



Ototoxicity: Tinnitus as a Drug Side Effect

What Healthcare Providers (and Patients) Should Know

By Robert M. DiSogra, AuD

Determining the cause of tinnitus

in most cases remains elusive to the medical and audiology communities. True, on the basis of the patient's medical, social, or occupational history, some causes, such as blast explosion, concert noise, recreational noise, and head trauma, can be readily linked (but not limited) to tinnitus.

When the cause of tinnitus is unknown, exploration of the patient's drug regimen is the next step in the differential diagnosis. The mechanism causing drug-induced ototoxicity remains unclear. It may involve biochemical and consequent electrophysiological changes in the inner ear and eighth cranial nerve impulse transmission.¹ But exploring

the pathophysiology of tinnitus is beyond the scope of this article. Most physicians and audiologists working with tinnitus patients would agree that damage to the outer cells of the cochlea or changes in the biochemistry within the cochlea would explain the cause of the tinnitus.

Ototoxicity: Tinnitus as a Drug Side Effect

The major classes of drugs known to be ototoxic are antimicrobials, antimalarial drugs, organic and industrial solvents, and some topically administered agents. Added to the list are salicylates, nonsteroidal anti-inflammatory drugs (NSAIDs), aminoglycoside antibiotics, loop diuretics, and chemotherapy agents (e.g., platins and vincristine).²

The Side Effect Resource Database (SIDER 2; <http://sideeffects.embl.de>) reported a total of 996 drugs with a combined side effects total of 4,192. Of these, 275, or 6.5 percent, listed tinnitus as a reported side effect using synonyms such as "ringing in ears" and "ear noise."

Keep in mind that there is no common language for reporting tinnitus during a drug's pre-FDA-approval clinical trials. Therefore, coinvestigators might report tinnitus using descriptors provided by the subject (humming,

buzzing, whistling, ear disturbance, auditory dysfunction, etc.).

It is essential for healthcare providers to understand the risk factors for ototoxicity, which often lead to drug accumulation and an increased potential for permanent hearing loss. These risk factors include medication dose, therapy duration, cumulative lifetime dose, impaired kidney function, infusion rate of certain medications (e.g., IV furosemide, aminoglycosides), co-administration of multiple ototoxic medications (e.g., aminoglycosides with loop diuretics), age, previous exposure to head and neck radiation (chemotherapeutic agents), genetic susceptibility, and family history of ototoxicity.³

Websites for Drug Side Effects Information — Especially Tinnitus

No one knows every drug's indication dosaging and side effects. However, the internet can be a tremendous resource, even though anyone can put up a website (e.g., www.howicuredmytinnitus.com). Winker et al. proposed a list of guidelines for using websites that offer medical information.⁴ One recommendation is that consumers and professionals look only at websites

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that have established credibility, operate under an advisory board, and are updated regularly. Websites should also include appropriate disclaimers that the information on the site is not a substitute for proper medical care.

Consumers and professionals can visit several excellent websites to determine whether any medication has tinnitus as a reported side effect. These include (but are not limited to) the following sites:

www.drugs.com

www.rxlist.com

When you visit a drug information website, simply type in the name of the drug (generic or brand name) and go the “Side Effects” tab. Next, look under “Special Senses” or “Central Nervous System.” If tinnitus is listed, then the next step is to confirm the start date of the drug (or date a drug dosage was increased) with the pharmacist. If the start date of the drug is established and the patient is sure of the start date of the tinnitus, it can be concluded whether the tinnitus is truly an adverse drug reaction.

The prescribing physician should be made aware of this discovery and correlation. The medication dosage might be decreased or the medication discontinued or changed altogether. However, if the prescribed medication is the best one for a particular medical

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condition and is clearly established as the cause of the tinnitus, the management strategy changes.

Onset of Tinnitus

The onset of tinnitus as a result of a drug is usually immediate (within 15 to 20 minutes for oral medications). When a drug enters the bloodstream, it is considered systemic, and therefore both ears would experience tinnitus. If there is a preexisting hearing loss without tinnitus, the poorer ear may be more susceptible to tinnitus. However, if there is preexisting hearing loss with tinnitus, the tinnitus could get louder.

