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Original Article

Rapid Drug Desensitization to Platinum-based Chemotherapy Agents: A Single-center Experience

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ABSTRACT

OBJECTIVE: To characterize the clinical features of patients with platinum-based hypersensitivity reactions (HSRs) and to evaluate rapid drug desensitization (RDD) outcomes across different platinum agents.

MATERIAL AND METHODS: This retrospective study included patients who underwent RDD for platinum agents between 2019 and 2023 at a tertiary adult allergy clinic. Index reaction characteristics, RDD procedures, and breakthrough reactions (BTRs) were systematically recorded and analyzed.

RESULTS: Of 2,131 patients receiving chemotherapy, 105 (5.0%) developed platinum-induced HSRs and were included in the analysis. The cohort comprised 75 (71.4%) females, with a mean age of 61.3±10.3 years. Carboplatin was the most frequently implicated agent (n = 56, 53.3%), followed by oxaliplatin (n = 35, 33.3%) and cisplatin (n = 14, 13.3%). Index reactions occurred at a median of 5 cycles (range: 1–20) and, according to Brown's classification, were mild in 26 patients (24.8%), moderate in 73 patients (69.5%), and severe in 6 patients (5.7%). A total of 430 RDD procedures were performed, with 62 (14.4%) BTRs occurring in 40 patients (38.1%). The proportion of RDD procedures completed without BTRs did not differ significantly among carboplatin (226/266, 85.0%), oxaliplatin (110/126, 87.3%), and cisplatin (32/38, 84.2%) ($P = 0.800$). Overall, 414 (94.1%) desensitization procedures were successfully completed. Sex distribution differed significantly by culprit platinum agent, with a male predominance observed among patients reacting to oxaliplatin compared with those reacting to cisplatin and carboplatin ($P < 0.001$).

CONCLUSION: This study demonstrates that desensitization to platinum-based chemotherapy achieved high success rates and produced comparable outcomes across different platinum agents. Notably, HSRs to oxaliplatin were observed significantly more frequently among male patients than HSRs to other platinum agents.

KEYWORDS: Chemotherapy desensitization, breakthrough reactions, platinum agents

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INTRODUCTION

Hypersensitivity reactions (HSRs) occur in approximately 5% of patients receiving chemotherapeutic agents, representing a significant challenge in oncology practice.[1] Among platinum-based compounds, carboplatin is most frequently implicated in HSRs; its incidence increases cumulatively with repeated exposure and may reach up to 46% after seven or more treatment cycles.[1] Oxaliplatin is associated with HSRs in approximately 15% of patients (range: 1–25%), although severe reactions occur in fewer than 1%. Cisplatin has been reported as the culprit agent in approximately 5% of cases.[1,2]

The pathophysiological mechanism underlying immediate HSRs to platinum agents is thought to be predominantly immunoglobulin E (IgE)–mediated. This mechanism is supported by characteristic clinical features such as the

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requirement for repeated exposures to induce sensitization, the demonstration of positive skin test responses, and the detection of platinum-specific IgE antibodies in some patients.[3] Rapid drug desensitization (RDD) has emerged as an essential therapeutic strategy for patients who have experienced HSRs to first-line chemotherapeutic agents and for whom no equally effective alternative treatments exist.[4] RDD enables the safe and timely reintroduction of culprit agents by inducing a temporary state of tolerance. Previous platinum desensitization studies have reported that most RDD procedures were completed without breakthrough reactions (BTRs), with rates ranging from 71.0% to 75.8%.[5-7] Nevertheless, published studies indicate that severe BTRs may occur in approximately 5.8–11% of desensitization procedures, typically during the first or second RDD cycle.[5,8,9]

Although several studies have evaluated the incidence and characteristics of HSRs associated with individual platinum agents, real-life data describing desensitization outcomes and reaction patterns during RDD remain limited, with heterogeneous outcomes reported across studies.[5-7,9] Therefore, the present study aimed to characterize the clinical features of patients referred to our center for suspected platinum-based chemotherapy HSRs and, among those requiring continued treatment with the culprit agent, to evaluate the success of RDD and the frequency, severity, and nature of BTRs occurring during desensitization.

