Ototoxicity of Polymyxin B, Neomycin, and Hydrocortisone Suspension in Tympanoplasty Surgery

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Abstract

Objectives. (1) To determine the safety of using a commercially available suspension of polymyxin B, neomycin, and hydrocortisone (PNH) in tympanoplasty surgery. (2) To apply evidence-based medicine to tympanoplasty surgery when considering potential ototoxicity.

Study Design. Case series with chart review.

Setting. Tertiary otology practice, single surgeon.

Methods. Approval for this study was obtained from the St. Dominic–Jackson Memorial Hospital Institutional Review Board. Data were gathered on 272 consecutive type 1, underlay tympanoplasties for which both pre- and postoperative audiometric data were available over a 10-year period. In each surgery, gelatin sponge saturated in a commercially available PNH suspension was placed in the middle ear to support the graft. Patients ranged in age from 3 years to 79 years. Preoperative and postoperative bone conduction thresholds were measured at 500, 1000, 2000, 3000, and 4000 Hz.

Results. The average change in sensorineural hearing as measured by bone conduction thresholds was negligible, with a slight improvement in all frequencies tested except 4000 Hz. The changes by frequencies were as follows: 500 Hz (−1.624 dB), 1000 Hz (−1.399 dB), 2000 Hz (−0.975 dB), 3000 Hz (−0.596 dB), and 4000 Hz (−0.560 dB). The 5-frequency average change was −0.545 dB.

Conclusions. The commonly used otic solution containing polymyxin B, neomycin, and hydrocortisone demonstrates no ototoxicity in tympanoplasty surgery and is safe to use in this setting.

Keywords

ototoxicity, Cortisporin, tympanoplasty, evidence-based medicine

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preponderance of pediatric patients. There was 1 more right ear than left ear. Fifty-three percent of the ears were female.

One surgeon using a temporalis fascia or tragal perichondrial graft in an underlay fashion performed all the surgeries. Gelfoam, a commercially available gelatin sponge, was saturated with a PNH solution and placed in the middle ear and the external canal to support the graft. An audiologic evaluation was performed no sooner than 4 months postoperatively by licensed audiologists. Paired data for pre- and postoperative audiometric bone conduction thresholds were measured at 500, 1000, 2000, 3000, and 4000 Hz in 5-dB increments.

Results
There was no overall significant change in the audiometric thresholds. A slight improvement was noted in the lower frequencies, trending to a slight decline in the highest frequency. The changes in bone conduction thresholds were as follows: 500 Hz (–1.624 dB), 1000 Hz (–1.399 dB), 2000 Hz (–0.975 dB), 3000 Hz (–0.596 dB), and 4000 Hz (+0.560 dB; Table 1). There were no incidences of a dramatic change in sensorineural hearing. The greatest change was observed in 1 ear with an 18-dB average improvement in hearing. Two ears were observed to experience a 15-dB average decline in hearing. The greatest change at any one frequency was a 35-dB decline at 4000 Hz (Table 2).

Discussion
It is well known that aminoglycosides can cross the round window membrane of mammals and cause vestibular and cochlear toxicity. Numerous animal studies have shown hair cell loss and hearing loss with topical application of neomycin and polymyxin B to the round window membrane.5 Also, hearing loss can occur in patients undergoing gentamicin perfusion of the inner ear via the round window to achieve a chemical labyrinthectomy in treatment of Meniere’s disease and other vestibular disorders.6,7 This knowledge, along with the advent of commercially available quinolone topical otic preparations, led to an investigation of the safety of aminoglycosides in the treatment of otologic disease with nonintact tympanic membranes (NITM) through a consensus panel commissioned by the AAO-HNS in 2004.5 Several studies were reported by the panel, including an investigation of animal studies,5 a review of clinical reports of SNHL with topical solutions in NITM patients,8 and an analysis and recommendation report.4

In the review of animal studies, more than 30 investigations looking at numerous topical medications including neomycin and polymyxin B were analyzed. These studies were conducted on a variety of animals, including primates. The studies demonstrated loss of inner and outer hair cells in the cochlea and loss of hearing through electrophysiologic measurements.5

In an exhaustive review of the literature from 1966 to 2003, Matz et al8 found evidence for 11 cases of cochlear and 2 cases of vestibular toxicity attributed to long-term use of neomycin in mastoid cavities.

Based on these investigations, the AAO-HNS consensus panel report discussed the poor correlation of animal studies and clinical experience, offering several possible explanations. These included differences between humans and animals in the round window and the organ of Corti. The panel referenced studies that demonstrated no hearing loss associated with use of PNH in NITM patients. The panel admitted that it was charged with using an evidence-based medicine approach in the analysis. The panel could use only a grade C for evidence. The panel concluded that potentially ototoxic preparations should not be used routinely despite lack of clinical evidence that ototoxicity is likely but rather because other preparations are available.4

In response to these recommendations, otologists at the Lippy group in Warren, Ohio, published 2 studies based on their observation of safety in using PNH for years in NITM patients.9,10 One study examined 500 patients receiving PNH at a dose of 3 drops, 3 times a day, for 5 days. There were no cases of hearing loss.9 The second study evaluated distortion product otoacoustic emissions in 30 patients treated in a similar fashion compared with a control group of 30 patients. Again, no ototoxicity was demonstrated.10
Other studies have also demonstrated no hearing loss in NITM patients treated with PNH.\textsuperscript{11,12} All of these studies reported on short-term use of PNH.

A recent study by Antonelli and colleagues\textsuperscript{13} from the University of Florida examined this question in an ambitious study reviewing the database for Medicaid recipients in 29 states, over a 7-year period, involving 134,598 children. The study determined ototoxicity based on the record of tympanostomy tube placement, prescriptions for PNH or quinolone ototopicals, and an ICD code for SNHL. No audiometric studies were examined. Patients who received quinolones showed no increase in the SNHL diagnosis. Patients receiving 1 prescription of PNH showed a slightly less incidence of SNHL, whereas those with 2 prescriptions for PNH demonstrated a statistically higher rate of SNHL diagnosis. Interestingly, the group that had 3 or more prescriptions for PNH had a slightly lower correlation with the SNHL diagnosis than the group that received 2 prescriptions. The authors concluded that repeated applications of PNH in patients with an NITM might result in SNHL. The obvious difficulty in this study is the absence of any audiometric studies. Another weakness is the inexact use of diagnoses in clinical practice. When submitting a bill for services, many possible diagnoses can be used. Rarely are all possible diagnoses used.\textsuperscript{13}

Our present investigation of possible ototoxicity using PNH in tympanoplasty has several limitations. A retrospective analysis inherently lacks the weight of a prospective, randomized, blinded study. Many patients did not have postoperative audiograms to review, introducing the possibility of missed SNHL. Also, there is no control group with which to compare these patients.

Conclusions

This study demonstrates grade B evidence that the use of a commercially available solution of polymyxin B, neomycin, and hydrocortisone (Cortisporin) shows no evidence of cochlear ototoxicity when used in tympanoplasty surgery.

Author Contributions

James R. House III, data analysis, drafting, final approval; Laura K. House, data analysis, drafting, final approval.

Disclosures

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References