Intratympanic Administration of Alpha-Lipoic Acid-Loaded Pluronic F127 Nanoparticles Ameliorates Acute Hearing Loss

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Information/ Background

- The purpose of this study was to develop a therapeutic method for acute hearing loss using an antioxidant-containing nanoparticle based on pluronic F127. In our previous study, nanoparticles coated with polyethylene glycol (PEG) showed an advantage in penetrating the mucosa when delivering drug to inner ear. Pluronic F127 is approved by FDA for use in ear, and has two PEG blocks.

Materials and Methods

- We selected alpha lipoic acid as a drug to be loaded in nanoparticles through literature search. The safety of nanoparticle in HEI-OC1 cells and the protective effect of nanoparticles against aminoglycoside toxicity were investigated. Then, we measured the intracellular levels of ROS in response to kanamycin with or without alpha lipoic acid-loaded nanoparticle, as well as levels of antioxidant proteins. In mice, we treat the nanoparticles by intratympanic injection 4h before ototoxicity induction and analyzed the therapeutic ability of the nanoparticles in acute hearing loss.

Results

- The size of particles was about 109.1 nm, and in the analysis of drug release, about 28% of the drug was released gradually from nanoparticle for 40 hours at room temperature. In vitro results showed the nanoparticles were safe in MTT assay and provided protective effects at concentrations from 0.25 mg/ml to 2.5 mg/ml. It also showed an increase in antioxidant proteins such as Nrf2, HO-1, SOD-1 and SOD-2. In animal study, the hearing of mice injected with the nanoparticles into the middle ear cavity was significantly preserved after ototoxicity induction compared to the control group. The increase of Nrf2 was also observed in cochlea of these animals, which indicated that the nanoparticles showed the protective effect of hearing through the same antioxidant mechanism.

Conclusion

ALa-loaded Pluronic F127 nanoparticles showed effective hearing protection in acute hearing loss, which could be mediated through the Nrf2 / HO-1 pathway. Considering the safety and sustained drug release of the nanoparticles, it appears to be a potential new drug formulation for intratympanic injections.