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Cell-specific accumulation of gentamicin and doxycycline within the guinea pig cochlea after intratympanic application

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Introduction: Intratympanic medication might alter cochlear NO-production resulting in damage or protection, respectively. In this study, the quantitative distribution patterns of gentamicin and doxycycline were determined after intratympanic application in the guinea pig animal model.

Materials & Methods: Gentamicin or Doxycycline were injected into both middle ears of male animals (n=24 and n=3, respectively). The cochleae were removed 1, 2 and 7 days after gentamicin injection or 1, 6 and 24 h after doxycycline application, transferred into fixative and embedded in paraffin. The cellular staining reactions by specific antibodies against gentamicin and doxycycline were quantified computer-assisted on sections for seven different cochlear regions.

Results: Gentamicin was identified in all experimental groups in numerous regions of the cochlea but with quantitative cell-specific differences. An intense accumulation was observed within the spiral ligament, organ of Corti, nerve fibers, interdental cells and fibrocytes in the limbus-area. A low gentamicin accumulation was seen in spiral ganglion cells and no accumulation in the striavascularis. Statistic analysis revealed fixed effects of cell type and an interaction between treatment and cell type, but no effects of cochlea turn and of treatment. Analysis over time identified a reduction of gentamicin within the spiral ligament and nerve fibers. Doxycycline was preferentially located in the striavascularis and in hair cells.

Conclusion: In respect to the route of infiltration, a contribution of the vessel systems is discussed. The identified accumulation of gentamicin in those cochlea regions which are responsible for potassium recycling might result in a local NO-increase leading finally to cochlear damage. The specific accumulation of doxycycline in the striavascularis and hair cells might prevent an NO up-regulation in stress situations in these areas. Knowledge of cell specific accumulation of different pharmaceutical products offers a promising approach for human medication.

Biography

Kai Helling is presently working in Johannes Gutenberg University Medical School, Department of Otorhinolaryngology, Head and Neck Surgery and Neuro-Otology. His research interest includes vestibular disorders and experimental neurootology.

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