MATERIAL AND METHODS

This retrospective study included adult patients (≥18 years) who were evaluated for immediate HSRs to platinum-based chemotherapeutic agents and subsequently underwent RDD between 2019 and 2023 in the adult allergy and clinical immunology department of a tertiary referral center. Patients receiving non-platinum chemotherapies, patients desensitized at other institutions, patients with incomplete medical documentation, and patients with delayed-type HSRs were excluded. The primary aim of the study was to characterize the clinical features of patients with platinum-based HSRs. The secondary aim was to assess RDD outcomes among different platinum agents.

Immediate HSRs were defined as reactions occurring during the infusion or within 6 hours after drug administration, including reactions developing after completion of the infusion, in accordance with current guidelines.[1,10,11] Initial reactions were graded according to Brown's[10] classification: grade 1 reactions were limited to skin or subcutaneous tissue; grade 2 reactions included respiratory, gastrointestinal, or cardiovascular symptoms without hypotension; and grade 3 reactions involved hypoxia, hypotension, or neurologic compromise.

Main Points

- Rapid drug desensitization (RDD) for platinum-based chemotherapy is generally successful; however, real-life data on desensitization outcomes and patterns of immediate hypersensitivity reactions (HSRs) remain limited and heterogeneous.
- This study demonstrates a high overall success rate for RDD (94.1%). The success rate without breakthrough reactions was 85.6% in the overall platinum cohort, with no statistically significant differences among platinum agents, including carboplatin (85.0%), oxaliplatin (87.3%), and cisplatin (84.2%).
- Notably, HSRs to oxaliplatin were observed significantly more frequently in male patients compared with other platinum agents.

Skin testing was performed at least two weeks after the index reaction in accordance with established recommendations.[12] Both skin prick testing (SPT) and intradermal testing (IDT) were conducted. For SPT, undiluted commercial preparations were used: carboplatin 10 mg/mL, cisplatin 1 mg/mL, and oxaliplatin 5 mg/mL.[8,11] When SPT was negative, IDT was performed using increasing concentrations (1:100, 1:10, and 1:1). A positive IDT was defined as a wheal enlargement of ≥3 mm with erythema at 20 minutes. Concentrations used for IDT were: carboplatin 0.1, 1, and 5 mg/mL; cisplatin 0.01, 0.1, and 1 mg/mL; and oxaliplatin 0.005, 0.5, and 5 mg/mL.[1,11] In clinical practice, IDT with carboplatin at the full concentration (10 mg/mL) is generally avoided due to irritant effects and reported risk of local skin necrosis and scarring.[12]

RDD was carried out using modified protocols based on the Castells desensitization regimen.[8] Depending on reaction severity, comorbidities, and skin test results, patients received a 12-step (three-bag), 16-step (four-bag), or 20-step (five-bag) protocol. The 12-step protocol included three dilutions of the final dose (X/100, X/10, X). For patients with previous grade 3 reactions or high-risk features, an additional dilution (X/1000) was added to create a 16-step protocol. A 20-step protocol was used in selected high-risk patients and involved serial dilution of chemotherapy solutions to achieve 1/10, 1/100, and 1/1000 concentrations.[13,14] All desensitization procedures were administered in an inpatient monitored unit. Premedication consisted of intravenous methylprednisolone (40 mg), an H1 antihistamine (pheniramine 45.5 mg), and an H2 antagonist (famotidine 20 mg or ranitidine 50 mg), administered 30 minutes prior to RDD, according to institutional practice.[5]

