme form, which significantly interferes with the quality and productivity of life. Despite numerous identifiable or idiopathic causes of tinnitus (Table 1), the variety of therapies used for its eradication or reduction has been uniformly disappointing, offering only temporary or no relief (Table 2) [2].

Chemical perfusion is a treatment option that involves the delivery of medication directly into the inner ear via the round-window membrane, thus achieving higher cochlear concentration without systemic side effects. Chemical perfusion shows great promise in controlling severe peripheral tinnitus either as the sole symptom or in association with other symptoms present from a variety of causes (Menière's disease, frequent attacks of vertigo, failed vestibular nerve section, sudden sensorineural hearing loss, inner ear vestibular dysfunction, and failed endolymphatic sac shunt surgery).

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This study describes the application of glucocorticoids, specifically dexamethasone, or gentamicin to the round-window membrane in individuals who have various inner ear diseases and in whom disturbing tinnitus is one of the symptoms. Various reports have shown that, in selected cases, these medications can control vertigo, improve hearing, and reduce tinnitus [3–11].

PATIENTS AND METHODS

Twenty patients in this study suffered from various inner ear diseases (Table 3). All had tinnitus of varying degrees of severity in association with other symptoms. Patients rated their tinnitus from 0 to 10, with 10 being the loudest. Three patients had severe tinnitus as their most disturbing symptom; hearing loss, vertigo, and ear fullness were of greater concern to 17 patients. Patient evaluation and testing were dictated by the diagnosis and, for Menière's disease, by stage (Shea I–V). Where indicated, tests included comprehensive audiometry, tinnitus matching, electronystagmography, electrocochleography, vestibular autorotation testing [12], osmotic diuresis, and radiological studies. Failure to respond to reassurance, dietary and lifestyle changes, medical intervention (diuretics, vestibular suppressants, systemic steroids, calcium channel blockers, vasodilators, anticholinergics, and lipid reduction), and vestibular physical therapy, considered in conjunction with the stage of the disease, resulted in the option of chemical perfusion with dexamethasone or gentamicin.

In this study, chemical perfusion of the inner ear with dexamethasone was offered as a treatment for patients suffering from sudden sensorineural deafness, se-

Table 1. Classification of Tinnitus

Identifiable Causes	Idiopathic Causes
Vascular	Sudden sensorineural hearing loss
Arterioventricular malformation	Normal hearing
Carotid stenosis	
Fibromuscular dysplasia of internal carotid artery	
Persistent stapedial artery	
Ectopic carotid artery	
Vascular compression of cranial nerve VIII	
Glomus tumors	
Venous hum	
Dehiscent jugular bulb	
Hypertension	
Atherosclerosis	
Nonvascular	
Medication	
Acoustic neuroma	
Intracranial neoplasms (temporal bone)	
Metabolic disorders	
Temporomandibular joint dysfunction	
Middle ear disease	
Menière's disease	
Sudden sensorineural hearing loss	
Palatal myoclonus	
Middle ear myoclonus	
Patulous eustachian tube	
Otosclerosis	
Benign intracranial hypertension	

vere tinnitus, early-stage Menière's disease (i.e., Shea I: tinnitus, fullness, fluctuant low-tone loss), Shea II (same as Shea I plus dizzy spells) or Shea III (fullness, tinnitus, dizzy spells, nonfluctuant hearing loss), or bilateral Menière's disease for the better-hearing ear. Dexamethasone for Shea IV (no dizzy spells, severe hearing loss, fullness, tinnitus) or stage V (no dizziness, less fullness and tinnitus; worse hearing; unsteadiness) does not appear to be effective [13]. Dexamethasone has as its probable mechanism an increase in blood flow to the cochlea, a decrease in any inflammatory component, and antioxidant properties [14].

Chemical perfusion of the inner ear with gentamicin was offered to patients who had Menière's disease, frequent vertigo with attacks, and fair to poor hearing and in whom vestibular nerve section or endolymphatic sac surgery had failed or who were poor surgical candidates.

