

University of South Florida and Indiana University researchers find hearing loss after cisplatin-based chemotherapy in testicular cancer survivors

TAMPA, FL – Many testicular cancer survivors experience hearing loss after cisplatin-based chemotherapy, according to researchers at Indiana University.

The researchers, Biomedical Engineering Professor Robert Frisina, Lois B. Travis, M.D., Sc.D., the Lawrence D. Einhorn Professor of Cancer Research at the IU School of Medicine and a researcher at the Indiana University Melvin and Bren Simon Cancer Center, studied for the first time the cumulative effects of cisplatin-based chemotherapy on hearing levels in testicular cancer survivors through comprehensive audiometry measurements. They found that increasing doses of cisplatin were associated with increased hearing loss at most of the tested frequencies, involving 4, 6, 8, 10, and 12 kHz.

The <u>research</u> was published June 27 in the Journal of Clinical Oncology.

"In addition to hearing loss, about 40 percent of patients also experienced tinnitus (ringing-in-the-ears), which was significantly correlated with reduced hearing," Dr. Travis, also director of the cancer center's Survivorship Research Program, said.

Although this study was conducted in patients with testicular cancer, the authors point out that the general conclusions are likely applicable to patients with other types of adult-onset cancers that are commonly treated with cisplatin. They indicate that it will be important to follow patients given cisplatin-based chemotherapy long-term to better understand the extent to which the natural aging process may further add to hearing deficits, as it does in the general population.

"The results show the importance of comprehensive hearing assessments, preferably, both before and after treatments," Dr. Travis said. "Our findings suggest that health care providers should, at a minimum, annually query patients who have received cisplatin-based chemotherapy about their hearing status, consulting with audiologists as indicated. Patients should also be urged to avoid noise exposure, drugs having adverse effects on hearing, and other factors that may further damage hearing."

Co-first author Robert Frisina, Ph.D., added: "We are the first to show definitively that in a significant number of the cancer survivors, they have hearing loss above-and-beyond age-related hearing loss. They were of different ages --20s to 60s -- so this was a new analysis." Dr. Frisina is a professor in the Department of Chemical and Biomedical Engineering, director of the Biomedical Engineering Program,

and director of the Global Center for Hearing and Speech Research at the University of South Florida. He designed the auditory portion of the study.

Platinum-based cisplatin is one of the most commonly used drugs in medical oncology that also has toxic effects on the inner ear. Despite its use for more than 40 years, knowledge about the effects of cumulative cisplatin dose on hearing loss in survivors of adult-onset cancer has remained limited.

The researchers found that every 100 mg/m² increase in cumulative dose of cisplatin resulted in a 3.2 dB impairment in hearing. The researchers also found high blood pressure was significantly related to hearing loss in these patients, even when cisplatin dose was taken into account. Thus, they emphasized the importance of high blood pressure control.

The researchers pointed out that because alterations in the highly successful testicular cancer regimens are unlikely for patients with advanced disease, their results underscore the importance of ongoing research aimed at the identification of genetic variants associated with cisplatin-related ototoxicity. An ultimate goal is to use the genetic results to develop effective agents that will protect the ear during the administration of cisplatin. For patients treated with cisplatin-based regimens for other types of cancer, it might also influence a physician to offer an alternative to those patients found to be genetically susceptible to the ototoxic effects of cisplatin after carefully weighing the risks and benefits of alternative treatments.

<u>Lawrence Einhorn</u>, M.D., Indiana University Distinguished Professor, Livestrong Foundation Professor of Oncology, and a physician scientist at the IU Simon Cancer Center, also was an author of the study.

In 1974, Dr. Einhorn tested cisplatin with two additional drugs that were effective in killing testis cancer cells. The combination became the cure for this once deadly disease. The results of this three-drug regimen were stunning. Tumors dissolved within days. Subsequent clinical research directed by Dr. Einhorn minimized the extremely toxic side effects of treatment; shortened the duration of two years of therapy to nine to 12 weeks; and established a model for a curable tumor, which has served as a research roadmap for generations of oncologists.

The researchers studied 488 men enrolled in the Platinum Study, which is open at the IU Simon Cancer Center and seven other cancer centers in the United States and Canada. The aim of the study is to gain new information that can benefit future testicular cancer patients and other patients treated with cisplatin-based chemotherapy.

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