The issue of hearing loss due to ototoxicity is of concern to all audiologists. As new bioactive pharmacological agents are introduced into therapeutic regimens, healthcare providers must be alert for ototoxic side effects, which are frequently unpredictable. Additionally, a number of potential environmental ototoxins have been identified that complicate the clinical picture (see review by Rybak, 1992). These agents include organic solvents, asphyxiant gases, and heavy metals.

One frustration to healthcare providers and patients is the intersubject variability of ototoxicity in general. The amount of hearing loss for a given dose and duration can vary widely across individuals. Hearing loss, typically high frequency and symmetric, may be asymmetric and occur in a variety of configurations. With repeated dosing, a patient may show no change after several administrations, then have a sudden marked change with one additional dose. Further, hearing loss may first appear or progress after discontinuation of the ototoxic agent.

Aminoglycosides have been known to cause hearing loss since they were introduced in the 1940s. Advances in the development of other antibiotics, new formulations of aminoglycosides, and routine monitoring of peak and trough levels, creatinine clearance, serum albumin, dosing levels, and duration have reduced, but not eliminated, aminoglycoside ototoxicity (Meyerhoff, Maale, Yellin, & Roland, 1989). Aminoglycosides are still used in the treatment of moderate to severe infections, frequently in combination with other agents or other aminoglycosides. In these cases, the synergistic effects of these combinations may increase ototoxicity unpredictably (Brummett et al., 1990). Additionally, the patient’s history of aminoglycoside use may be unavailable, yet prior use potentiates the development of ototoxicity. Unfortunately, even when possible, many studies and many clinicians do not monitor bone conduction levels or middle ear function in addition to air conduction monitoring. Because patients with moderate to severe infections could have (or develop) otitis media, the absence of these data complicates interpretation.

Animal studies have demonstrated interactive effects among development, noise exposure, and aminoglycosides (Dodson, Bannister, & Douek, 1982; Uziel, 1985). Combinations of these factors produce hearing losses that exceed simple additive effects. In studies of altricious animals that are not fully developed at birth, there appears to be a critical period of exposure. During this critical period, at least for some species, the animal is markedly susceptible to aminoglycoside ototoxicity. With the survival of increasingly premature infants (who are more likely to receive aminoglycosides than are term infants), the risk of ototoxicity may also be higher. The combination of noise exposure and aminoglycosides may be of clinical importance, as when older inpatients use their Walkmans or when infants are placed in incubators. Further studies in humans will be required to investigate these potential interactive effects.

Loop diuretics, including furosemide, bumetanide, and ethacrynic acid, produce hearing losses that are generally reversible; however, irreversible ototoxicity can be increased when these drugs are used in combination with aminoglycosides. Because concomitant use is sometimes unavoidable, guidelines need to be developed for audiologic monitoring according to dosage levels. Furthermore, there is recent evidence that furosemide may cause permanent sensorineural hearing loss in neonates (Brown, Watchko, & Sabo, 1991).

Aspirin has been studied extensively and appears to produce hearing loss that is entirely reversible. For patients who require chronic, high-dosage salicylate administration and cannot be readily switched to other analgesic/anti-inflammatory agents, the tinnitus and hearing loss may still prove problematic.

Aminoglycosides have been known to cause hearing loss since they were introduced in the 1940s. Advances in the development of other antibiotics, new formulations of aminoglycosides, and routine monitoring of peak and trough levels, creatinine clearance, serum albumin, dosing levels, and duration have reduced, but not eliminated, aminoglycoside ototoxicity (Meyerhoff, Maale, Yellin, & Roland, 1989). Aminoglycosides are still used in the treatment of moderate to severe infections, frequently in combination with other agents or other aminoglycosides. In these cases, the synergistic effects of these combinations may increase ototoxicity unpredictably (Brummett et al., 1990). Additionally, the patient’s history of aminoglycoside use may be unavailable, yet prior use potentiates the development of ototoxicity. Unfortunately, even when possible, many studies and many
extremely difficult time for the patient and his or her family. If these patients are not monitored for ototoxicity, their communication difficulty could be attributed to cognitive impairment, malaise, or emotional stress.

Several agents have been suggested as protective or rescue agents to ameliorate the ototoxicity of cisplatin agents (Gandara, Perez, Wiebe, & Gregorio, 1991) but none are being used clinically yet. Hopefully, further research will identify a safe, effective protective agent.

Currently the audiologist has a wide array of options for monitoring auditory ototoxicity. Standard audiometrics, high frequency air conduction, ABR testing, otoacoustic emissions, and tinnitus monitoring are all under investigation. Monitoring issues are further complicated by several patient factors. Patients may be too ill for extensive behavioral measures and may be unable to be transported to the audiology clinic. Bedside testing is frequently limited by the ambient acoustic and electrical noise of the hospital room. Because some insurance companies provide limited or no coverage for audioligic testing, cost may be a factor for the repeated testing needed. We need to determine the procedures that are most effective in terms of audiologic management and cost for providing services to these patients.

Clinical studies and basic science research in ototoxicity are both progressing in a variety of areas. For a more comprehensive review of current issues in ototoxicity, the reader is referred to the upcoming 1993 issue of the Otolaryngologic Clinics of North America (in press), which will address the issue of ototoxicity and will include a chapter on audiologic monitoring.

Ototoxicity is an exciting and rapidly expanding area of audiologic practice and research. Working in conjunction with otolaryngologists, neonatologists, oncologists, infectious disease specialists, and basic scientists, we can improve patient care and our understanding of the underlying mechanisms of ototoxicity.

Acknowledgment

Financial support for the preparation of this manuscript was provided by the NIDCD, National Institutes of Health, Bethesda, MD, Grant 1K08 DC00040-01

References


Contact author: Kathleen C. M. Campbell, PhD, Division of Otolaryngology, SIU School of Medicine, P.O. Box 19230, 301 North Eighth Street, Springfield, IL 62794-9230.

Key Words: Ototoxicity, hearing loss, aminoglycosides, chemotherapeutic agents, loop diuretics.