Evidence-Based Systematic Review: Drug-Induced Hearing Loss—Tobramycin

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Introduction

Tobramycin was introduced in 1967, several years after the discovery of gentamicin, and is indicated for the treatment of infections caused by gram-negative bacteria. Although similar in pharmacokinetic properties to gentamicin, tobramycin has been shown to be more effective in the treatment of infections caused by *Pseudomonas aeruginosa* (*P. aeruginosa*; Siegenthaler, Bonetti, & Luthy, 1986). Tobramycin is commonly used to treat pulmonary complications in individuals with cystic fibrosis (Bates et al., 1997) and has also been studied in the treatment of neonatal bacterial infections (deHoog, van Zanten, Hoeve, Blom, & van den Anker, 2002), peritonitis (Nikolaidis et al., 1991), and renal impairment with bacterial infections (Gorse, Bernstein, Cronin, & Etzell, 1992). In the treatment of cystic fibrosis patients with *P. aeruginosa*, tobramycin is typically administered via inhalation of a solution. TOBI® is one such prescription solution. The product information for TOBI indicates that although patients receiving TOBI did not demonstrate symptoms of hearing loss during clinical studies, some patients reported hearing loss post marketing. Patients also reported transient tinnitus. The product information additionally urges caution when prescribing TOBI to patients with pre-existing auditory or vestibular impairment (TOBI, 2006, p. 1015). A systematic review (Govaerts et al., 1990) summarized the incidence of

ototoxicity and vestibulotoxicity for several aminoglycosides. The incidence of ototoxicity in individuals administered tobramycin ranged from 0.5% (Andreu et al., 1985, as cited in Govaerts et al., 1990) to 25% (Tablan, Reyes, Rintelmann, & Lerner, 1984). Tablan et al. noted that patients received high doses of tobramycin for extended time periods.

The intent of this systematic review is to evaluate the evidence regarding the incidence and persistence of hearing loss in patients receiving tobramycin. Additionally, the possible effects of dosage, schedule of administration, route of administration, and concurrent ototoxic drug use are examined. This review may provide audiologists with valuable evidence that will help them better advise physicians on potential hearing risks, monitor the hearing of patients receiving tobramycin, and provide hearing amplification as appropriate to those who need it.

This systematic review is part of a series exploring the effects of aminoglycoside use on hearing function. Two other aminoglycosides (i.e., gentamicin and amikacin) are included in the series. Additional information pertaining to the objectives of these systematic reviews and procedures for searching, sifting, and appraising the evidence is included in the introductory paper titled Evidence-Based Systematic Review (EBSR): Drug-Induced Hearing Loss—Aminoglycosides.

The following six clinical questions were formulated to guide the review process:

1. What is the likelihood of persons treated with tobramycin developing hearing loss?
2. What is the persistence of hearing loss in persons treated with tobramycin?
3. Is the likelihood of tobramycin-induced hearing loss affected by dosage?
4. Is the likelihood of tobramycin-induced hearing loss affected by route of administration?
5. Is the likelihood of tobramycin-induced hearing loss affected by schedule of administration?
6. Is there evidence of a synergistic effect on hearing loss if multiple ototoxic drugs (e.g., aminoglycosides, antineoplastics, etc.) are taken concomitantly with tobramycin?

Results

Twelve studies were identified for inclusion in this review. The studies provided sufficient information to address five of the six clinical questions. No studies provided sufficient information to address Clinical Question 2 regarding the persistence of hearing loss (see Table 1).

Table 1. Included studies and corresponding clinical questions addressed.

Study	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6
Bates et al., 1997	X			X	X	
de Hoog et al., 2003	X		X	X		X
de Hoog et al., 2002	X		X	X		
Fausti et al., 1999	X					
Gorse et al., 1992	X					
Li et al., 1991	X			X		
Mukhopadhyay et al., 1993	X		X	X		
Nikolaidis et al., 1991	X		X	X		
Ramsey et al., 1993	X		X	X	X	
Ramsey et al., 1999	X		X	X	X	
Sánchez-Alcaraz et al., 1998	X		X	X	X	
Smyth et al., 2005	X		X		X	

Study Quality and Participant Characteristics

Table 2 details the participant characteristics and methodological quality of the included studies. The studies consisted of two controlled trials, eight case series, and two case control studies, together totaling 842 participants and 28 ears (Fausti et al., 1999, reported data by ear) with analyzable data. Half of the studies (six) assessed tobramycin administration in children and adults with pulmonary complications secondary to cystic fibrosis. The remaining studies examined the effects of tobramycin administration to neonates with possible infection, adults with infection secondary to renal disease, adults receiving a bone marrow transplant, or individuals with serious infections.

