

Incidence of The Risk of Ototoxicity in Patients Undergoing Treatment with Aminoglycosides

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ABSTRACT

Hearing is considered one of the fundamental human senses and is essential for maintaining an adequate quality of life. Currently, hearing loss is recognized as a serious problem and is classified as a disability, with affected individuals being susceptible to social stigmatization and isolation. This condition may even lead to increased risk of accidents, such as traffic incidents, thereby generating additional complications for the patient.

Aminoglycoside-induced ototoxicity is an irreversible adverse effect, typically presenting bilaterally and causing permanent sensory cell degeneration. Multiple mechanisms may contribute to its development during treatment with these drugs, ultimately leading to hearing loss. Although the exact mechanisms underlying this toxicity are not fully understood, reports of this severe adverse effect are increasing. Despite this, aminoglycosides continue to be widely used worldwide due to their low cost, availability, and effectiveness.

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INTRODUCTION

The history of aminoglycosides began in 1944 with the discovery of streptomycin. Later developments included kanamycin in 1957, followed by gentamicin and tobramycin, which represented significant advances in the treatment of infections caused by gram-negative bacilli. Consequently, these antimicrobials became standard therapy for such infections.

In the 1970s, semisynthetic aminoglycosides such as dibekacin, amikacin, and netilmicin demonstrated activity against resistant bacterial strains and exhibited different toxicological profiles. However, widespread use revealed significant issues, including toxicity, bacterial resistance, and superinfection. It was also established that modifying aminoglycoside molecules to reduce toxicity often compromised their antimicrobial activity. As a result, the development of new aminoglycosides has slowed considerably.

In recent decades, however, advances in pharmacodynamic, experimental, and clinical research have led to a better understanding of these drugs and to the implementation of improved dosing strategies.

Aminoglycosides have been used for over 40 years and are primarily active against aerobic gram-negative bacilli and mycobacteria. Despite their broad therapeutic spectrum, their use has been limited due to nephrotoxicity and ototoxicity.

Therefore, recommendations have been established to minimize these adverse effects while maintaining their clinical utility.

FRAMEWORK

Ototoxicity can be defined as cellular degeneration and functional disruption of the cochlea and vestibular system in the inner ear caused by pharmacological agents. Aminoglycosides are a major contributor to ototoxicity due to their widespread use.

Prolonged use (≥ 6 weeks) predisposes patients to hearing loss. Ototoxicity may appear even after treatment has ended and often becomes irreversible. The risk is proportional to both the dose and duration of therapy. Additional risk factors include age, renal dysfunction, mitochondrial mutations, concurrent use of other ototoxic drugs (e.g., loop diuretics), and noise exposure.

Clinically, ototoxicity may present as cochlear damage (permanent hearing loss) or vestibular damage (dizziness, ataxia, nystagmus). Aminoglycosides primarily affect sensory hair cells in the cochlea, typically beginning at the basal turn and progressing toward the apex. Streptomycin and gentamicin are predominantly vestibulotoxic, whereas neomycin and kanamycin are more cochleotoxic.

Toxic effects are first observed in outer hair cells of the basal cochlear turn. Damage progresses from inner to outer rows

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and extends to higher cochlear turns, initially affecting high-frequency hearing before involving lower frequencies. Inner hair cells remain intact until surrounding outer hair cells are destroyed. In severe cases, the organ of Corti collapses, and the spiral ganglion undergoes degeneration.

Mechanistically, aminoglycosides induce cell death via reactive oxygen species (ROS), activating pathways such as JNK and mitochondrial apoptosis. The Bax protein promotes apoptosis, while Bcl-2 inhibits it. ROS generated by mitochondria further exacerbate cellular damage.

Dong et al. demonstrated that NaHS protects cochlear hair cells from gentamicin-induced toxicity by inhibiting mitochondrial apoptosis. Their findings showed increased cell viability in treated cultures.

Following hair cell death, replacement by scar tissue leads to profound deafness. Abbas et al. used gerbil models to study this process, demonstrating that a single dose of kanamycin combined with furosemide effectively induces significant hearing loss, while preserving some neuronal structures.

Aminoglycosides also produce nephrotoxicity. Early renal damage can be detected by biomarkers such as N-acetyl- β -glucosaminidase (NAG). Blunston et al. showed that nephrotoxicity may be reduced by administering high doses during specific circadian periods.

In neonates, strict monitoring of serum gentamicin levels is essential to reduce ototoxicity risk. In patients with cystic fibrosis, repeated aminoglycoside exposure increases the risk of hearing loss. High-frequency audiometry (EHF) and otoacoustic emissions (DPOAE) are more sensitive methods for early detection.

DISCUSSION

Aminoglycosides are widely used for severe infections, including multidrug-resistant gram-negative infections and tuberculosis. With the increasing incidence of tuberculosis globally, the use of these ototoxic drugs has also increased.

