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Clinical Outcomes of Chemotherapy Desensitization: A Retrospective Single-Center Experience in an Allergy and Immunology Clinic

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ABSTRACT

Objective: Patients receiving repeated chemotherapy cycles may develop hypersensitivity reactions due to sensitization. Rapid drug desensitization protocols allow safe reintroduction of the culprit chemotherapeutics. This study aimed to evaluate the clinical characteristics of patients who underwent rapid drug desensitization in our clinic and to analyze the features and predictors of breakthrough reactions.

Materials and Methods: After ethics committee approval, patients who underwent rapid drug desensitization with chemotherapeutic agents between 2019 and 2024 were retrospectively reviewed. Demographic data, initial hypersensitivity reaction profiles, skin test results, and breakthrough reactions were analyzed.

Results: 29 patients, including 26 females and 3 males with a mean age of 53.1 ± 10.8 years, were included. Rapid drug desensitization was performed with platinum agents in 18 patients and with taxanes in 11 patients. The platinum group was older than the taxane group, with mean ages of 56.5 ± 10.3 and 47.5 ± 9.6 years, respectively ($p = 0.028$). Initial hypersensitivity reactions were type I (immediate) hypersensitivity reactions in 14, cytokine release reaction in 1, and mixed-type in 3 platinum cases, and type I (immediate) hypersensitivity reactions in 8, cytokine release reaction in 1, and mixed-type in 2 taxane cases. Platinum-related reactions occurred at the 6th cycle after 30 minutes, versus the 1st cycle at 5 minutes for taxanes ($p < 0.05$). Skin tests were positive in 11 platinum patients and 1 taxane patient ($p = 0.027$). Breakthrough reactions were more frequent in patients with positive skin tests ($p = 0.024$) and in those with urogenital malignancies ($p = 0.024$). Of the 104 desensitization procedures, all but one were successfully completed.

Conclusion: Rapid drug desensitization is a safe and effective approach for managing chemotherapy-induced hypersensitivity reactions. Taxane-related reactions occur earlier, and positive skin tests or urogenital malignancy may predict breakthrough reactions.

Keywords: Desensitization, chemotherapy, hypersensitivity, platinums, taxanes

INTRODUCTION

Although the first discovery of chemotherapy dates back to the 1940s, agents that are widely used today, such as platinum compounds and taxanes, were first introduced into clinical practice in the 1970s (1-3). While these drugs serve as a powerful weapon against cancer, their use is limited by associated adverse effects—such as nausea and vomiting, alopecia, neuropathies, and others—as well as hypersensitivity reactions (HSRs), which are exagger-

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ated or inappropriate immune responses to the drugs (4,5). Patients who develop HSRs to chemotherapeutic agents may exhibit a wide range of clinical manifestations, ranging from mild urticaria to severe anaphylaxis and death. HSRs occur more frequently with platinum-based agents (e.g. oxaliplatin, carboplatin), taxanes (e.g. paclitaxel, docetaxel), L-asparaginase, epipodophyllotoxins, and procarbazine than others (6).

Among platinum agents, carboplatin and cisplatin are most frequently used in the treatment of genitourinary cancer, lung, and head and neck cancers, whereas oxaliplatin is predominantly used in colorectal cancer. These drugs may trigger type I (immediate) HSRs, cytokine release reactions, or mixed reactions. Taxanes are widely employed in the treatment of breast, prostate, head and neck, gynecological, and lung cancers. Although taxane-related HSRs were initially thought to be non-IgE mediated and mainly associated with infusion solvents such as Cremophor EL and Polysorbate 80, subsequent studies have demonstrated that the majority of patients exhibit true allergic responses to taxanes, with evidence suggesting cross-reactivity with tree pollens. Infusion reactions with cytokine release can also induce mild to moderate symptoms such as fever, chills, rash, muscle pain, and headache that occur within the first few hours and mostly following first exposure to the drug (7,8).

Skin tests are important indicators in detecting type-1 (immediate) HSRs. They are useful in particular for platinum agents and taxanes in some cases. Skin tests can provide information for diagnosis, prevention, risk evaluation and cross-reactivity with platinum compounds. Skin test positivity reaches 100%, especially in cases of carboplatin hypersensitivity with a history of severe reactions (8).

When an HSR occurs, the first approach is usually to switch the treatment to an alternative agent. If no alternative therapy is available, or if the alternative agent is less effective than the culprit drug, desensitization should be considered. Rapid drug desensitization (RDD) is a procedure that allows patients to receive the optimal treatment by administering the drug in gradually increasing doses at a controlled rate (9).

