Differential presentation of hypersensitivity reactions to carboplatin and oxaliplatin: phenotypes, endotypes and management with desensitization.

Teodorikez Jimenez-Rodriguez¹, Leticia De las Vecillas Sánchez², Marina Labella³, Donna-Marie Lynch⁴, Kylie Marie Besz⁴, Kathleen Marquis⁴, Amparo Burgos¹, Victor Soriano Gomis¹, Inmaculada Lozano¹, Rosa Ana Montoyo Antón¹, Francisco Marco de la Calle¹, Purificacion Gonzalez Delgado¹, Aurora Gutiérrez², Estefanía Montenegro², Fernando Rodríguez², Javier Fernandez¹, and Mariana Castells⁴

¹Dr Balmis General University Hospital Alicante Institute for Health and Biomedical Research (ISABIAL)
²Hospital Universitario Marques de Valdecilla
³ARADyAL Spanish Network (RD16/0006)
⁴Brigham and Women’s Hospital Harvard Medical School

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Abstract

Background Drug hypersensitivity reactions (DHRs) to platinum-based drugs are heterogeneous and restrict their access, and drug desensitization (DD) has provided a ground-breaking procedure for their re-introduction, although the response is heterogeneous. We aimed to identify the phenotypes, endotypes and biomarkers of reactions to carboplatin and oxaliplatin and their response to DD. Methods Seventy-nine patients presenting with DHRs to oxaliplatin (N=46), and carboplatin (N=33) were evaluated at the Allergy Departments of two tertiary care hospitals in Spain. Patient symptoms, skin testing, biomarkers, and outcomes of 267 DDs were retrospectively analyzed. Results Oxaliplatin-reactive patients presented with predominantly type I (74%), cytokine release reaction (CRR) (11%), and mixed (Mx) (15%) phenotypes. In contrast, carboplatin reactive patients presented with predominantly type I (85%) and Mx (15%) but no CRRs. Out of 267 DDs, breakthrough reactions (BTRs) to oxaliplatin occurred twice as frequently as carboplatin (32% versus 15%; p<0.05). Phenotype switching from type I to another phenotype was observed in 46% of oxaliplatin DDs compared to 21% of carboplatin DDs. Tryptase was elevated in type I and Mx reactions, and IL-6 in CRR and Mx, indicating different mechanisms and endotypes. Conclusion Carboplatin and oxaliplatin induced three different types of reactions with defined phenotypes and endotypes amendable to DD. Although most of the initial reactions for both were type I, oxaliplatin presented with unique CRR reactions. During DD, carboplatin reactive patients presented mostly type I BTR, while oxaliplatin reactive patients frequently switched from type I to CRR, providing a critical difference and the need for personalized DD protocols.

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