Ethical approval was obtained from the Hacettepe University Ethics Committee (approval number: SBA 25/917, date: 09.12.2025). Owing to the retrospective study design, informed consent was waived.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 27.0 (SPSS Inc., Chicago, IL). The normality of continuous variables was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Non-normally distributed continuous variables were compared using the Mann–Whitney U test. Normally distributed continuous variables were compared using Student's t-test. Categorical variables were analyzed using the Pearson chi-square test or Fisher's exact test, as appropriate. Data are presented as medians (minimum-maximum) for continuous variables and as numbers (percentages) for categorical variables. Risk factors associated with the development of BTRs were evaluated using univariate regression analyses followed by multivariate models. All results are reported with 95% confidence intervals. A P value <0.05 was considered statistically significant.

RESULTS

A total of 2,131 patients received chemotherapy during the study period, of whom 105 (5.0%) experienced platinum-induced immediate HSRs. Among these patients, 75 (71.4%) were female, and the mean age was 61.3±10.3 years. The demographic and clinical characteristics of the study cohort are summarized in Table 1.

Carboplatin was the most frequently implicated platinum agent, identified in 56 (53.3%), patients followed by oxaliplatin in 35 (33.3%) patients and cisplatin in 14 (13.3%) patients.

Table 1. Demographic and clinical characteristics of patients with and without BTRs during rapid drug desensitization with platinum agents

Variables, n (%)	All patients (n = 105)	Patients with BTRs (n = 40)	Patients without BTRs (n = 65)	*P* value
Age at diagnosis (years), mean (± SD)	61.3±10.3	61.7±12.7	61.0±8.9	0.745
Sex				
Male	30 (28.6)	11 (27.5)	19 (29.2)	0.849
Female	75 (71.4)	29 (72.5)	46 (70.8)	
BMI, median, (min–max)	26.3 (16.7–55.1)	25.7 (18.6–36.7)	26.6 (16.7–55.1)	0.266
Obesity (BMI ≥30 kg/m²)	29 (27.6)	9 (22.5)	20 (30.8)	0.357
Other drug allergy diagnosis*	16 (15.2)	8 (20.0)	8 (12.3)	0.287
Comorbidity†	50 (47.6)	22 (55.0)	28 (43.1)	0.235
Hypertension	33 (31.4)	15 (37.5)	18 (27.7)	0.293
Antihypertensive treatment††				
Beta-blocker	4 (15.4)	2 (18.2)	2 (13.3)	0.426
ACE inhibitor/ARB	15 (57.7)	5 (45.5)	10 (66.7)	
Beta-blocker and ACE inhibitor/ARB	1 (3.8)	0 (0.0)	1 (6.7)	
Other	6 (23.1)	4 (36.4)	2 (13.3)	
CVD, n (%)	8 (7.6)	6 (15.0)	2 (3.1)	0.051
Family history of drug allergies, n (%)	7 (6.7)	1 (2.5)	6 (9.2)	0.248
Type of chemotherapy, n (%)				
Monotherapy	2 (1.9)	1 (2.5)	1 (1.5)	1.000
Combination therapy	103 (98.1)	39 (97.5)	64 (98.5)	
Culprit chemotherapeutic agent, n (%)				
Cisplatin	14 (13.3)	4 (10.0)	10 (15.4)	0.330
Carboplatin	56 (53.3)	25 (62.5)	31 (47.7)	
Oxaliplatin	35 (33.3)	11 (27.5)	24 (36.9)	
Time to index reaction (minutes), median (min–max)	30.0 (2.0–180.0)	20.0 (5.0–180.0)	30.0 (2.0–180.0)	0.884
Cycle of index reaction, median (min–max)	5.0 (1.0–20.0)	6.0 (1.0–16.0)	5.0 (1.0–20.0)	0.303
Total cumulative chemotherapy dose (mg), median (min–max)	250.0 (37.5–720.0)	290.0 (80.0–700.0)	240.0 (37.5–720.0)	0.376
Index reaction severity (Brown's classification), median (min–max)				
Mild	26 (24.8)	7 (17.5)	19 (29.2)	0.365
Moderate	73 (69.5)	30 (75.0)	43 (66.2)	
Severe	6 (5.7)	3 (7.5)	3 (4.6)	
Skin test positivity with the culprit drug, n (%)	33 (31.4)	14 (35.0)	19 (29.2)	0.690
Number of chemotherapy cycles with RDD, median (min–max)	3.0 (1.0–17.0)	4.0 (1.0–17.0)	3.0 (1.0–12.0)	0.081
Number of chemotherapy cycles without BTRs	3.0 (0.0–16.0)	2.5 (0.0–16.0)	3.0 (1.0–12.0)	0.198