This study aimed to assess the phenotypic profiles of patients who received RDD in our clinic, as well as the characteristics of breakthrough reactions (BTRs) occurring during the RDD procedure.

MATERIALS and METHODS

Study Design and Patients

After receiving approval from the local ethics committee (approval number: TABED-1-24-465), we retrospectively reviewed patients who underwent RDD with chemotherapy at the Immunology and Allergy Diseases Clinic between 2019 and 2024.

We reviewed patients' medical records to evaluate sociodemographic characteristics (e.g. age, sex, occupation), the type of chemotherapeutic agent used, the dose number and minute at which the initial HSR occurred, the severity of the HSR, skin test results, type of malignancy, the organ systems involved in the initial HSRs together with their specific symptoms and/or findings, and the treatments administered for the management of the initial HSRs, as well as the features (e.g. number and severity) of BTRs.

The severity of patients' initial HSRs was classified as mild, moderate, or severe according to the Brown classification scale of anaphylaxis. Cases presenting with skin and subcutaneous tissue involvement, such as erythema, urticaria, or angioedema, were classified as mild HSRs; those with gastrointestinal, respiratory, or circulatory symptoms—such as dyspnea, abdominal pain, nausea, vomiting, dizziness, or presyncope—were considered moderate; and patients exhibiting vital sign changes, including hypotension, hypoxia, confusion, loss of consciousness or incontinence, were classified as having severe HSRs (10).

Classification of HSRs

The symptoms of type l (immediate) HSRs included pruritus, urticaria, angioedema, nasal congestion, sneezing, wheezing, cough, throat tightness, tongue swelling, hypotension, and syncope. Cytokine release reaction symptoms included chest pain, back or abdominal pain, headache, rigors, chills, numbness, hypertension, hypotension, and fever. Mixed reactions were characterized by the coexistence of clinical features from both Type I (immediate) and cytokine release reaction phenotypes (11,12).

Skin Testing

Skin testing was performed in patients with a history of immediate HSRs to chemotherapy agents, 2 to 4 weeks after the initial reaction. The skin prick test (SPT) was conducted first, using concentrations of 10 mg/mL for carboplatin, 5 mg/mL for oxaliplatin, 6 mg/mL for pacli-

taxel, and 1 mg/mL for docetaxel. Histamine and saline were used as positive and negative controls, respectively. In patients with negative SPT results, intradermal tests (IDTs) were subsequently performed. For paclitaxel and docetaxel, 1:100 and 1:10 dilution were used; for carboplatin, 1:10 dilution was administered. In the case of oxaliplatin, IDT was performed at 1:10 dilution, and the undiluted drug (8,13,14). A positive result in either the SPT or the IDT was considered indicative of a positive skin test.

Desensitization Protocol

A standardized 12-step, 3-solution desensitization protocol was administered to patients who had experienced immediate HSRs to chemotherapeutic agents. This protocol was the first-line approach unless the initial HSR was classified as high-grade (according to the Brown anaphylaxis grading scale), or a high-grade BTR occurred during RDD. In such cases, a 16-step protocol was preferred in order to enhance safety and minimize the risk of severe HSRs during re-exposure. In the standard 12-step protocol, 3 solutions were prepared at concentrations of 1:100, 1:10, and 1:1. In the extended 16-step protocol, an additional 1:1000 dilution was included as the initial step.

Written informed consent was obtained from all patients prior to the procedure. The intervention was performed on an outpatient basis. For each patient, the entire procedure was conducted under the supervision of an experienced nurse and physician. Premedication regimens were determined based on the clinical characteristics of each patient. While most patients received H1-antihistamines and glucocorticoids, acetylsalicylic acid was administered to those with a history of flushing, paracetamol to those with fever or chills, and montelukast to those with wheezing or bronchospasm (15). Beta-blockers were discontinued 24 hours prior to the procedure.

For patients who experienced BTRs, the infusion was immediately discontinued. Management was tailored according to the affected organ system and the severity of the HSR. Once all clinical signs and symptoms had resolved, the infusion was restarted. The severity of BTRs was graded based on the Brown classification scale (10).

Statistical Analysis

Descriptive statistics were used for the comparison of demographic data, while the Pearson Chi-square test and Fisher's exact test were used for the comparison of categorical variables. Normally distributed continuous variables were presented as mean ± standard deviation, whereas non-normally distributed continuous variables were presented as median (minimum–maximum). A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA).