The methodological quality of the included studies ranged from 3/6 to 6/6. The majority of studies (83%) received quality markers of 4/6 or 5/6. Common areas of methodological weakness included failure to blind assessors to the intervention; failure to hold dosage, schedule, or route of administration constant across participants (or to adjust results in consideration of these variables); and, to a lesser extent, failure to report the pre-treatment hearing status of participants.

Table 2. Methodological quality and patient characteristics of included studies.

Study	Study design	Medical diagnosis	Mean age yrs (range)	Sample clearly defined	Pre-hearing status reported	> 80% follow up	Outcome measure(s) clearly defined	Assessor blinded	Same treatment regime or stratified	Quality score
Bates et al., 1997	Case series	Cystic fibrosis with pulmonary exacerbation	24.6 (6.6–44.8)	Y	Y	Y	Y	N	N	4/6
deHoog et al., 2003	Case control	Neonates admitted to the NICU	Median 19 days (0–286 days)	Y	N	Y	Y	N	Y	4/6
de Hoog et al., 2002	Case control	Children admitted to the NICU as neonates with suspected septicemia	(3–4)	Y	N	Y	Y	Y	N	4/6
Fausti et al., 1999	Case series	Not stated	Not stated	N	Y	Y	Y	N	N	3/6
Gorse et al., 1992	Case series*	Serious bacterial infections and pre-existing renal impairment	66.4	Y	Y	Y	Y	Y	N	5/6
Li et al., 1991	Case series*	Cystic fibrosis with pulmonary infection	23	Y	Y	Y	Y	N	N	4/6

(continued)

Table 2 (continued)

Study	Study design	Medical diagnosis	Mean age yrs (range)	Sample clearly defined	Pre-hearing status reported	>80% follow up	Outcome measure(s) clearly defined	Assessor blinded	Same treatment regime or stratified	Quality score
Mukhopadhyay et al., 1993	Case series	Cystic fibrosis with respiratory infection	11.6 (4–19)	Y	Y	Y	Y	N	Y	5/6
Nikolaidis et al., 1991	Case series	End-stage renal disease	60.2 (19–80)	Y	Y	Y	Y	N	Y	5/6
Ramsey et al., 1993	Case series[a]	Cystic fibrosis with history of severe infection	16.6–17.7	Y	Y	Y	Y	Y	Y	6/6
Ramsey et al., 1999	Case series[a]	Cystic fibrosis with history of severe infection	20.8 *N* = 118 < 18 yrs *N* = 140 ≥18 yrs	Y	N	Y	Y	Y	Y	5/6
Sánchez-Alcaraz et al., 1998	Controlled trial	Severe infection	54.7 (16–80)	Y	Y	Y	Y	N	Y	5/6
Smyth et al., 2005	Controlled trial	Cystic fibrosis with pulmonary infection	14.8 (5.1–50.4)	Y	Y	Y	Y	Y	N	5/6

Note. [a]These studies are controlled trials by design; however, the studies are classified as "case series" for the purposes of this review for one of two reasons: (1) Only one arm of the study is applicable for inclusion in the review, or (2) the comparative piece is not pertinent to this review; therefore, the results of the two arms are collapsed in the results of this review. NICU = neonatal intensive care unit.

Clinical Question 1: What Is the Likelihood of Persons Treated With Tobramycin Developing Hearing Loss?

All twelve studies provided sufficient information to address this question. Details of hearing measures are listed in Table 3. The incidence of hearing loss in individuals treated with tobramycin ranged from 0% to 33%. One study, Fausti et al. (1999), reported hearing loss by ears rather than by individual at an incidence of 18%. The heterogeneity of the included studies—particularly the variability in hearing loss criteria—does not allow for a reliable calculation of the pooled incidence of hearing loss for the purposes of meta-analysis. Additionally, factors such as medical diagnosis, age, methodological quality, study design, and hearing loss criteria, contributed to the differences among the included studies. Given this, the results of this question are further stratified in order to note trends among these factors. Fausti et al. (1999) is not included in these analyses, as it did not report incidence by individual.

