

# Medications Use & Hearing Loss

A Quantitative Correlational Study focused on Active-duty Sailors.

By Adeolu Farohun, Ph.D.

## Abstract

The extent to which ototoxic pharmaceuticals impacted the human auditory system has been repeatedly highlighted in various scientific literature. The mechanisms underlying their selective toxicity to the inner ear remained subjects of concern despite years of investigations. The aim of this retrospective non-experimental correlational study was to determine if the confirmed hearing loss cases among active-duty sailors are associated with the use of ototoxic pharmaceuticals. Over 14,000 samples from age 17 through 62 across the Navy occupations and pay groups were used in this study. The results of this study revealed statistically significant positive correlations between 25 of 106 selected medications and the sailors' confirmed hearing-loss threshold values. The outcome of this study could be helpful in the development of relevant policies to safeguard sailors against combined drug and noise induced hearing loss.

## Background

A 2023 paper from *Annual Review of Pharmacology and Toxicology* reported that over half a million people are diagnosed with permanent hearing loss caused by treatment with therapeutic drugs with ototoxic side effects annually. Hearing loss is the most common sensory disorder in the U.S. and afflicts over 36 million people. Data from the National Health and Nutrition Examination Survey (NHANES) demonstrate that not only is hearing loss highly prevalent among the elderly, but approximately one-third of those aged 40–49 already suffer from hearing loss. In 2006, *Hearing Research* published a paper which was used to shed lights on the sensory cell uptake of ototoxic drugs. It was reported that inner-ear hair cells cannot clear ototoxic drugs such as aminoglycosides, loop

diuretics, analgesics antipyretics, and certain antineoplastic agents from their cytoplasm. These drugs are being retained by the hair cells for extended periods of time. The sensory cell uptake of these drugs, disruption of intracellular physiological pathways, and drug trafficking across endothelial and epithelial barrier layers of the inner ears remained subjects of concerns. Other specific factors that increase the risk of drug-induced toxicity include sustained exposure to higher levels of ambient noise and selected therapeutic agents such as loop diuretics and glycopeptides. Thus, it is thought that the retention of these drugs alongside the higher metabolic rate of hair cells contributes to the human auditory system susceptibility to these drugs.

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### *Synergistic Drug and Noise-induced Hearing Loss*



An AI-generated Image, 2024 February

Considering growing awareness on medications ototoxicity, it became necessary to examine the associations between ototoxic pharmaceuticals and sailors' confirmed hearing-loss threshold values. This study was aimed at determining if cases of hearing loss among active-duty sailors are associated with ototoxic medications commonly being prescribed to sailors. Hence, the overarching hypothesis for this study was that an increase in the ototoxic medications prescribed for or used by active-duty sailors would yield an increase in the hearing-loss threshold values between 2008 and 2023. This study is an essential first step in examining how ototoxic medications might be contributing to the active-duty sailors' hearing loss cases.

#### **Research Method and Design**

This correlational study used retrospective de-identified secondary data collected from the Defense Health Agency, Hearing Center of Excellence (DHA-HCE). The non-experimental correlational study approach often provides more information to initiate future studies than simple experimental studies. Over 14,000 data samples across the Navy occupational codes or rates, pay groups, ranks, ages, gender, and education

levels were provided by the DHA-HCE from 2008 through 2023. Descriptive and multiple linear regression analyses were conducted to assess whether presumed ototoxic medications, days of supply issued, drug form, age, and sex, would significantly predict confirmed hearing loss threshold values at 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hertz. Active-duty sailors' confirmed hearing-loss threshold values at these frequencies were considered as hearing-loss objective indicators in this study. Only samples with confirmed and qualified hearing loss cases and who have taken any of the 106 presumed ototoxic medications as prescribed by their healthcare providers were included in the final analyses.