*Cetuximab, iron supplement, Sinovac vaccine (inactivated SARS-CoV-2 virus), proton pump inhibitor, and granulocyte colony-stimulating factor therapy, NSAID, antibiotic

†Asthma, hypertension, cardiovascular disease

††Percentages calculated among patients with hypertension

BTRs: breakthrough reactions, SD: standard deviation, min: minimum, max: maximum, BMI: body mass index, ACE: angiotensin-converting enzyme, ARB: angiotensin receptor blocker, CVD: cardiovascular disease, RDD: rapid drug desensitization, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, NSAID: non-steroidal anti-inflammatory drug

Index reactions occurred at a median of 5 chemotherapy cycles (range: 1.0–20.0). According to Brown's[10] classification, index reactions were mild in 26 (24.8%) patients, moderate in 73 (69.5%) patients, and severe in 6 (5.7%) patients. The most common clinical manifestations of index reactions were cutaneous symptoms (80 patients, 76.2%); respiratory (61 patients, 58.1%); cardiovascular (27 patients, 25.7%); neurological (17 patients, 16.2%); gastrointestinal (11 patients, 10.5%); fever (9 patients, 8.6%); and back pain (2 patients, 1.9%). Skin testing was performed in 84 patients (80.0%), of whom 33 (39.2%) had positive results. SPT was positive in 7 of 84 patients (8.3%). Among patients with negative prick test results (n = 77), IDT yielded positive results in 27 (33.7%) patients (Table 1).

A total of 430 chemotherapy administrations were performed using RDD; the median number of procedures per patient was 3 (range: 1–17). Overall, 40 (38.1%) patients experienced a total of 62 (14.4%) BTRs among all desensitization procedures. BTRs occurred at a median cycle of 2.0 (range: 1.0–16.0) and most frequently at the 16th step of the desensitization protocol (range: 1.0–20.0). Among the 62 BTRs, 49 involved cutaneous symptoms, 10 involved respiratory symptoms, and 14 involved cardiovascular symptoms. Epinephrine administration was required in 4 BTRs, and no fatalities occurred. Overall, 414 of 430 (94.1%) desensitization procedures were successfully completed.

Analysis stratified by platinum agent showed that index reactions occurred at median cycles of 4.0 (range: 2.0–10.0) for cisplatin, 6.0 (range: 1.0–20.0) for carboplatin, and 5.0 (range: 1.0–14.0) for oxaliplatin, with no statistically significant difference among the three agents (P = 0.157). The proportion of desensitization procedures completed without BTRs was similar among carboplatin (226/266, 85.0%), oxaliplatin (110/126, 87.3%), and cisplatin (32/38, 84.2%) (P = 0.800) (Figure 1). Skin test positivity rates by culprit agent were 33.3% (4/14) for cisplatin, 31.8% (14/43) for carboplatin, and 53.5% (15/35) for oxaliplatin, with no statistically significant differences among groups (P = 0.118). A significant difference in sex distribution according to the culprit platinum agent was observed: HSRs were more frequent in males receiving oxaliplatin (20 patients, 57.1%) than in males receiving cisplatin (1 patient, 7.1%) or carboplatin (9 patients, 16.1%) (P < 0.001). The distribution of malignancies differed among platinum agents, with gastrointestinal malignancies accounting for a higher proportion of cases in the oxaliplatin group (34/35, 97.2%) than in the carboplatin (2/56, 3.5%) and cisplatin (1/14, 7.1%) groups (P < 0.001) (Table 2). Desensitization characteristics and BTR outcomes, stratified by culprit platinum agent, are summarized in Table 3.