Gentamicin was used to take advantage of its known biphasic ototoxicity. Thereby, it (1) blocks calcium channels and competitively displaces divalent cations (transient and reversible effects); (2) destroys hair cells; and (3) destroys endolymph-producing dark cells in the ampullae, utricle, and common crus [15].

TECHNIQUE

Intratympanic Drug Administration

Dexamethasone

Of the 20 patients reported in this study, the initial 14 patients (5 male, 9 female; age range, 27–79 years) underwent chemical perfusion of the round window. Of these 14 patients, 6 suffered Menière's disease, 6 had severe tinnitus, and 3 had experienced sudden deafness. According to procedure, 0.6 ml of dexamethasone (4 mg/ml) was placed into the middle ear via a tuberculin syringe (27-gauge needle, 1.5 inches long) through an intact tympanic membrane just posterior to the umbo of the malleus. Patients remained supine with their head turned away 30 degrees for 45 minutes. Then tympanostomy with ventilation tube placement was performed. Patients were instructed to instill dexamethasone ophthalmic solution (1 mg/ml), five drops twice daily, and to massage the tragus to help tube perfusion. Most patients received two office injections. Of these 14 patients, tinnitus was reduced in 5 and completely eliminated in 3 (Table 4).

Table 2. Management of Tinnitus

Reassurance	Masking	Medication	Surgery	Alternative Therapies	Psychiatric Intervention
	Ambient noise	Anxiolytics (alprazolam [Xanax])	Cranial nerve VIII section	Biofeedback	
	Household noise	Vasodilators (papaverine [Pavabid], dipyridamole [Persantine], niacin, pentoxifylline [Trental])		Electrical stimulation	
	Designated masker	Local anesthetics		Habituation therapy	
	Hearing aids	Anticonvulsants (carbamazepine [Tegretol], phenytoin sodium [Dilantin])		Acupuncture, yoga, tai-chi, massage therapy	
		Antihistamines		Three-dimensional tapes	
		Antidepressants (amitriptyline, nortriptyline, fluoxetine [Prozac]			
		Other			

Table 3. Inner Ear Diseases That Might Benefit from Chemical Perfusion with Dexamethasone or Gentamicin

Menière's disease
Frequent vertigo attacks
Failed vestibular nerve section
Sudden sensorineural hearing loss*
Severe peripheral tinnitus
Inner ear vestibular dysfunction
Failed endolymphatic sac shunt surgery

*Dexamethasone only.

Gentamicin

Three patients had intratympanic chemical perfusion with gentamicin (40 mg/ml) 1 week apart. These patients had dry Gelfoam placed into the round-window niche through an extended tympanostomy incision, allowing the practitioner to inspect the round window to ensure the absence of false membranes or mucosal bands [16]. A ventilation tube was placed, the gentamicin was instilled, and patients remained supine with their head turned away 30 degrees for 45 minutes. All three patients had severe vertigo or imbalance and severe tinnitus, two had poor hearing, and one had no hearing. Of the three, two experienced significant reduction in and one experienced elimination of tinnitus (Table 5).

Intraear Drug Administration

The intratympanic method of chemical perfusion does not permit accurate instillation of any medication into the inner ear. This impediment is significant to the precision necessary to control, monitor, and gain a desired outcome and not a failed or deleterious effect.

The Round Window Microcatheter (IntraEar, Inc., Denver, CO) appears to be a major advance in permitting the precise delivery of medication over a specified period. The catheter tip of the dual-lumen microcatheter is a fenestrated, hollow, compressible bulb that fits snugly into the round-window niche. The inflow-outflow design permits the physician, with the device in place, (1) to add medication, (2) to remove medication, (3) to flush the device, and (d) to relieve or avoid build-up of air or fluid pressure. Attachment to an infusion pump allows continuous and exact delivery of medication to the inner ear. The IntraEar Round Window Microcatheter was used in three patients in this report (Table 6). Although each patient had different underlying pathology, all three had severe cochlear tinnitus. Under general anesthesia, the patients had their catheters—filled with the gentamicin solution (1.25 ml)—placed into the round-window niche via a tympanomeatal flap and were released to home. At a follow-up office visit,

Table 4. Results of Chemical Perfusion with Dexamethasone in 14 Patients with Inner Ear Disease

Posttherapy Hearing State	Hearing (n = 14)	Tinnitus (n = 14)	Vertigo (n = 13)	Ear Pressure (n = 13)
Normal	—	3	2	7
Better	5	5	5	3
Same	9	5	6	2
Worse	—	1	—	1

Note: Follow-up period ranged from 1 to 21 months.