#### **Findings**

Results showed that there are positive correlations between hypothesized ototoxic medications and the confirmed hearing-loss threshold values at 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hertz between 2008 and 2023. *Adalat CC, Amlodipine Besylate, Antivert, Butalbital-Acetaminophen CA, Compazine, Gralise, Hydrochlorothiazide, Jardiance, LMX 4, Nifedipine, Tylenol Extra Strength, Pain and Fever, Banophen, Mapap, Pain Reliever, Motion Sickness Relief, Pain Relief, Lidocaine, Lidocaine HCL, Meclizine HCL, Ofirmev, Nifedipine ER, Diltiazem 24HR ER, Gabapentin, and Prax* have statistically significant correlation  $p < .001$  with the confirmed hearing-loss threshold values. An increase in these ototoxic medications use resulted in an increase in the mean values of hearing-loss threshold values across all selected hearing frequencies. The results answered the research question. At least 150 days of these 25 medications' use significantly predicted an increase in the mean values of hearing-loss threshold values at 500, 1000, 2000, 3000, 4000, and 6000 Hertz. In addition, the



age group 32-41years significantly predicted an increase in the mean values of hearing-loss threshold values at 2000, 3000, 4000, 6000 and 8000 Hertz. Based on the reviewed literature, the outcome of the analyses was expected. Related studies showed that high doses of nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to be ototoxic in animals and in human case reports, potentially through a reduction in cochlear blood flow. Pre-exposure to salicylates and NSAIDs may potentiate noise-induced hearing loss. Unlike other studies that mostly examined ototoxic chemicals such as solvents, Asphyxiants, Nitriles, metals, and other compounds, this study focused on calculating the association between commonly used medications by sailors (prescription only) and sailors' confirmed hearing-loss threshold values over 15years period.

### Discussion

The outcome of this study necessitates the need to consider all contributing factors to hearing loss when it comes to setting standards. Considering the effects of ototoxic drugs on individuals, it is difficult to argue that the Navy OEL (85dBA) is accurate to safeguard against the synergistic drug and noise-induced hearing loss. This study sheds light on the need to reduce the Navy OEL. Increased use of these medications by the active-duty sailors between age 32 and 41 led to increased mean values of hearing-loss threshold levels at 2000, 3000, 4000, 6000, and 8000 Hertz. This is an indication that drugs or medications with known or reported ototoxicity remained a considerable factor in people's development of hearing loss. Medications that this study revealed are being used to treat High Blood Pressure, Nausea and Vomiting, Muscle Tension and Headache, Diabetes, Fever, Pain, Allergic

Reaction, Motion Sickness, Seizure or Nerve Pain, and Itching.

### Limitations

This study has limitations. The interaction of ototoxic medications and other medications that subjects might be taking could not be investigated. The population of samples used was mostly (91.16%) active-duty males. Thus, the results may not be generalized to non-males. Also, there was no specific information on the exact dose of the ototoxic medications taken, purpose of taking the medication, drug formulations, and confirmation that the medications were used or taken as prescribed. Therefore, calculating the drugs duration-dose or indication-related ototoxicity was not feasible. Consequently, this study focused solely on calculating the associations between ototoxic medications use and hearing-loss threshold values.

### Recommendations

Future studies using larger population-based cohorts of service members across all services are needed to reexamine the extent to which the variance in the hearing-loss threshold values explains the variance in the ototoxic medications. Using only in-patients drug intake data to conduct related future studies will rule out the assumption that all prescribed medications were taken by the sailors. Further research might identify specific variables that influenced the results of this study.

### Conclusions

Without having preventive measures against drug-induced hearing loss, one could infer that the Navy's noise OEL is subjected to an assumption that all personnel are free of exposure to ototoxic pharmaceuticals. In 2018, the National Institute for Occupational Safety and Health (NIOSH) via Publication No. 2018-124 stated that synergistic effects

from the combined ototoxicant and noise exposure could result in hearing loss even when exposures are below the Permissible Exposure Limits (PEL). As published in *Therapies*, a 2023 review conducted with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) using PubMed® database stated that “clinical strategies to limit ototoxicity include identifying patients at risk, monitoring drug concentrations, performing serial hearing assessments and switching to less ototoxic therapy.” The outcome of this study could be helpful in the development of relevant policies to safeguard sailors against combined drug and noise induced hearing loss.

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