Temporary or Permanent?

Most tinnitus patients report that their drug-related tinnitus lasts for as long as they are taking the medication. In other words, the tinnitus can be

temporary, as in the case of aspirin, nonsteroidal anti-inflammatory drugs, and diuretics. Although the ototoxicity of many drugs resolves after treatment discontinuation, the use of platinum derivatives and aminoglycosides is associated with permanent hearing loss.⁵

The Role of the Pharmacist

In pursuing a drug as the cause of tinnitus, the patient’s pharmacist can provide exact start dates and dates of increased dosaging. Once a time line has been established of when the drug was dispensed (or increased) and tinnitus reported, the audiologist and pharmacist are in a unique position to work together, helping the patient understand and manage the tinnitus. The prescribing physician is also included for medical management.

“What medications do you take and why?”

This is a typical case history question a physician or audiologist asks. The clinician does additional work to pursue the possibility or probability that the patient’s tinnitus complaint may be a drug side effect. With over 220 drugs listing tinnitus as a reported side effect or adverse drug reaction (ADRs)⁶, more detective work is needed to establish whether the tinnitus is truly pathological or not. The terms “side effect” and “adverse drug reaction” are used interchangeably.

Audiometric Testing

When tinnitus is a symptom of a drug side effect or other medical problem, an audiological evaluation should be scheduled to rule out hearing loss as a cause. An audiologist will evaluate hearing and help differentiate between certain types of losses — some of which could be medically or surgically correctable. If there is preexisting hearing loss, the medication could aggravate the condition and the tinnitus could emerge. This is why the information from the pharmacist is critical to determine whether the tinnitus is an adverse event or a sign that hearing loss is getting worse.

“Should I stop my medication if I get tinnitus?”

No! Patients should consult their prescribing physician before cutting back or discontinuing any medication. According to noted auditory researcher Kathleen C. M. Campbell: “The health benefits of the drug far outweigh the risk of tinnitus (or hearing loss).” (K. C. M. Campbell, PhD, personal communication, 2012).

Summary

Despite being a side effect or adverse drug reaction, drug-related tinnitus is manageable and in most cases, is usually temporary and limited to the time the drug is taken. For chemotherapy patients or patients with chronic medical conditions, the health benefits of the drug outweigh the risk of tinnitus. Therefore, counseling is a critical component of tinnitus management. 🌈



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To read DiSogra’s article, “Over-the-Counter Dietary Supplements for Tinnitus: Do They Really Help?” see Tinnitus Today (Winter issue, 2014.)

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- 2 Byung, I. H., Lee, H. W., Kim, T. Y., Lim, J. S., & Shin, K. S. (2009). Tinnitus: Characteristics, causes, mechanisms, and treatments. *Journal of Clinical Neurology*, 5, 11–19.
- 3 Coggins, M. D. (2014). Medication-related ototoxicity. *Today’s Geriatric Medicine*, 7, 6.
- 4 Winker, M. A., Flanagan, A., Chi-Lum, B., White, J., Andrews, K., Kennett, R. L., . . . Musacchio, R. A. (2000). Guidelines for medical and health information sites on the internet — principles governing AMA web sites. *Journal of the American Medical Association*, 283, 1600–1606.
- 5 Lanvers-Kaminsky, C., Zehnhoff-Dinnesen, A. A., Parfitt, R., & Ciarimboli, G. (2017). Drug-induced ototoxicity: Mechanisms, pharmacogenetics, and protective strategies. *Clinical Pharmacology and Therapeutics*, 101, 491–500.
- 6 DiSogra, RM Adverse drug reactions and audiology practice, 3rd edition *Audiology Today*, American Academy of Audiology, September, 2008.



“Thank you for the kindness you have done for me tonight, calling me on a Friday night.”

— Nanette L., daughter of someone with tinnitus