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Oral Presentations

O.04 Renal and Auricular Adverse Drug Reactions are Linked Through a Predictive Mechanistic Commonality

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Background: Drug-induced ototoxicity is a subject of interest, as many diseases are treated with drugs which have potential toxic effects on the ear. There is evidence that both inner ear and kidney tissue are immunologically, biochemically and functionally related. It has been suggested that drugs affecting transport of sodium and/or potassium change ionic homeostasis in the inner ear, hence inducing functional disturbances, such as hearing loss, tinnitus and vertigo.

Objectives: The aim of the study was to assess whether renal suspected adverse drug reactions (sADRs) have predictive value for auricular sADRs and whether involved drug classes influence ion transport systems.

Study design: Data were obtained from the Netherlands Pharmacovigilance Centre Lareb. The study base comprised all reports of sADRs, till January 1st, 2007. Cases were all sADRs for relevant renal disorders, and all sADRs for relevant auricular disorders. All other reported sADRs were selected as non-cases. The relationship between drug classes and auricular and renal sADRs was evaluated by calculating reporting odds ratios (RORs). A ROR ≥1.50 was regarded as a cut-off value for an association. We defined four groups: A) ROR kidney<1.50 and ROR ear<1.50 or no reports on auricular sADRs (reference), B) ROR kidney<1.50 and ROR ear≥1.50, C) ROR kidney≥1.50 and ROR ear<1.50 or no reports on auricular sADRs, and D) ROR kidney≥1.50 and ROR ear≥1.50. For each group, we calculated odds ratios (ORs) for the association between the group classification and effect on ion channels/ion transport systems in kidney and ear tissues.

Results: Fourteen out of 193 drug classes had a ROR≥1.50 for the association between drug class and both renal and auricular sADRs. Among these drug classes were several with a well-known ability of inducing renal and auricular ADRs, such as loop diuretics, aminoglycosides and quinine. The percentage of drugs having the ability to affect ion transport systems differed between the four groups. The ORs for group D and B were significantly higher compared to the reference group (OR 12.2 and OR 8.7, respectively), whereas there was no association for group C (table I).

Association between drug class with effect on ion transport systems and classification into drug class group based on ROR kidney and ROR ear

Group		Drug classes (N)	Drug classes with effect on ion systems (N) (%)	OR	(95% CI)
A	ROR kidney < 1.50; ROR ear < 1.50 and/or no reports on auricular sADRs	86	5 (5.8)	1.0	(reference)
B	ROR kidney < 1.50; ROR ear 1.50	20	7 (35.0)	8.7	(2.4-18.7)
C	ROR kidney 1.50; ROR ear < 1.50 and/or no reports on auricular sADRs	73	8 (11.0)	2.0	(0.6-3.1)
D	ROR kidney 1.50; ROR ear 1.50	14	6 (42.9)	12.2	(3.0-30.5)

OR = odds ratio; **CI** = confidence interval; **ROR** = reporting odds ratio.

Conclusion: Our data suggest that potential renal ADRs as such are no marker for drug-induced auricular events. However, the ability of drugs to act on ion transport systems, and therefore influences ionic homeostasis in kidney and ear, might be a predictor for the possible occurrence of drug-related ototoxicity.