Table 5. Intratympanic Chemical Perfusion with Gentamicin in Three Patients with Inner Ear Disease

Patient Data (Initials, Gender, Age)	Diagnosis	Treatment	Result
AW (male, 69 yr)	Anacusis, AD; S/P meningioma resection, cranial nerve VIII intact; severe imbalance; severe tinnitus (10); ENG: peripheral dysfunction 75%	0.6 ml gentamicin (40 mg/ml) 9/11/97, 9/16/98; vestibular rehabilitation	Complete resolution of dizziness; ENG: 100% ablation, AD; no tinnitus (0)
BD (female, 63 yr)	Menière's disease, AD; S/P endolymphatic shunt; moderate (40 dB) SNHL, AD; imbalance (not TRV); tinnitus (7)	0.6 ml gentamicin (40 mg/ml) 9/26/97, 10/6/97	Complete resolution of dizziness; speech discrimination reduced 88%–36%; ENG: 11/10/97; 100% ablation, AD; tinnitus (2)
JR (male, 22 yr)	Menière's disease, AD; S/P endolymphatic shunt, 5/14/98 AD; recurrent TRV; SNHL, 55 dB; speech discrimination 72%; tinnitus (5)	0.6 ml gentamicin (40 mg/ml) 5/7/98, 5/14/98	Complete resolution of dizziness; hearing PTA 55→63→60 (92% speech discrimination); tinnitus (2)

AD = *auris dextra* (right ear); ENG = electronystagmography; S/P = status post; PTA = pure tone average; SNHL = sensorineural hearing loss; TRV = true rotational vertigo.

Table 6. Intraear Round-Window Microcatheter Chemical Perfusion in Three Patients with Inner Ear Disease

Patient Data (Initials, Gender, Age)	Diagnosis	Treatment	Result
DK (male, 42 yr)	S/P stapedectomy, AD 7/97; severe SNHL, AD 12/97; speech discrimination 25%; no vertigo; severe tinnitus, AD (9)	0.2 ml dexamethasone (4 mg/ml), 1/13/98 1/19/98, 1/27/98	Initial hearing gain; subsequent loss; no tinnitus (0)
ME (female, 66 yr)	Menière's disease, AU; SNHL, AS > AD; vertigo; severe tinnitus, AD (9)	0.2 ml gentamicin (40 mg/ml), 2/12/98, 2/24/98	Hearing unchanged; no vertigo; no tinnitus (0)
VB (female, 54 yr)	Severe SNHL, AD for 6 wk; no vertigo; severe tinnitus, AD (10)	0.2 ml dexamethasone (4 mg/ml), 7/23/98, 7/29/98	Hearing unchanged; no tinnitus (0)

AD = *auris dextra* (right ear); AS = *auris sinistra* (left ear); AU = *auris unitas* (both ears); S/P = status post; SNHL = sensorineural hearing loss.

the gentamicin within the catheter was removed and was replaced with new solution. No patients complained of any pain or discomfort from this brief procedure (approximately 40 minutes). All IntraEar patients experienced complete cessation of their tinnitus.

CONCLUSION

Although these results are preliminary, a number of observations appear to be acceptable. The delivery of medications into the inner ear (chemical perfusion) shows promise in controlling a host of cochleovestibular symptoms, including tinnitus, without systemic effects. Additionally, chemical perfusion may lessen the need for some types of traditional surgery and for alternative therapies provided for tinnitus.

Precise delivery of medication into the inner ear is a goal, which is obtainable because the round-window microcatheter technique can deliver the required precise quantity of medication into the inner ear. This precise delivery of medication suggests an array of future applications of medications in this fashion (e.g., antioxidants, nerve growth factor, cytotoxic drugs, antivirals). However, further investigation and analysis of chemical perfusion's role in the control of tinnitus are needed.

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