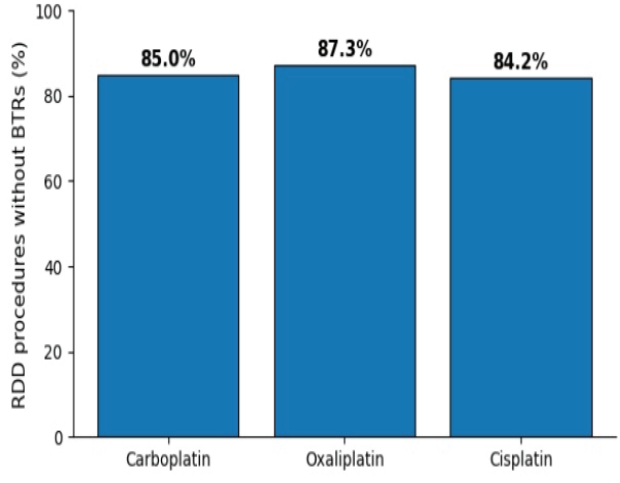

Figure 1. Breakthrough reaction-free desensitization rates by platinum agent

RDD: rapid drug desensitization, BTRs: breakthrough reactions

Potential risk factors for BTRs, including age, sex, type of chemotherapy, body mass index, history of other drug allergy, atopy, hypertension, culprit platinum agent, index reaction severity, skin test positivity, and the total number of desensitizations, were evaluated using univariate and multivariate logistic regression analyses. In univariate analysis, atopy [odds ratio (OR): 4.62, 95% confidence interval (CI): 1.03–20.7; P = 0.046], skin test positivity (OR: 3.69, 95% CI: 1.33–10.2; P = 0.012), and total number of desensitizations (OR: 1.18, 95% CI: 1.01–1.37; P = 0.034) were associated with an increased risk of BTRs. However, none of these variables remained statistically significant in the multivariate model. Detailed results are presented in Supplementary Table S1.

DISCUSSION

Current literature supports the safe continuation of platinum-based chemotherapy through RDD, with success rates approaching 98.7%; however, data directly comparing outcomes among different platinum agents are limited.[3,6,7] Consistent with these data, our study demonstrated a high overall desensitization completion rate of 94.1%, confirming the effectiveness and safety of RDD in a real-life clinical setting and demonstrating comparable success rates for carboplatin, oxaliplatin, and cisplatin.

Previous studies have shown that cutaneous symptoms are the most frequent and earliest manifestations of platinum-induced HSRs across all platinum agents, followed by respiratory symptoms, while cardiovascular involvement, although less common, is associated with greater severity.[15,16] In our cohort, index reactions most commonly presented with cutaneous symptoms, followed by respiratory and cardiovascular manifestations. In the study by Gorgulu Akin et al.,[7] HSRs occurred at a median of the fifth infusion, with significant differences in reaction onset according to the specific platinum agent, occurring at a median of 6 cycles for carboplatin and 3 cycles for both cisplatin and oxaliplatin. In our cohort, index HSRs occurred after a median of five chemotherapy cycles. Although the median cycle number at reaction onset was similar across platinum agents (6 for carboplatin, 4 for cisplatin, and 5 for oxaliplatin), no statistically significant difference in reaction timing was observed. Although carboplatin HSRs are generally reported to occur after a higher number of treatment cycles, the earlier onset observed in our cohort may be explained by our status as a tertiary referral center, where close collaboration with oncologists and heightened awareness of chemotherapy-related HSRs facilitate earlier recognition and referral.[3,13]

