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Title:

EXPLORATION OF THE RELATIONSHIP BETWEEN CUMULATIVE EXPOSURE TO TOBRAMYCIN AND OTOTOXICITY IN PATIENTS WITH CYSTIC FIBROSIS

Lay Title: Cumulative ototoxicity of tobramycin

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What was your research question?

Aminoglycosides, like tobramycin, are antibiotics which cause irreversible hearing toxicity, without the relationship being clearly described in the literature. Our objective was to propose a mathematical model describing the relationship between the cumulative exposure in tobramycin and the auditory toxicity, in young patients with cystic fibrosis.

Why is this important?

Evaluate the relationship between the cumulative exposure in tobramycin and the auditory toxicity is important because tobramycin is an essential antibiotic in the management of pulmonary infections in patients with cystic fibrosis. Children with cystic fibrosis are exposed to tobramycin from the beginning of their lives, and the accumulation of this antibiotic induces irreversible auditory toxicity in them. The interest in creating a mathematical model linking auditory toxicity to cumulative exposure to tobramycin would allow treatment regimens to be adapted to limit this toxicity.

What did you do?

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For 106 children with cystic fibrosis, information on each course of intravenous tobramycin was collected, and auditory toxicity was evaluated with audiogram. With these data, a mathematical model was created, liking the cumulative exposure to tobramycin to auditory toxicity.

What did you find?

We found a significant relationship between cumulative exposure to tobramycin and hearing loss, which confirms the need to monitor the number of tobramycin courses received by the patient during his lifetime. The hearing loss was highly variable from subject to subject: two individuals treated identically will not have the same level of hearing loss. Finally, auditory toxicity was not clinically perceptible in these children.

What does this mean and reasons for caution?

Over time, patients receive an increasing number of courses of IV tobramycin therapy because of more frequent respiratory infections associated with the progression of cystic fibrosis. Patients in our paediatric study cohort may not have reached a sufficient cumulative exposition to tobramycin to generate clinically quantifiable hearing loss.

What's next?

As auditory toxicity was not clinically perceptible in the children of our study, it is essential to continue hearing tests in adults to document hearing during adulthood. Once the cumulative exposure at which deafness occurs is identified, this will allow to define an optimal administration strategy to limit their auditory toxicity.

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