The majority of included studies (10/12) assessed hearing loss with pure-tone averages (PTAs). The remaining two studies (de Hoog, van Zanten, Hoeve, Blom, & van den Anker, 2002; deHoog et al., 2003) assessed hearing via auditory brainstem response (ABR). In addition to ABR, deHoog et al. (2002) also assessed hearing with otoacoustic emissions (OAE).

Hearing loss criteria

As shown in Table 3, the criteria for hearing loss differed across studies. One study (Gorse, Bernstein, Cronin, & Etzell, 1992) selected a relatively sensitive criteria for hearing loss (≥ 15-dB increase in at least one frequency in one ear) and reported an 11.1% incidence of hearing loss. Several studies (Bates et al., 1997; Li et al., 1991; Mukhopadhyay, Baer, Blanshard, Coleman, & Carswell, 1993; Nikolaidis et al., 1991; Ramsey et al., 1993) utilized moderate criteria (≥ 20-dB increase in at least one frequency in one ear or ≥ 15-dB increase in at least two frequencies in one ear). The incidences for these studies with moderate criteria ranged from 0% to 25%. Two studies (Ramsey et al., 1999; Smyth et al., 2005) defined hearing loss with relatively specific criteria (bilateral increase of ≥ 15 dB in two consecutive frequencies in both ears or ≥ 20-dB increase in at least two frequencies in one ear) with no incidence of hearing loss reported in either study.

Medical diagnosis

Notably, six studies with a total of 566 participants addressed tobramycin administration to children and adults with pulmonary complications secondary to cystic fibrosis (Bates et al., 1997; Li et al., 1991; Mukhopadhyay et al., 1993; Ramsey et al., 1993, 1999; Smyth et al., 2005) and reported 0% incidence of hearing loss. The incidence of hearing loss in infants, children, and adults administered tobramycin to

treat infection or prevent infection in immunocompromised patients ranged from 0% to 33%.

Age

Two studies (de Hoog et al., 2002, 2003) investigated the hearing outcomes of children and infants administered tobramycin in the neonatal period. The incidence of hearing loss ranged from 2% to 33%. Note, however, that the incidence of 33% is based on a sample size of nine children. Only one study (Ramsey et al., 1999) had analyzable results for children between 6 and 18 years of age. None of the 118 children demonstrated hearing loss. Several studies included a mixed age range of children and adults (Bates et al., 1997; Mukhopadhyay et al., 1993; Sánchez-Alcaraz et al., 1998; Smyth et al., 2005); the incidence of hearing loss in these populations ranged from 0% to 2%. Two studies (Nikolaidis et al., 1991; Ramsey et al., 1999) analyzed the effects of tobramycin applied to an adult population; the incidences of hearing loss ranged from 0% to 25%. Several studies were not included in these analyses, as the age range of individuals was not stated. Three studies (Gorse et al., 1992; Nikolaidis et al., 1991; Sánchez-Alcaraz et al., 1998) reported the mean age of participants to be over 50 years. Hearing loss in these studies ranged from 2% to 25%. The mean age of participants in the Gorse et al. (1992) and Nikolaidis et al. (1991) studies was above 60 years, with corresponding incidences of 11.1% (2/18) and 25% (10/40), respectively.

Study design

The majority (67%) of included studies were case series. The incidence of hearing loss in these studies ranged from 0% to 25%. The two case control studies (de Hoog et al., 2002, 2003) reported incidences of 33% and 2%, respectively. The two controlled trials (Sánchez-Alcaraz et al., 1998; Smyth et al., 2005) reported 2% and 0% incidences, respectively.

Methodological quality

It is also important to consider the incidence of hearing loss after tobramycin exposure in the context of methodological quality and hearing loss criteria. The methodological quality of the included studies ranged from 3/6 to 6/6. The reported incidence of hearing loss for the single study (Ramsey et al., 1993) that met the highest quality level (6/6) was 0% (0/71). For the studies meeting 4/6 or 5/6 quality measures, the incidence of hearing loss ranged from 0% to 33%.

Table 3. Studies addressing incidence of hearing loss post-tobramycin treatment.