The sensitivity of skin testing to platinum drugs varies among studies, with an overall reported sensitivity of approximately 66%.[3]

Table 2. Baseline demographic and clinical characteristics of patients according to culprit platinum agent

Variables, n (%)	Cisplatin (n = 14)	Carboplatin (n = 56)	Oxaliplatin (n = 35)	*P* value
Age at diagnosis (years), median (min–max)	61.0 (42.0–70.0)	61.0 (36.0–86.0)	63.0 (34.0–81.0)	0.489
Sex				
Male	1 (7.1)	9 (16.1)	20 (57.1)	**<0.001**
Female	13 (92.9)	47 (83.9)	15 (42.9)	
BMI, median (min–max)	27.0 (22.0–37.6)	27.9 (16.6–55.1)	25.3 (17.3–36.8)	0.164
Obesity (BMI ≥30 kg/m²)	4 (28.6)	19 (33.9)	6 (17.1)	0.218
History of other drug allergies	4 (28.6)	7 (12.5)	5 (14.3)	0.320
Drug allergy type				
NSAID	0 (0.0)	1 (14.3)	2 (40.0)	
Antibiotic	1 (25.0)	2 (28.6)	3 (60.0)	0.361
Others*	3 (75.0)	4 (57.1)	0 (0.0)	
Comorbidity†	6 (42.9)	26 (46.4)	18 (51.4)	0.834
Hypertension	4 (28.6)	16 (28.6)	13 (37.1)	0.672
Antihypertensive treatment††				
Beta-blocker	1 (25.0)	2 (16.7)	1 (10.0)	
ACE inhibitor/ARB	3 (75.0)	6 (50.0)	6 (60.0)	0.796
Beta-blocker and ACE inhibitor/ARB	0 (0.0)	1 (8.3)	0 (0.0)	
Other	0 (0.0)	3 (25.0)	3 (30.0)	
CVD	0 (0.0)	5 (8.9)	3 (8.6)	0.513
Family history of drug allergy	13 (92.9) 1 (7.1)	52 (92.9) 4 (7.1)	33 (94.3) 2 (5.7)	0.962
Type of malignancy				
Gynecologic cancers	11 (78.7)	38 (67.8)	1 (2.8)	
Head and neck tumors	2 (14.2)	1 (1.7)	0	**< 0.001**
Gastrointestinal malignancies	1 (7.1)	2 (3.5)	34 (97.2)	
Lung cancer	0	10(17.8)	0	
Others**	0	5 (8.9)	0	
Type of mutation				
HER/neu	1 (16.7)	1 (5.6)	1 (25.0)	
TP53	4 (66.7)	13 (72.2)	0 (0.0)	0.098
Others##	1 (16.7)	4 (22.2)	3 (75.0)	
Type of chemotherapy				
Monotherapy	2 (14.3)	0 (0.0)	0 (0.0)	**0.001**
Combination therapy	12 (85.7)	56 (100.0)	35 (100.0)	
Time to index reaction (minutes), median (min–max)	30.0 (2.0–110.0)	20.0 (3.0–80.0)	30.0 (5.0–180.0)	0.118
Cycle of index reaction, median (min–max)	4.0 (2.0–10.0)	6.0 (1.0–20.0)	5.0 (1.0–14.0)	0.157
Index reaction severity (Brown's classification), median (min–max)				
Mild	6 (42.9)	11 (19.6)	9 (25.7)	
Moderate	8 (57.1)	40 (71.4)	25 (71.4)	0.275
Severe	0 (0.0)	5 (8.9)	1 (2.9)	
Skin test positivity with the culprit drug	4 (33.3)	14 (31.8)	15 (53.5)	0.118

*Cetuximab, iron supplement, Sinovac vaccine (inactivated SARS-CoV-2 virus), proton pump inhibitor, and granulocyte colony-stimulating factor therapy

