
Drug Treatments for Tinnitus: The Tulane Experience

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Abstract: It has recently been estimated that 12 million Americans have a severe form of tinnitus and that nearly 40 million Americans suffer from some form of tinnitus-related complaints [1]. The nature of patients' concerns at the time of the initial evaluation is very important in our overall patient management. Specific issues that we address in our practice include the following: (1) Why are patients here? (2) What do patients want and what do they expect of me? (3) Whom have they seen before and what if anything has been tried and proved ineffective in treating their condition? Each of these basic questions must be answered to ensure that we are addressing affected patients' concerns and are targeting our efforts according to individual patients' needs.

The meaning ascribed to tinnitus varies widely across patients. Some patients are extremely concerned about whether their tinnitus complaint is associated with the onset of irreversible deafness. Elderly patients who complain of tinnitus seem to be more concerned about the possibility that the onset of tinnitus indicates an impending cerebral vascular accident. Some patients do not have a specific fear or concern associated with the tinnitus; such patients generally are concerned that their tinnitus simply indicates that something medical might be seriously wrong with them. Recognizing that some patients are concerned about the general health implications of tinnitus versus specific disease-related implications helps to guide us in our approach to the evaluation and management of tinnitus sufferers.

We emphasize the importance both of the neurootological evaluation of patients presenting with tinnitus and of the overall general medical history and physical examination. The latter is particularly important to those patients who have undiagnosed or untreated underlying medical conditions, such as diabetes mellitus, high blood pressure, arteriosclerosis, altered blood flow, temporomandibular joint disorder, hyperlipidemia, or

hypothyroidism, or those conditions secondary to adverse reactions to medications that they are taking for any of these medical diseases. The opportunity to direct our efforts at the underlying cause most often will yield the best results for affected patients. This is particularly important when in considering that roughly 50% of the time the underlying etiology causing tinnitus is unknown. Twenty-five percent of new tinnitus patients will have a history of noise exposure, 7% will have some form of middle or inner ear pathology (or both), 6% will have had an antecedent history of head or neck trauma, and 15% will have other causes [1]. Although 90% of tinnitus sufferers ultimately will receive diagnoses of some form of ear disease, the cause-and-effect relationship is not always clear. Consequently, a thorough review of affected patients' general medical condition is pursued prior to specific audiological and neurootological examinations.

Our audiological evaluation includes a comprehensive audiometric examination plus a tinnitus evaluation. Our tinnitus evaluation consists of pitch matching, minimal masking levels, and subjective severity ratings. Additionally, all new tinnitus patients are asked to complete the Tinnitus Handicap Inventory; to those in whom an underlying neuropsychiatric component is suspected, the Beck Depression Inventory also is administered [2,3]. Typically, auditory brainstem responses and magnetic resonance imaging are used only in those patients in whom retrocochlear pathology or other neurological abnormalities are suspected. Other medical

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testing, such as skin testing, frequently is used for those patients presenting with tinnitus and having a strong underlying allergic diathesis.

A specific form of tinnitus complaint that we feel deserves special evaluation is that of pulsatile tinnitus. Pulsatile tinnitus may be the result of glomus (tympanicum or jugulare) tumors, patulous eustachian tube, or cholesterol granuloma, as has been seen in an unusual number of patients in our practice [4,5]. Arteriosclerotic carotid artery disease, hypertension, and twisted arteries also have been found in patients complaining of pulsatile tinnitus. More recently, several patients received diagnosis of benign intracranial hypertension, as described in the recent otological literature [6,7]. Because pulsatile tinnitus may be caused by both otological and nonotological conditions, having an organized approach to evaluation, treatment, or referral for all tinnitus patients is important.

We have proposed a tinnitus patient algorithm (Fig. 1). Typically, most patients with undiagnosed or untreated system diseases (e.g., hypertension and diabetes) are referred to our colleagues in internal medicine for appropriate treatment of such conditions. Patients having underlying vascular problems (e.g., arteriosclerotic carotid artery disease) usually are referred to our colleagues in vascular surgery for noninvasive studies and appropriate surgery, as indicated. We all are aware that many patients with a tinnitus complaint have a very strong psychological overlay. Our recent efforts have incorporated our colleagues in the neuropsychiatric department to assist us in the evaluation and treatment of affected patients, as indicated. Usually, such identified ear diseases as cholesteatoma, otosclerosis, or glomus tumor are treated with standard otological surgery. A significant number of patients have a strong underlying allergic component, which necessitates better control using newer non-sedating antihistamines in conjunction with topical nasal steroids. During acute exacerbations, systemic steroids also may be indicated; for those sufferers with perennial symptoms, skin testing with appropriate immunotherapy often is recommended. However, the majority of our patients fall into the idiopathic or nonsurgical category, and patients in this group undergo the more typical tinnitus evaluation (as outlined).

