Regular Analgesic Use May Increase Risk for Hearing Loss

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March 11, 2010 — Regular use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), or acetaminophen may increase the risk for hearing loss in men, and the impact is larger on those younger than 60 years, according to a prospective study published in the March issue of the *American Journal of Medicine*.

"Aspirin, acetaminophen, and ibuprofen are the 3 most commonly used drugs in the US," write Sharon G. Curhan, MD, ScM, from Brigham and Women's Hospital, Boston, Massachusetts, and colleagues. "Given that analgesic use might result in pathophysiologic changes in the cochlea and that regular use of these analgesics is so common, the relation of these medications and hearing loss might be an important public health issue."

However, Curhan and colleagues point out several study limitations that may affect the results of their study. Two independent commentators interviewed by *Medscape Family Medicine* reiterate these limitations and emphasize that causality cannot be determined from the study results. Yet, both agree that the study focuses on an important issue.

Findings of the Study

The aim of this study was to determine if there was an association between regular analgesic use and the risk for hearing loss.

The study subjects were participants in the Health Professionals Follow-up Study, which enrolled 51,529 male dentists, optometrists, osteopathic physicians, pharmacists, podiatrists, and veterinarians aged 40 to 75 years at baseline in 1986. The participants filled out detailed questionnaires about their diet, medical history, and medication use, including their use of aspirin, NSAIDs, and acetaminophen, at baseline and every 2 years thereafter. Regular analgesic use was defined as 2 or more times per week.

In 2004, the questionnaire asked participants if they had been professionally diagnosed with hearing loss and, if so, the year of their diagnosis. Incident cases were defined as hearing loss diagnosed after 1986.

The authors analyzed 26,917 men from the original cohort. They excluded men who were diagnosed with hearing loss before 1986; those who had been exposed to ototoxic chemotherapeutic agents; and, because age is such a strong risk factor and the prevalence of hearing loss is so high among the elderly population, those who had reached age 75 years during follow-up.

During 369,079 person-years of follow-up, 3488 cases of hearing loss were reported. Regular analgesic use was independently associated with an increased risk for hearing loss for all 3 types of analgesics.

After controlling for age, race, profession, body mass index, alcohol intake, folate intake, physical activity, smoking, hypertension, diabetes, and the use of other classes of analgesics, the hazard ratios of hearing loss in regular users vs those who used aspirin, NSAIDs, or acetaminophen less than twice per week were 1.12 (95% confidence interval [CI], 1.04 - 1.20) for aspirin, 1.21 (95% CI, 1.11 - 1.33) for NSAIDs, and 1.22 (95% CI, 1.07 - 1.39) for acetaminophen.

These results were further adjusted for a history of elevated cholesterol, cardiovascular disease, use of furosemide, rheumatoid arthritis, and osteoarthritis, and remained the same, the study authors report.

The risk for hearing loss also increased with longer duration of regular use. Men who used aspirin regularly for 1 to 4 years were 28% (95% CI, 17% - 40%) more likely to develop hearing loss than those who did not, although this risk did not increase with longer duration of use, the study authors report.

Men who used NSAIDs for 4 or more years were 33% (95% CI, 18% - 49%) more likely to develop hearing loss, and men who used acetaminophen for 4 or more years were also 33% (95% CI, 14% - 56%) more likely to develop hearing loss.

The study authors also report that the magnitude of the association between analgesic use and hearing loss was substantially higher in younger men. For men younger than 50 years, the hazard ratio (HR) for hearing loss was 1.33 for regular aspirin use, 1.61 for NSAIDs, and 1.99 for acetaminophen. No such association was observed in men 60 years and older.

Combining 2 classes of analgesics also increased the risk for hearing loss, the study authors report. The risk was highest when NSAIDs and acetaminophen were combined (HR, 1.58; 95% CI, 1.16 - 2.16).

Study Limitations

That the diagnosis of hearing loss was self-reported is a limitation of this study. Another is the lack of information on lifetime noise exposure, which is a known risk factor for hearing loss.

In addition, the study population consisted of predominantly white men; therefore, the results may not be generalizable to other racial groups. Other studies in women, younger men, and other racial groups are needed to examine whether similar associations between analgesic use and hearing loss exist in these groups, the study authors write.

Hearing loss because of regular use of analgesics represents an important public health issue, "given the high prevalence of regular analgesic use and health and social implications of hearing impairment," the study authors conclude.

Can Definitive Conclusions Be Made From the Study?

Commenting on the study in an interview with *Medscape Family Medicine*, Pamela Roehm, MD, PhD, of the New York University School of Medicine, New York, NY, said it was potentially interesting but had certain limitations that make it difficult to draw any definite conclusions.

Dr. Roehm comments on the limitations cited by the study authors: "The study was not designed to look at the link between hearing loss and analgesic use. They don't have any measures of noise exposure, and this is a huge issue, especially with sensory neural hearing loss in men."

The issue of familial hearing loss was not addressed, and neither was the type of hearing loss. "The genetic predilection for hearing loss was not taken into account. Also, this was a study of professional men, mainly Caucasian. There are going to be some genetic tendencies for hearing loss that have not been taken into account by the study," she said.

She agreed that the association between NSAID use and hearing loss has yet to be explained. However, the association between aspirin and hearing loss is well known to be reversible and therefore a problem that is easily remedied.

With regard to the link between acetaminophen and hearing loss, Dr. Roehm said she would have liked to know if codeine was also involved.

"There is not a lot of literature on acetaminophen on its own being linked to hearing loss. In fact, I couldn't find any at all. But there is quite a bit of recent literature on acetaminophen plus codeine and sensory neural hearing loss. This study brings up interesting associations, but a lot of avenues still need to be explored further," she said.

Medscape Family Medicine also interviewed John K. Niparko, MD, director of otolaryngology at Johns Hopkins Medicine in Baltimore, Maryland, for an independent comment on the study. Dr. Niparko told *Medscape Family Medicine* that the fact that there is no information about noise exposure is a very serious limitation of the study.

"This is a study of observation and association and does not prove that these medicines caused the hearing loss," he said. "These are very valuable medications for a variety of disorders, so we have to be cautious in interpreting results that show an association but do not prove causality."

However, he congratulated the study authors for investigating the potential causes of hearing loss, which "has become a major public health concern in the US."

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