Once-daily aminoglycosides

We applaud the efforts of Stankowicz et al. in reviewing once-daily aminoglycoside dosing and specifically stating that “Otorrhea has not been sufficiently addressed in studies comparing aminoglycoside dosing regimens to warrant a reasonable risk assessment.” We are concerned, however, with their broad conclusion that implies that once-daily administration may limit toxicity in general.

While we agree that once-daily aminoglycoside administration reduces nephrotoxicity when appropriately dosed and monitored, this is simply not true for aminoglycoside-induced ototoxicity. Targeted hair-cell injury caused by aminoglycosides appears to damage the auditory and vestibular apparatus of the inner ear. Auditory dysfunction results from cochlear damage, while vestibular damage results from injury to the vestibular organ; these effects generally occur independently. Risk factors for aminoglycoside-associated auditory damage and hearing loss include advanced age and a specific mitochondrial DNA mutation referred to as m.1555A-G. Consequently, cochlear hair-cell damage has not been associated with specific aminoglycoside doses, dosage frequencies, or achieved serum concentrations. Aminoglycoside-induced vestibular toxicity is believed to result from prolonged drug exposure, since most cases have occurred after at least 5 days of therapy and a median exposure of 28 days. No analysis has ever demonstrated a causal relationship between vestibular toxicity and elevated trough or postdose aminoglycoside concentrations or method of administration.

While there are advantages to once-daily aminoglycoside dosing in terms of effectiveness and simplification of administration and monitoring, the take-home message is that there is no evidence that such dosing decreases the risk of cochlear or vestibular damage. Such toxicity can manifest even after completion of therapy and is, unfortunately, not prevented by therapeutic drug monitoring. Furthermore, given the inherent and unpredictable ototoxicity associated with aminoglycosides, their use—for as short a duration as possible—should be restricted to circumstances in which less-toxic alternatives are not available.


The recent article by Stankowicz et al. on once-daily aminoglycoside dosing included relevant literature and summarized significant findings but did not address the literature on such dosing in pregnancy. The article supports a 1997 recommendation in which Bailey et al. advised against once-daily aminoglycosides in pregnancy due to limited data in the pregnant population. Since 1997, evidence has emerged to suggest that once-daily aminoglycoside administration may be safe and effective in pregnancy.

Locksmith et al. randomized women in labor who had reached at least 34 weeks’ gestation with clinical chorioamnionitis to receive gentamicin i.v. once daily (5.1 mg/kg; 18 patients) or every eight hours (first dose of 120 mg