RESULTS

Clinical and Demographic Characteristics of the Patients

The study group consisted of 29 patients, including 26 females and 3 males, with a mean age (±SD) of 53.1 (±10.8) years. The sociodemographic and clinical characteristics of the study group, the type of chemotherapy used, and the severity of initial HSRs and BTRs are summarized in Table I. The mean age of patients receiving taxane-based chemotherapy was significantly lower than that of those receiving platinum-based chemotherapy (47.5±9.6 vs. 56.5±10.3 years, respectively; p=0.028).

Platinum-based chemotherapy was administered with RDD in 18 patients (62.1%), while a taxane regimen was used in 11 patients (37.9%). Among the patients who received platinum-based chemotherapy (n=18), 11 received carboplatin (61.1%) and 7 received oxaliplatin (38.9%). In the taxane group (n=11), 6 patients received paclitaxel (54.5%) and 5 received docetaxel (45.5%).

When the malignancy diagnoses of the patients were compared, the most common cancer type was found to be urogenital system malignancies (n=15, 51.7%), followed by gastrointestinal system malignancies (n=8, 27.6%) and breast cancer (n=6, 20.7%). Among the patients with urogenital system malignancies (n=15), 12 had ovarian cancer (80.0%), while cervical, endometrial, and prostate cancer were each observed in 1 patient (6.7% each). Among those with gastrointestinal system malignancies (n=8), colon cancer was identified in 4 patients (50.0%), primary peritoneal cancer in 2 (25.0%), rectal cancer in 1 (12.5%), and gastric cancer in 1 (12.5%).

Characteristics of Initial HSRs

Among the initial HSRs, type 1 (immediate) reactions were the most frequent (n=22, 75.9%), followed by mixed reactions (n=5, 17.2%) that display features of both type 1 (immediate) and cytokine release reactions, with cytokine release reactions being the least common (n=2, 6.9%).

Table I: Sociodemographic and clinical characteristics of the study group

Variables	Values
Age (year)	53.1 (±10.8)
Sex	
Female	26 (89.7)
Male	3 (10.3)
Occupation	
Housewife	15 (51.7)
Government Officer	3 (10.3)
Retired	10 (34.5)
Worker	1 (3.4)
Type of administered CT	
Platinum	18 (62.1)
Carboplatin	11 (37.9)
Oxaliplatin	7 (24.1)
Taxane	11 (37.9)
Paclitaxel	6 (20.7)
Docetaxel	5 (17.2)
Type of Initial HSRs	
Type 1 (immediate)	22 (75.9)
Cytokine Release	2 (6.9)
Mixed	5 (17.2)
Skin testing	
Positive	12 (41.4)
Negative	11 (41.4)
Severity of Initial HSRs	
Grade 1	5 (17.2)
Grade 2	16 (55.2)
Grade 3	8 (27.6)
BTR during RDD	
Yes	17 (58.6)
Grade 1	12 (41.3)
Grade 3	5 (17.2)
No	12 (41.4)
Diagnosis of malignancy	
Urogenital System	15 (51.7)
Gastrointestinal System	8 (27.6)
Breast	6 (20.7)

Values are presented as number (%) or mean (±SD).

CT: Chemotherapy, **HSR:** Hypersensitivity Reaction, **RDD:** Rapid Drug Desensitization, **BTR:** Breakthrough Reaction

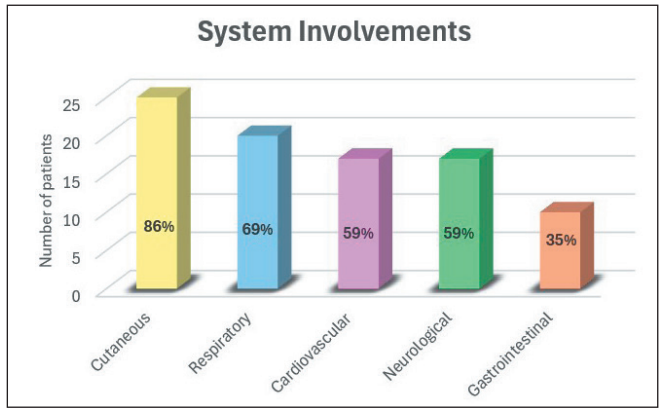


Figure 1: Distribution of system involvement in initial HSRs.

