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

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Abstract

Background Drug hypersensitivity reactions (DHRs) to platinum-based drugs are heterogenous 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 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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