



Drug Induced Ototoxicity – Reply

*Richard K Albert

Denver Health and University of Colorado, Denver, CO 80206, USA

Ryan and Sachin [1] express concern that chronic use of macrolide antibiotics can cause permanent hearing loss and cite a Cochrane Review in support of this contention [2]. Only six studies of macrolides were included in the Cochrane Review and, of these, only three reported adverse events [3-5]. Our study of azithromycin [3] was the by far the largest of these (N = 1142 compared, with N = 110 and 36 in references 4 and 5, respectively) and was the only one that systematically evaluated the effect of the macrolide on hearing by having research coordinators or audiologists perform audiograms and ask about subjective changes in hearing at pre-designed intervals during the course of treatment [3]. We indeed found that hearing decrements occurred more commonly in patients receiving azithromycin than in those receiving placebo (25% vs. 20%, $P < 0.05$) but 32% of the participants who developed hearing decrements while receiving azithromycin had *reversal* of these decrements on subsequent testing despite the fact that, because of an error in our protocol, they continued to receive the medication. A comparable percent of reversal in hearing decrements also occurred at subsequent measurements in the patients receiving placebo leading us to conclude that the audiograms performed by our research coordinators were likely too non-specific to confirm that the hearing decrements recorded actually occurred [3].

Ototoxicity is a well-recognized side effect of erythromycin and is attributed to high blood levels of the medication. Hearing decrements

have been reported in patients given azithromycin in doses of 500 or 600 mg/day orally, but many of these patients were receiving other medications known to be ototoxic and/or to decrease the metabolism of macrolides. Whether ototoxicity occurs in response to long-term azithromycin at the dose that we administered (i.e., 250 mg/day), after screening for, and excluding patients taking concurrent medications known to alter macrolide metabolism, as we did in our study, remains to be determined.

References

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*Corresponding author: Richard K. Albert MD, Denver Health and University of Colorado, Denver, CO 80206 USA, Tel: 303-556-2400; E-mail: ralbert@dhha.org

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