†Asthma, hypertension, cardiovascular disease

††Percentages calculated among patients with hypertension

**Skin tumors, hematolymphoid malignancies, ocular tumors, and breast cancer

##EGFR, c-KIT, KRAS, BRCA, PD-L1 expression, mismatch repair deficiency, microsatellite instability, and PMS2 loss

min: minimum, max: maximum, BMI: body mass index, NSAID: non-steroidal anti-inflammatory drug, ACE: angiotensin-converting enzyme, ARB: angiotensin receptor blocker, CVD: cardiovascular disease, HER/neu: human epidermal growth factor receptor 2, TP53: tumor protein p53, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, EGFR: epidermal growth factor receptor, c-KIT: KIT proto-oncogene, receptor tyrosine kinase, KRAS: Kirsten rat sarcoma viral oncogene homolog, BRCA: breast cancer gene, PD-L1: programmed death-ligand 1

Table 3. Desensitization characteristics and breakthrough reaction outcomes according to platinum agent

Variables, n (%)	Cisplatin (n = 14)	Carboplatin (n = 56)	Oxaliplatin (n = 35)	*P* value
Total RDD procedures	38 (8.8)	266 (61.9)	126 (29.3)	**<0.001**
Chemotherapy cycles with RDD per patient, median (min–max)	2.0 (1.0–9.0)	4.0 (1.0–17.0)	3.0 (1.0–10.0)	0.119
Number of patients with BTRs	4 (29.6)	25 (44.6)	11 (31.4)	0.330
Chemotherapy cycles without BTRs per patient, median (min–max)	1.5 (0.0–9.0)	3.0 (0.0–16.0)	3.0 (0.0–9.0)	0.159
RDD procedures completed without BTRs	32 (84.2)	226 (85.0)	110 (87.3)	0.800
Cutaneous BTR symptoms	7 (63.6)	31 (55.4)	12 (63.2)	0.660
Respiratory BTR symptoms	1 (9.1)	6 (10.7)	3 (15.8)	0.780
Cardiovascular BTR symptoms	2 (18.2)	10 (17.9)	2 (10.5)	0.790
Febrile BTR symptoms	0 (0.0)	5 (8.9)	2 (10.5)	0.940
Anaphylaxis events during BTRs	0 (0.0)	4 (7.1)	0 (0.0)	0.270

RDD: rapid drug desensitization, BTRs: breakthrough reactions

The diagnostic sensitivity of skin testing to platinum agents differs according to the specific compound. In contemporary studies, carboplatin has consistently demonstrated the highest skin test sensitivity, reported in approximately 60–70% of patients, whereas oxaliplatin and cisplatin show lower and more heterogeneous sensitivities, generally ranging from 30–60% and 20–50%, respectively.[1,11,12,17,18] In our cohort, skin test positivity rates were 31.8% for carboplatin, 53.5% for oxaliplatin, and 33.3% for cisplatin. Oxaliplatin showed higher positivity rates, consistent with known variability in oxaliplatin-associated HSRs. The lower carboplatin skin test positivity observed in our study may be explained by the use of lower IDT concentrations, as the predictive value of skin testing is known to be concentration dependent.[19] Although platinum-induced HSRs are generally considered IgE-mediated, the low rate of positive skin tests in our cohort suggests that non-IgE-mediated mechanisms may also contribute. Pathways such as cytokine release or complement activation may be involved, particularly in patients undergoing RDD who have negative skin tests. Because acute-phase cytokine markers, including interleukin-6, were not routinely measured in our study, we were unable to further delineate the relative contributions of these mechanisms.

