



Ear drops and ototoxicity

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Summary

Ototoxicity is a rare but potentially serious complication of the use of aminoglycoside and other cochleo-toxic ear drops. This risk is increased when there is a perforation of the tympanic membrane or a patent grommet. Until recently, no alternatives to potentially ototoxic antibiotic ear drops were approved in Australia. The approval of fluoroquinolone ear drops means that an alternative to the aminoglycosides is now available for use in the open middle ear. Guidelines from the Australian Society of Otolaryngology Head and Neck Surgery state that non-ototoxic antibiotic ear drops are preferable for the management of a discharging middle ear.

Key words: aminoglycosides, antibiotics, fluoroquinolones, hearing.

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Introduction

The risks of systemic ototoxicity from various drugs, such as the aminoglycosides, are well known. Less well known is the potential for ototoxicity when these drugs are prescribed as ear drops for patients with tympanic membrane perforations. Although some antibiotic ear drops have been used for 40 years in Australia, ototoxicity has become an increasing concern globally over the last ten years. Aminoglycoside ototoxicity can affect not only the cochlea (hearing) but also the vestibular (balance) system.

Aminoglycoside ototoxicity

The most frequently prescribed antibiotic ear drops in Australia are a combination of framycetin (an aminoglycoside), gramidicin and dexamethasone. Aminoglycoside ear drops may cause hearing loss or balance disorder in about 1 in 10 000 patients, but the true incidence of topical ototoxicity is unknown. It may be much more common, but not recognised for various reasons, including:

- lack of pre- and post-treatment audiograms or balance assessment
- lack of audiologic testing for frequencies greater than 8000 Hz
- attribution of any hearing loss to the underlying disease process.

There is no doubt that some ingredients of older ear drops, especially but not limited to aminoglycosides, have the potential to cause severe cochlear and vestibular ototoxicity. Neomycin is probably the most toxic of the aminoglycosides followed by gentamicin and tobramycin. (Framycetin is a major component of neomycin.) Repeated and prolonged courses of treatment increase the risk of toxicity.

In a survey of 2235 American otolaryngologists, 3.4% reported having seen a patient with probable ototoxicity secondary to the use of potentially ototoxic ear drops in the presence of a tympanic membrane perforation or open mastoid cavity.¹ In a Canadian series of nine patients prescribed gentamicin drops (not generally used in Australia except for deliberate ablation of vestibular function in Ménière's disease) four developed balance symptoms that were so incapacitating that they required mechanical aids to help them walk.²

Factors affecting topical ototoxicity

A clinician may prescribe ototoxic ear drops for an apparent otitis externa or wax-obstructed ear canal, but if there is an undetected tympanic membrane perforation a profound sensorineural hearing loss may result. In the presence of a tympanic membrane perforation, open mastoid cavity or patent grommet, topical antibiotics can cause ototoxicity within a few days, although most cases follow prolonged therapy. The absorption of drops is affected by the presence or absence of thickened middle ear mucosa and round window membrane (the latter being the portal of entry of the drops to the inner ear). The presence of granulation tissue, webs or polypoid tissue can also prevent ear drop access to the round window. There are genetic factors in some patients of Asian or Arabic origin causing them to be uniquely sensitive to the ototoxic effects of ear drops.

Ototoxic ear drops – overseas recommendations

The British³, Canadian⁴ and US⁵ guidelines or protocols for the use of ototoxic ear drops in the open middle ear recommend against the use of aminoglycosides with a tympanic membrane perforation. The evidence-based recommendations of the expert consensus panel of the American Academy of Otolaryngology – Head and Neck Surgery regarding efficacy and safety of topical antibiotics in the treatment of ear disease have been adopted, with minor variations, by the Australian Society of Otolaryngology Head and Neck Surgery pharmaceutical sub-committee (see box).⁶

The Australian situation

The majority of prescriptions for antibiotic ear drops in Australia have been for potentially ototoxic aminoglycoside-containing drops. Six cases of deafness in patients using combination ear drops have been reported to the Adverse Drug Reactions Advisory Committee. The product information states the drops are contraindicated in the presence of tympanic membrane perforations yet they are still used as first-line management of discharging middle ears. In children with chronic suppurative otitis media, particularly Aboriginal and Torres Strait Islander children, repeat courses of potentially ototoxic drops have been used for prolonged periods, placing these often audiotically unmonitored children at risk of sensorineural hearing loss. The Therapeutic Guidelines: Antibiotic recommends aural toilet for chronic suppurative otitis media and limits any aminoglycoside drops to seven days of treatment. If there is no response after seven days a topical fluoroquinolone is recommended.

A study by the National Aboriginal Community Controlled Health Organisation compared fluoroquinolone ear drops with a combination of framycetin, gramicidin and dexamethasone. In 111 children with ears infected by the usual organisms isolated in chronic suppurative otitis media (*Pseudomonas aeruginosa*, *Staphylococcus aureus*), the efficacy of ciprofloxacin was significantly greater.⁷ There was a clinical cure in 42 of the 55 children given ciprofloxacin, compared with 29 of the 56 children given the combination.

The recommended duration of ciprofloxacin therapy is nine days, and safety and efficacy are unknown beyond 14 days. There is concern about bacterial resistance to the fluoroquinolones, but no controlled studies with pre- and post-treatment minimum inhibitory concentration/sensitivity testing have detected fluoroquinolone resistance in the absence of previous systemic fluoroquinolone treatment. The local high

Australian Society of Otolaryngology Head and Neck Surgery recommendations⁶

1. Non-ototoxic eardrops are preferable in the presence of tympanic membrane perforations.
2. If potentially ototoxic drops are used for discharging middle ears, they should be ceased immediately the infection resolves.
3. Patient's/parental informed decision making should be documented for use of potentially ototoxic eardrops.
4. If hearing loss, vertigo, or tinnitus develop while using potentially ototoxic ear drops the patient should be instructed to return to their doctor.
5. If the tympanic membrane is known to be intact and the middle ear and mastoid are closed, then the use of potentially ototoxic preparations presents no risk of ototoxic injury.

concentration of topical drops ensures that they are bactericidal to bacteria in the middle ear and mastoid, although a bacterial biofilm may persist.

Ciprofloxacin drops as an ear preparation have been approved by the Therapeutic Goods Administration, and the Pharmaceutical Benefits Scheme subsidises them for use in chronic suppurative otitis media in Aboriginal and Torres Strait Islander patients over the age of one month. A private prescription is necessary for other patients.

Conclusion

The ototoxicity of commonly prescribed aminoglycoside ear drops, although rare, poses a therapeutic dilemma for the prescribing physician. The use of ototoxic ear drops should be avoided in patients with perforations of the tympanic membrane. The Australian recommendations provide a clear plan of management for the discharging middle ear and raise awareness of an alternative therapeutic option using non-ototoxic fluoroquinolone rather than potentially ototoxic ear drops.

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Further reading

For a list of further references see this article online at www.australianprescriber.com in Vol. 31 No. 2.

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