Study	Assessment instrument			HL criteria (dB loss post-treatment)	% HL post-treatment
	PTA	ABR	OAE		
Bates et al., 1997	X			≥ 20 dB increase in at least 1 freq. in 1 ear	0% (0/18)
de Hoog et al., 2002		X	X	Pass/fail: CEOAE at 82 dB SPL; DPOAE f1 at 60 dB SPL; f2 at 55 dB SPL, confirmed with ABR (pass criteria not stated)	33% (3/9)
de Hoog et al., 2003		X		Pass with response at 35 dB	2% (3/166)
Fausti et al., 1999	X			≥ 20 dB increase in at least 1 freq.; ≥ 10 dB increase in 2 consecutive freqs.; or loss of response at 3 consecutive freqs.	18% (5/28; by ear)
Gorse et al., 1992	X			≥ 15 dB increase in at least 1 freq. in 1 ear	11.1% (2/18)
Li et al., 1991	X			≥ 15 dB increase in at least 2 freqs. in 1 ear	0% (0/100)
Mukhopadhyay et al., 1993	X			≥ 20 dB increase in at least 1 freq. in 1 ear	0% (0/10)
Nikolaidis et al., 1991	X			≥ 15 dB increase in at least 2 freqs. in 1 ear; or ≥ 20 dB increase in 1 freq. in 1 ear	25% (10/40)
Ramsey et al., 1993	X			≥ 20 dB increase in at least 1 freq. in 1 ear	0% (0/71)
Ramsey et al., 1999	X			Bilateral decrease of ≥ 15 dB increase in 2 consecutive freqs. in both ears	0% (0/148)

(continued)

Table 3 (continued)

Study	Assessment instruments			HL criteria (dB loss post-treatment)	% HL post - treatment
	PTA	ABR	OAE		
Sánchez-Alcaraz et al., 1998	X			≥ 15 db increase in at least 2 freqs. in 1 ear; or ≥ 10 db increase in all tested freqs. in both ears	2% (1/43)
Smyth et al., 2005	X			≥ 20 dB increase in at least 2 freqs. in 1 ear	0% (0/219)

Note. PTA = pure tone audiometry; ABR = auditory brainstem response; OAE = otoacoustic emissions; HL = hearing loss; freq. = frequency; CEOAE = click-evoked otoacoustic emission; DPOAE = distortion product otoacoustic emission; dB = decibel; SPL = sound pressure level.

Clinical Question 2: What Is the Persistence of Hearing Loss in Persons Treated With Tobramycin?

No studies addressed this clinical question.

Clinical Questions 3: Is the Likelihood of Tobramycin-Induced Hearing Loss Affected by Dosage?

Eight studies (deHoog et al., 2002, 2003; Mukhopadhyay et al., 1993; Nikolaidis et al., 1991; Ramsey et al., 1993, 1999; Sánchez-Alcaraz et al., 1998; Smyth et al., 2005) provided sufficient information to address this question. Intravenous daily dosage ranged from 4 mg/kg to 15 mg/kg, with reported incidences ranging from 0% to 33%. There does not appear to be a correlation between daily dosage and hearing loss, as studies providing individuals with higher daily dosages did not consistently report higher incidences of hearing loss. The daily dosage of inhaled tobramycin ranged from 400 mg to 1,800 mg. No incidence of hearing loss was reported in any studies utilizing inhalation administration, regardless of dosage. One study (Nikolaidis et al., 1991) administered 8 mg/L tobramycin intraperitoneally after an initial loading dose of 1.7 mg/kg/body weight. A 25% incidence of hearing loss was reported.

Clinical Question 4: Is the Likelihood of Tobramycin-Induced Hearing Loss Affected by Route of Administration?

Ten studies (Bates et al., 1997; de Hoog et al., 2002, 2003; Li et al., 1991; Sánchez-Alcaraz et al., 1998; Smyth et al., 2005; Mukhopadhyay et al., 1993; Ramsey et al., 1993, 1999; Nikolaidis et al., 1991) addressed the route of tobramycin administration (see Table 4). Six studies administered tobramycin intravenously, with incidences ranging from 0% to 33%. Three studies, (Mukhopadhyay et al., 1993; Ramsey et al., 1993, 1999) administered tobramycin via inhalation. All three studies reported no incidence of hearing loss. The one study (Nikolaidis et al., 1991) administering tobramycin intraperitoneally noted a 25% incidence of hearing loss.

Clinical Question 5: Is the likelihood of Tobramycin-Induced Hearing Loss Affected by Schedule of Administration?