REVIEW OF RECENT CLINICAL INVESTIGATIONS

Typically, in our practice annually we see approximately 400–500 new patients with a tinnitus complaint. Since 1994, the male-to-female ratio has remained equal, and 50% of patients localize their complaint to one ear, whereas the remainder complain of tinnitus in both ears or, as they occasionally describe

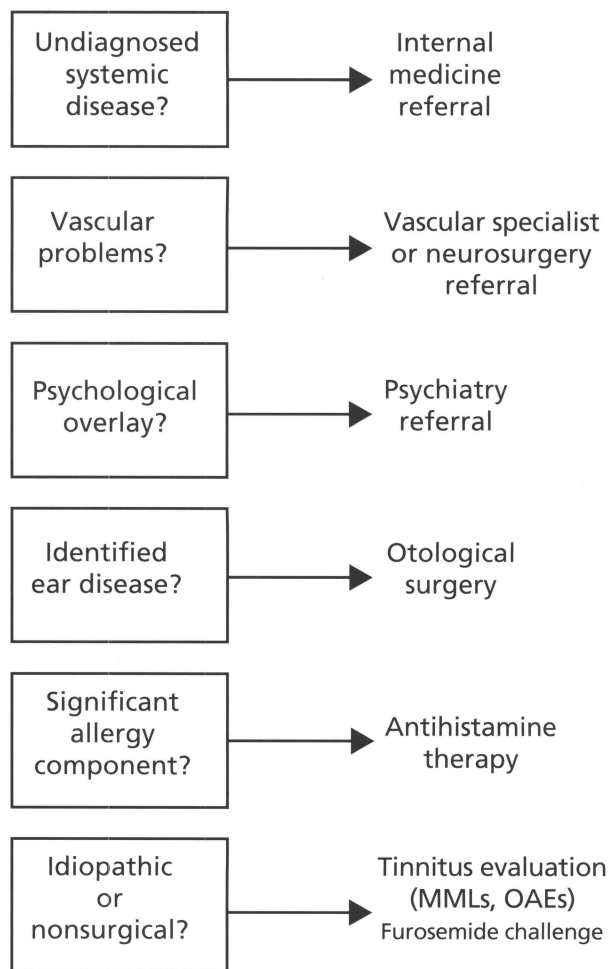


Figure 1. Algorithm for workup of tinnitus patients.

it, “noise in their head.” A review of our audiological parameters shows that the involved frequencies range between 125 and 10,000 Hz, with a peak incidence between 3,000 and 5,000 Hz. Probably, this range is associated with a previous occupational noise exposure or the onset of presbycusis (or both). Tinnitus associated with a conductive hearing loss seems to involve the lower frequencies, whereas tinnitus associated with a sensorineural hearing loss usually involves the higher frequencies. In addition to conductive or sensorineural pathologies, various drugs are known to be associated with tinnitus complaints. In our practice, these have included salicylates, quinine, tobacco, caffeine, alcohol, oral contraceptives, and heavy metals. In particular, cocaine and marijuana also have been associated with an exacerbation of tinnitus complaints. Patients affected by the foregoing factors (on occasion) will undergo a toxicology screen, particularly on suspicion of chronic usage of these products in the face of a tinnitus com-

plaint. An obviously important factor is to identify and, where possible, remove potential sources of tinnitus generation or exacerbation before instituting any type of pharmacological therapy.

Many different drugs have been used at one time or another in treating patients with tinnitus. By classification, these drugs have included antianxiolytics, anticonvulsants, antidepressants, antiinflammatories, antipsychotics, diuretics, and the like. These medications by action serve to reduce anxiety; reduce the polysynaptic responses; improve mood and reduce emotional distress; suppress spontaneous otoacoustic emissions; reduce panic attacks; or reduce the endocochlear potential. By name, these products include Buspar, Tegretol, Elavil, aspirin, Zoloft, and Lasix (Table 1). Some of these medications have had only empirical trials, whereas others have been tested under controlled conditions.

The anticonvulsant aminooxyacetic acid (AOAA) originally was selected by our research group for clinical investigation as a pharmacologic treatment for tinnitus. This drug appeared to reduce the endocochlear potential, which additionally inhibited firing rates of the auditory nerve. For patients with tinnitus of presumed cochlear origin, use of AOAA was hypothesized to allow us to potentiate the severity of cochlear-generated tinnitus by modulating cochlear function. A pilot study indicated a 30% success rate using this drug; consequently, our initial studies were followed by a federally funded contract project involving 66 patients [8,9]. This double-blinded placebo crossover study revealed a 21% success rate using this medication. However, most of the patients who responded positively to this drug experienced side effects, precluding its continued or chronic use. The idea of targeting a drug specifically at the cochlea continued to have theoretical appeal and led us to our second approach to tinnitus treatment: furosemide.

