Chronic Cisplatin Tubulopathy in Humans and Animals: Clear-Cut Discrepant Findings

C.	Christina	Kanaka
O.H.	Oskar H.	Oetliker
M.G.	Mario G.	Bianchetti

Department of Pediatrics, University of Berne, Switzerland

Dr. Mario G. Bianchetti, Department of Pediatrics, University of Berne, Inselspital, CH-3010 Berne (Switzerland)

Dear Sir,

The experimental animal has been extensively used to delineate and possibly minimize the chronic cisplatin tubulopathy, which often represents a limiting factor for the use of this agent [1–3]. Unfortunately, the morphological and the functional findings in human beings and in the experimental animal seem consistently discordant.

Histologic findings in humans with persisting cisplatin tubulopathy demonstrate predominant lesions in the distal portions of the nephron [1–3]. Renal magnesium wasting is the main chronic renal tubular complication of cisplatin reported so far in humans. Recent observations indicate that renal magnesium wasting is mostly linked with hypokalemic metabolic alkalosis and hypocalciuria [4, 5]. Apart from chronic cisplatin tubulopathy, the renal handling of calcium and magnesium is dissociated under the influence of thiazide diuretics, which exert their action in the distal convoluted tubule. It is therefore possible that these findings result from a defect in the distal convoluted tubule. Thus, in humans, both morphological and functional studies indicate persisting lesions affecting predominantly the distal portions of the nephron.

In the experimental animal, the persisting morphological changes observed after cisplatin are characterized by widespread tubular lesions of the proximal tubule. Functional studies report chronic renal magnesium wasting, hypercalciuria, and glycosuria, and suggest also a disturbance in the proximal tubule [1–3]. Thus, in the experimental animal, both histologic and functional studies indicate predominant alterations of the proximal tubule. The mode of administration (repeated injections in humans versus single injection in the animal), the concomitantly used antineoplastic agents in humans or intrinsic properties of renal tissue might likely account for the differential chronic toxicity of cisplatin in humans as compared with the experimental animal. Unfortunately, this fact has been often neglected in the literature. Models of cisplatin tubulopathy closely mimicking the human cisplatin tubulopathy might better delineate the underlying mechanisms and validate preventive measures.

References

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