Five of the included studies addressed this clinical question (Bates et al., 1997; Ramsey et al., 1993, 1999; Sánchez-Alcaraz et al., 1998; Smyth et al., 2005). Three studies assessed the incidence of hearing loss following a once-daily administration schedule (Bates et al., 1997; Sánchez-Alcaraz et al., 1998; Smyth et al., 2005), two studies (Ramsey et al., 1999; Sánchez-Alcaraz et al., 1998) assessed the incidence of hearing loss with twice-daily administration, and two studies (Ramsey et al., 1993; Smyth et al., 2005) assessed the incidence of hearing loss with thrice-daily administration. Of the five, all but one study (Sánchez-Alcaraz et al., 1998) reported 0% incidence of hearing loss. Sánchez-Alcaraz et al. (1998) noted a hearing loss in 1 of 21 participants (4.8%) administered tobramycin twice daily.

Two of the six studies (Sánchez-Alcaraz et al., 1998; Smyth et al., 2005) compared the effects of once-daily versus twice-daily and once-daily versus thrice-daily administration. Sánchez-Alcaraz noted a 0% (0/22) incidence with once-daily administration compared to 4.8% (1/21) twice-daily administration. Smyth et al. noted no difference (0% incidence) between once-daily and thrice-daily administration.

Table 4. Incidence of hearing loss by dosage, frequency, and route of administration.

Study	Route of administration	Dosage (mg/kg per day)	Frequency	*N*	% HL
Bates et al., 1997	Intravenous	Varied (7–15 mg/kg)	OD	0/18	0%
De Hoog et al., 2003	Intravenous	4 mg/kg	Varied	3/166	2%
de Hoog et al., 2002	Intravenous	4 mg/kg	Varied	3/9	33%
Li et al., 1991	Intravenous	Varied (avg. 8.56–9.56	Varied	0/100	0%
Sánchez-Alcaraz et al., 1998	Intravenous	4mg/kg	OD vs. BD	1/43 (OD: 0/22) (BD: 1/21)	2% (OD 0%) (BD: 4.8%)
Smyth et al., 2005	Intravenous	10mg/kg	OD vs. TD	0/219 (OD:0/107) (TD:0/112)	0%
Mukhopadhyay et al., 1993	Inhalation	400 mg (nebulized)	1 dose	0/10	0%
Ramsey et al., 1993	Inhalation	1,800 mg (nebulized)	TD	0/71	0%
Ramsey et al., 1999	Inhalation	600 mg (nebulized)	BD	0/148	0%
Nikolaidis et al., 1991	Intraperitoneal	8 mg/L (peritoneal; 1.7 mg/kg/body weight loading dose)	Not reported	10/40	25%

Note. avg. = average; OD = once daily; BD = twice daily; TD = three times daily.

Clinical Question 6: Is There Evidence of a Synergistic Effect on Hearing Loss if Multiple Ototoxic Drugs (e.g., Aminoglycosides, Antineoplastics, etc.) Are Taken Concomitantly With Tobramycin?

One study presented sufficient data to compare the incidence of hearing loss across neonates receiving tobramycin in isolation; tobramycin in combination with vancomycin or in combination with furosemide; or a combination of tobramycin, vancomycin, and furosemide. Data are presented in Table 5. Two percent of the neonates receiving tobramycin in isolation did not pass the automated auditory brainstem response (A-ABR) hearing test, whereas 9% of neonates receving tobramycin in combination with vancomycin and 9% of neonates receiving tobramycin in combination with furosemide failed to pass the hearing test. Eleven percent of the neonates receiving all three drugs (tobramycin, vancomycin, and furosemide) failed to pass the A-ABR. These differences are not statistically significant.

Table 5. Incidence of hearing loss with concomitant use of ototoxic drugs.

Study	**Concomitant ototoxic drugs**	***N***	**% HL**
de Hoog et al., 2003	tobramycin + vancomycin	11/122	9%
	tobramycin + furosemide	14/154	9%
	tobramycin + vancomycin + furosemide	7/66	11%
	tobramycin only	3/166	2%

Discussion

The objective of this review was to determine the likelihood of developing hearing loss after treatment with tobramycin. We also sought to determine (a) if hearing loss worsened or improved over time at follow-up and (b) the effect of dosage, schedule, and route of administration. Additionally, the effects of concurrent administration of other potentially ototoxic drugs on the likelihood of developing hearing loss were investigated. Due to the lack of current research regarding follow-up hearing results, we are unable to provide information to address the persistence of hearing loss after tobramycin administration. Further, given the heterogeneity of the included studies, results could not be meaningfully pooled to provide estimates of the likelihood of developing hearing loss; all data are reported in the form of incidence ranges.

