Response to Letter to the Editor Regarding Sensorineural Hearing Loss Associated with Neomycin Eardrops and Nonintact Tympanic Membranes
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Sensorineural Hearing Loss Associated with Neomycin Eardrops and Nonintact Tympanic Membranes

The recently published article “Sensorineural Hearing Loss Associated with Neomycin Eardrops and Nonintact Tympanic Membranes” sought to address a relevant concern. Does responsible use of neomycin eardrops cause hearing loss in people? Studies have clearly shown ototoxicity in animal models. Despite years of clinical use, however, resultant sensorineural hearing loss (SNHL) has not been shown in humans.

The conclusion of the current study was that repeated doses of neomycin present a significant risk of SNHL and that other eardrops such as fluoroquinolone should be used instead. Unfortunately, several issues appear to confound or bias the results obtained.

1. The use of an ICD-9-CM diagnosis code as the sole metric seems problematic. It does not show the severity or configuration of loss. There is no audiometric corroboration. Also as acknowledged in the study, the current concern about neomycin drops might have caused practitioners to disproportionately look for and diagnose hearing loss in these cases.

2. Also of concern were the years from which most of the cases in each group were drawn. Most subjects in the neomycin group were from 1999 to 2002. Most from the quinolone group were from 2003 to 2006. This may present bias due to the more recent adoption of newborn hearing screening and widespread use of otoacoustic emission testing. More children in the quinolone group may have been diagnosed early with SNHL and excluded from the results. It would be helpful to know how many children from each group were excluded because of prior SNHL.

3. Finally, all of the cases who had fluoroquinolone drops appeared to have been used as the reference that was compared against children who had 1 prescription of neomycin drops and again against the few children who had 2 or more prescriptions of neomycin. Would the difference have been significant if all of the neomycin cases had been compared against this reference? Would the difference have been significant if the children with more chronic infections requiring multiple antibiotics had been directly compared for the 2 groups?

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We thank Berenholz and colleagues for their interest in our study. We also appreciate the authors’ previous efforts to assess the neomycin ototoxicity in the presence of nonintact tympanic membranes (NITM).

The authors begin with a statement that no ototoxic effect of neomycin in NITM has been noted in clinical practice. The literature is replete with examples of uncommon safety issues not discovered in clinical practice and only appreciated through large population-based studies.
The authors state concerns about confounding or bias. As no concern about confounding is specified, we assume these terms were used interchangeably. Following are our thoughts about the three concerns about bias the authors specify.

Indeed the use of physician-assigned ICD9 coding to measure sensorineural hearing loss has not been validated, but several factors point to the validity of this approach. First, we did require charges for audiometric testing to assure appropriate diagnostic work up. Second, compromised sensitivity or specificity of measurement would have biased this study toward the null hypothesis (no ototoxic effect) and thus against our findings. Third, increased vigilance in neomycin users should have introduced bias in the analysis of first and not only after repeated doses. On the same note, we apologize for the lack of clarity in our analytic design. While we used all fluoroquinolone users as comparator, we adjusted the analysis for the number of repeat prescriptions, resulting essentially in a comparison of 1 dose neomycin : 1 dose fluoroquinolone, 2 doses : 2 doses, and so forth. A sensitivity analysis where we restricted the analysis to repeat users showed near identical results but wider confidence intervals. An analysis of all neomycin users versus all fluoroquinolone users as the authors suggest would lack the ability to find a cumulative effect and thus add no value to our research question. Note that repeat prescriptions was a statistically significant determinant of hearing loss, supporting the suggested association (as well as the importance for multivariate adjustment, as done in our analysis).

Finally, the authors suggest a secular effect, such that newborn hearing screening might have reduced the incidence of sensorineural hearing loss post-typanic membrane perforation in later study years, which in turn were more often attributed to fluoroquinolone users. As shown in Table 2 we did adjust for study year, which in fact was not associated with risk for hearing loss.

We conclude that the observed results, even though pointing to only a small increase in risk, along with solid biological plausibility and the availability of alternative treatment options support the existing labeling to avoid the use of neomycin in patients with NITM.

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Possible Errors in Hearing Recovery Results

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We read with great interest the article titled “Efficacy of 3 Different Steroid Treatments for Sudden Sensorineural Hearing Loss: A Prospective, Randomized Trial” by Lim et al.1 In this article, the authors demonstrated the clinical efficacy of steroid therapy on idiopathic sudden sensorineural hearing loss (ISSNHL) with different protocols in 60 patients. The treatment outcomes were similar among 3 groups: oral steroid for 10 days (group I), intratympanic dexamethasone injection (ITDI) 4 times (group II), and both (group III). Outcomes were measured by performing pure-tone audiometry before and after treatment, and hearing gains were then calculated in each group. The authors demonstrated that group III’s hearing gain was the highest (21.9 dB), although without statistical significance, followed by groups I and II (12.8 and 12.1 dB). However, on closer inspection, there were potentially incorrect data. According to the normative data provided in figure 3, comparing pure-tone average before and after treatment in each group, the hearing gain for group I should be 18.7 dB. Thus, the overall hearing gain for all 3 groups should be 17.5 dB. When comparing the hearing gains among 3 groups and overall hearing gain using the Kruskal-Wallis test in figure 4, the hearing gains for group I and total should be 18.7 dB and 17.5 dB, respectively. These potential errors might lead to different results as the hearing gains of group I and III become quite close. Therefore, we recommend that the authors take another look at the original data and correct any possible statistical errors in the hearing gain results that might have occurred.

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