Furosemide was viewed as a "second-generation"

drug by our research group because it, like AOAA, was known to affect the endocochlear potential of the inner ear. Unlike AOAA, however, furosemide was not known to cross the blood-brain barrier, and we hoped that we might be able to suppress tinnitus of cochlear origin without the attendant side effects caused by AOAA. Initial results using furosemide in patients with tinnitus of cochlear origin also have been published [10]. In addition to working with AOAA and furosemide, we investigated the potential value of antihistamines in tinnitus patient management.

The first of the nonsedating antihistamines, terfenadine, was investigated for its clinical efficacy in treating tinnitus as a result of anecdotal reports of patients. Terfenadine appeared to be useful in reducing tinnitus of peripheral origin; however, its average effect was found to be only a mild suppression of tinnitus. Terfenadine failed to abolish tinnitus totally in any treated patients, and it appeared to be most effective in patients whose symptom complaint was related to an underlying allergic condition [11].

TREATMENT OPTIONS

Our current treatment armamentarium includes surgery, prescriptive medications, herbal-homeopathic remedies, hearing aids, noise generators, psychological counseling, biofeedback, or electrical suppression. Our current drug trials are attempting to determine the efficacy of the selective serotonin reuptake inhibitors in ameliorating tinnitus in both depressed and nondepressed subjects. Our current tinnitus management tools also lean heavily on using self-help groups, education, and counseling. From the standpoint of counseling, psychological therapy has been emphasized. This includes *cognitive restructuring*, which challenges the accuracy of thought patterns [12]. Also, *attention diversion* has been used to help to develop methods of focus-

Table 1. Drugs Frequently Used in the Treatment of Tinnitus

By Classification	By Action	By Name(s)
Antianxiolytics	Reduce anxiety	Buspar
Anticonvulsants	Reduce endocochlear potential	AOAA
	Reduce polysynaptic responses	Tegretol
Antidepressants	Improve mood and reduce emotional distress	Elavil/Aventyl/Prozac
Antiinflammatory (N-S)	Suppress spontaneous otoacoustic emissions	Aspirin
Antipsychotics	Reduce panic attacks	Zoloft
Diuretics	Reduce endocochlear potential	Lasix
Herbal remedies	Unknown	Gingko biloba
Local anesthetics	Membrane stabilizer	Lidocaine
Nutritional supplements	Restore sensory nerve fiber function	Vitamin B ₁₂
Tranquilizers	Reduce anxiety	Xanax
Vasodilators	Improve blood circulation	Nicotinic acid

AOAA = anticonvulsant aminooxyacetic acid.

ing attention away from the tinnitus complaint. Finally, *imagery training* harnesses the powers of imagination to compete with tinnitus for affected patients' attention. Our psychology and psychiatry colleagues who are trained and knowledgeable in these techniques best perform these treatment approaches. In a less structured approach to nonmedical management, tinnitus retraining therapy has been employed [13]. Recent publications have emphasized the neurophysiological model of tinnitus and we have incorporated this approach into our nonmedical management strategy. This model postulates that although tinnitus may originate within the inner ear, processes within the central nervous system fail to suppress the ongoing tinnitus signal, leading to emotional reactions to the presence of the tinnitus. Tinnitus retraining therapy emphasizes control of this symptom through a prolonged application of education, directed counseling, and low-level noises delivered to the ears to invoke a process of habituation. Accomplishing such control may take as long as 12–18 months.

CONCLUSION

Tinnitus has an intimate relationship with other life events and influences affected patients' ability to perform their jobs, to relate to their families, and to participate in meaningful hobbies. Currently, we do not possess the magic bullet that completely eliminates the tinnitus complaint, but numerous opportunities exist for continued clinical and basic science research that may lead to a cure. As part of the tobacco settlements in many states, certain portions of award moneys have been set aside for ongoing medical research. We suggest that researchers apply for some of these moneys in the form of grants in an effort to better elucidate the association between nicotine and tinnitus complaints.

Finally, we instruct our patients to obtain the most up-to-date information about tinnitus from the American Tinnitus Association. Printed information is given to all our tinnitus patients concerning this organization, and we encourage them to support its efforts to educate patients and to assist in research efforts aimed at alleviating this disorder. Our firm hope and belief are that the

next millennium will bring a better understanding of patients with tinnitus and will offer clinicians and scientists a reliable source of treatment options to improve or even eliminate this malady.

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