Based on the studies included in this review, the range of hearing loss for individuals taking tobramycin was 0% to 33%. No trends emerged regarding the effects of dosage or schedule of administration on the likelihood of developing hearing loss. There was a potential effect of the route of administration on the incidence of hearing loss. Zero of three studies utilizing inhalation of tobramycin reported hearing loss in patients. Although the data from one study (de Hoog et al., 2003) appear to present a potential synergistic effect of concomitant ototoxic drug use on the incidence of hearing loss, these effects failed to reach statistical significance. Risk factors of craniofacial abnormalities, family history, cerebral complications, APGAR score, and syndrome likely had a larger effect on the incidence of hearing loss in the neonates tested in the de Hoog et al. (2003) study.

After further analysis of the studies included in the review, several population-specific trends appeared to emerge. Again, given the limited number of studies and the heterogeneity of the studies, these findings must be interpreted with caution. Trends across patients with cystic fibrosis, renal impairment, and neonates are discussed.

Cystic Fibrosis

The incidence of hearing loss in patients with cystic fibrosis receiving tobramycin was consistently 0% across studies. These effects do not appear to be related to dosage or frequency of administration. It is unclear whether route of administration affects the incidence of hearing loss. Half of the studies on cystic fibrosis patients administered tobramycin via inhalation, and half administered tobramycin intravenously. Additional research is needed to determine if the trends observed in patients with cystic fibrosis are valid, and if so, the implications of these findings.

Renal Impairment

Gorse et al. (1992) and Nikolaidis et al. (1991) studied individuals with renal impairment. The incidences of hearing loss in this population were 11.1% (2/18) and 25% (10/40), respectively. Without additional studies in this population, it is difficult to determine if these potential trends are secondary to medical diagnosis or other factors. Individuals with renal impairment may have a reduced ability to filter tobramycin from the system. Additionally, the mean age of participants in these studies is higher in comparison to the other studies included, which may have an effect on the incidence of hearing loss. It is of interest to note that between the two studies in this population, Nikolaidis et al. (1991) demonstrated a higher incidence of hearing loss despite the use of more stringent criteria for determining hearing loss. Given the small number of participants in both studies, no conclusions can be drawn.

Neonates

In the neonatal population, a 2% (3/166) to 33% (3/9) incidence of hearing loss was noted (de Hoog et al., 2002, 2003). These effects could indicate an increased risk of hearing loss due to tobramycin exposure in the neonatal period. The differences in sample size and incidence between the two studies should be noted and considered when attempting to draw conclusions.

The criteria for determining hearing loss differed across studies. Several studies used relatively sensitive criteria, which may inflate the incidence of hearing loss, whereas other studies utilized more specific criteria, which may lead to an underestimation of hearing loss. Without a uniform definition of hearing loss, the generalizability of incidence across studies is limited.

Additional research is necessary to further explore the effects of tobramycin on the likelihood of developing hearing loss. Comparative research is needed to determine if inhalation is a safer route of administration than intravenous or intraperitoneal methods. Additional research is also needed to address the possible differential impact of population on risk of hearing loss. It is important to consider how age, diagnosis, and severity may affect the likelihood of developing a hearing loss. Future research also should consider the discrepancies of hearing loss criteria across studies. Until consistent criteria are used, researchers should increase transparency of participants' decibel thresholds or make raw data available. The long-term effects on hearing are also very important to consider, as the effects of aminoglycoside-induced ototoxicity are often latent (American Speech-Language-Hearing Association, 1994). Finally, additional research is needed to further understand the potential synergistic effects of concomitant ototoxic drug exposure, as tobramycin is frequently administered with other antibiotics such as vancomycin or with other aminoglycosides such as amikacin.

As with all areas of clinical practice, audiologists must consider the evidence provided in this systematic review in conjunction with their own clinical experience, with the clinical expertise of their peers, and with the values and wishes of their patients. When making clinical decisions, audiologists should consider the risk of drug-induced hearing loss, other drug treatments available, the severity of the illness, and the patient's level of understanding and concern for their hearing preservation.

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