Previous platinum desensitization studies have reported that 71.0–75.8% of procedures were completed without BTRs.[6,7] In our study, approximately 85% of desensitization procedures were completed without BTRs, indicating a relatively lower rate of BTRs compared with previously published data. When stratified by platinum agent, desensitization procedures were completed without BTRs in 85.0% of carboplatin administrations, 87.3% of oxaliplatin administrations, and 84.2% of cisplatin administrations, with no statistically significant differences among agents. The higher reaction-free completion rate observed in our study may be attributable to the use of a 20-step desensitization protocol, which allows for more gradual dose escalation. Previous studies and current EAACI recommendations support increasing the number of desensitization steps in high-risk patients, particularly those receiving platinum agents, to improve tolerability and reduce BTRs.[1,4,5] Previous studies have reported that RDD is successfully completed in 94% to 98.7% of procedures.[5,7] Consistent with this range, our study demonstrated a similarly high overall completion rate: 414 of 430 desensitization procedures (94.1%) were successfully completed. From a clinical perspective, our findings indicate that desensitization outcomes do not differ meaningfully among platinum agents, supporting RDD as a safe and practical approach that enables patients with HSRs to continue essential chemotherapy.

Although germline BRCA1/2 mutations have been reported as independent risk factors for carboplatin HSRs, particularly in patients receiving repeated cycles, comparative analyses of mutation frequencies across different platinum agents remain limited.[20] In our cohort, the frequency of BRCA1/2 mutations did not differ significantly among patients treated with cisplatin, carboplatin, or oxaliplatin; this suggests that BRCA-related genetic susceptibility may not account for inter-agent differences in hypersensitivity patterns. Notably, sex-related differences were observed with respect to the culprit platinum agent. Kim et al.[17] previously reported a male predominance among patients experiencing oxaliplatin HSRs, with males constituting 54.2% of affected cases. In line with these findings, our study identified a significant difference in the sex distribution of HSRs among patients treated with platinum-based agents, with reactions observed more frequently in male patients receiving oxaliplatin (57.1%) than in those treated with cisplatin (7.1%) or carboplatin (16.1%). This pattern is considered to be related both to the significantly higher prevalence of gastrointestinal malignancies in the oxaliplatin-treated cohort and to existing epidemiological evidence demonstrating a higher incidence of gastrointestinal cancers in males.[21]

Study Limitations

The limitations of this study include its retrospective design, which inherently limits causal inference, and the potential for incomplete documentation and referral bias. Another limitation is that serum tryptase measurements during index or BTRs were not routinely available. In addition, the relatively small number of patients receiving cisplatin may have limited the statistical power for agent-specific comparisons. The strengths of this study include its relatively large real-life cohort, the

comprehensive evaluation of three commonly used platinum agents within the same clinical setting, and the standardized assessment of index reactions, skin testing, and desensitization outcomes, using predefined, risk-adapted protocols and a uniform premedication regimen applied across all procedures.

CONCLUSION

This study demonstrates a high overall success rate of RDD (94.1%). The success rate without BTRs in the overall platinum cohort was 85.6%, with comparable success rates for carboplatin (85.0%), oxaliplatin (87.3%), and cisplatin (84.2%). HSRs to oxaliplatin were observed more frequently in male patients compared with reactions to other platinum agents.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Hacettepe University Ethics Committee (approval number: SBA 25/917, date: 09.12.2025).

Informed Consent: Owing to the retrospective study design, informed consent was waived.

Footnotes

Authorship Contributions

Concept: H.K.,E.D., M.C., Design: H.K., K.Ç., E.H, Data Collection or Processing: H.K., E.D., Analysis or Interpretation: H.K., E.D., Literature Search: H.K.,K.Ç., E.H. Writing: H.K.,Ç.T., A.P.U., G.K., A.F.K.

Conflict of Interest: Ebru Damadoğlu, MD, is an Editor of the Thoracic Research and Practice. She was not involved in the peer review of this article and had no access to information regarding its peer review. The other authors have no disclosures.

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Supplementary Table S1. https://d2v96fxpocvxx.cloudfront.net/d18681b3-da48-42d0-9b05-c9e02fb8192c/content-images/add714ec-6985-4279-90ce-73fc11e42dd2.pdf

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