The findings of this review are consistent with previous studies, confirming that aminoglycoside-induced ototoxicity results from cellular degeneration. Prolonged exposure (≥ 6 weeks) can lead to complete hearing loss.

Hearing loss imposes significant social and economic burdens. Children with hearing impairment often experience delays in speech and cognitive development, while adults may face employment difficulties (WHO, 2014).

Given that ototoxicity risk is dose- and duration-dependent, alternative therapeutic strategies should be explored. Studies such as those by Dong suggest potential protective agents (e.g., NaHS). Abbas demonstrated that specific drug combinations can induce ototoxicity efficiently, highlighting the need for safer treatment protocols.

Further research is necessary to determine which aminoglycosides present the lowest risk.

CONCLUSIONS

This study confirms a strong association between aminoglycoside use and increased risk of ototoxicity and nephrotoxicity. Although both occur, this research focused on ototoxicity.

Aminoglycosides remain widely used in monotherapy for severe infections. Advances in pharmacokinetics support single-dose regimens, which maintain efficacy while reducing toxicity.

Clinicians must carefully consider treatment duration, daily dose, and total cumulative dose. Patient history, including prior aminoglycoside exposure and genetic predisposition, should also be evaluated.

As antibiotic use continues to rise, so does the risk of adverse effects such as ototoxicity. Continuous medical education is essential to minimize these risks and improve patient outcomes.

REFERENCES

- I. Sagit, M., Korkmaz, F., Gürgen, S., Kaya, M., Akcadag, A. and Ozcan, I. (2014). The protective role of thymoquinone in the prevention of gentamicin ototoxicity. *American Journal of Otolaryngology*, 35(5), pp.603-609.
- II. Papadakis a. maxine, stephen j. mcphree. *Current. cmdt. Medical diagnosis and treatment*. Elsevier. mcgraw-hill. 2015.
- III. Mohamed N. El-barbary, Rania I.H. Ismail, Adel A.A. Ibrahim. Gentamicin extended interval regimen and ototoxicity in neonates. M.N. El-barbary et al. / *International Journal of Pediatric Otorhinolaryngology* 79 (2015) 1294–1298.
- IV. Abbas, Leila, and Marcelo N. Rivolta. "Aminoglycoside Ototoxicity and Hair Cell Ablation in the Adult Gerbil: A Simple Model to Study Hair Cell Loss and Regeneration". *Hearing Research* 325 (2015): 12-26. Web.
- V. Dong, Yaodong et al. "Nahs Protects Cochlear Hair Cells From Gentamicin-Induced Ototoxicity By Inhibiting The Mitochondrial Apoptosis Pathway". *PLOS ONE* 10.8 (2015): e0136051. Web.
- VI. J.-W. Koo, L. Quintanilla-Dieck, M. Jiang, J. Liu, Z. D. Urdang, J.J. Allensworth, et. Al. Endotoxemia-mediated inflammation potentiates aminoglycoside-induced ototoxicity. *Sci Transl Med*. 2015 July 29; 7(298): 298ra118.
- VII. Sogebi O, Adefuye B, Adebola S , Oladeji S , Adedeji T. Clinical predictors of aminoglycoside-induced ototoxicity in drug-resistant Tuberculosis patients on intensive therapy. O.A. Sogebi et al. / *Auris Nasus Larynx* xxx (2016) xxx–xxx.
- VIII. BlunstonM, Yonovitz A, Woodahl E, Smolensky M. Gentamicin-Induced Ototoxicity and Nephrotoxicity Vary with Circadian Time of

Incidence of The Risk of Ototoxicity in Patients Undergoing Treatment with Aminoglycosides

- Treatment and Entail Separate Mechanisms. *Chronobiol Int.* 2015; 32(9): 1223–1232.
- IX. He, Jing-chun et al. "Streptomycin Ototoxicity In Rat Cochlear Organotypic Cultures". *Cell Biochemistry and Biophysics* 71.2 (2014): 851-856. Web. 26 Apr. 2017.
- X. Adebolajo A. Adeyemo, Odunayo Oluwatosin, and Olayemi O. Omotade. Study of streptomycin-induced ototoxicity: protocol for a longitudinal study. *Springerplus.* 2016; 5(1): 758.
- XI. Ghada Al-Malky, Sally J. Dawson, Tony Sirimanna, Emmanouil Bagkeris, Ranjan Suri. High-frequency audiometry reveals high prevalence of aminoglycoside ototoxicity in children with cystic fibrosis. *Journal of Cystic Fibrosis* 14 (2015) 248–254.
- XII. J. L.Llorente pendas, C. A. Álvarez Marcos, F. J. Nuñez Batalla. *Otorrinolaringología.* 1ra ed. México. Panamericana. 2011.
- XIII. Anil k. Lalwani. *Otorrinolaringología. Current diagnosis & treatment otolaryngology--head and neck surgery* third edition. 3th ed. USA. McGraw-Hill. 2012.