In the initial HSRs, cutaneous involvement was the most common finding, observed in 25 patients (86%). Respiratory involvement occurred in 20 patients (69%), while cardiovascular and neurological systems were each affected in 17 patients (59%), and gastrointestinal involvement was reported in 10 patients (35%) (Figure 1). Within the spectrum of cutaneous involvement, flushing/erythema was observed in 69.0% (n=20), angioedema in 27.6% (n=8), pruritus in 17.2% (n=5), and urticaria in 13.8% (n=4) of the patients. Regarding respiratory system involvement, dyspnea occurred in 48.3% (n=14), hypoxia in 24.1% (n=7), cough in 10.3% (n=3), and stridor and cyanosis each in 3.4% (n=1) of the patients. Regarding cardiovascular involvement, tachycardia was observed in 24.1% (n=7), syncope in 17.2% (n=5), hypotension in 10.3% (n=3), hypertension in 6.9% (n=2), and chest pain, dizziness, and presyncope each in 3.4% (n=1) of the patients. Regarding gastrointestinal involvement, nausea was reported in 27.6% (n=8), while vomiting and abdominal pain were each observed in 17.2% (n=5) of the patients. Regarding neurological involvement, numbness was observed in 27.6% (n=8), back pain in 17.2% (n=5), loss of consciousness in 13.8% (n=4), and confusion in 3.4% (n=1) of the patients. Fever was observed in 3.4% (n=1) of the patients, and an antipyretic was administered.

The initial HSRs was classified as grade 2 in 16 patients (55.2%), grade 3 in 8 patients (27.6%), and grade 1 in 5 patients (17.2%). Among patients in the platinum group, the initial HSR was grade 2 in 11 patients (61.1%), grade 1 in 4 patients (22.2%), and grade 3 in 3 patients (16.7%). In the taxane group, grade 2 and grade 3 HSRs were observed in 5 patients each (45.5%), while grade 1 HSRs were detected in 1 patient (9.1%) (p=0.219).

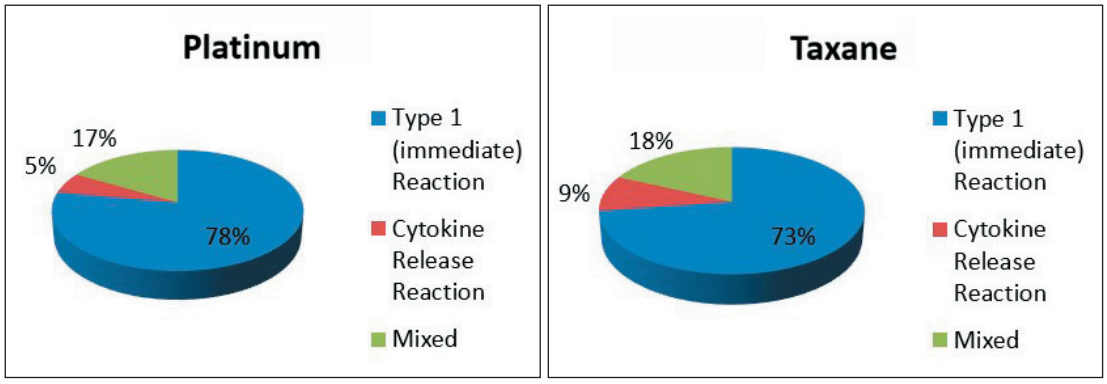


Figure 2: Comparison of initial HSR types in patients receiving platinum and taxane therapies.

When the platinum and taxane groups were evaluated separately, type 1 (immediate) HSRs were observed in 14 (78%) patients in the platinum group and in 8 (73%) patients in the taxane group. Mixed reactions were identified in 3 (17%) patients receiving platinum and 2 (18%) patients receiving taxanes. Cytokine release reactions were observed in 1 patient from each group (Figure 2).

In the platinum group, initial HSRs occurred at a median of the 6th cycle (2–15), whereas in the taxane group they were observed at the 1st cycle (1–3) (p=0.001). For infusion timing, initial HSRs in the platinum group occurred at the 30th minute (7–60), while in the taxane group they were observed at the 5th minute (1–15) (p=0.002).

Of the 29 patients, treatment data regarding the initial HSRs were available for 20. Among these 20 patients, adrenaline was administered in 20% (n=4), antihistamines in 95% (n=19), corticosteroids in 90% (n=18), oxygen therapy in 30% (n=6), analgesics/antipyretics in 10% (n=2), and an antiemetic in 5% (n=1).

Results of Skin Testing

Skin tests were performed on a total of 23 patients, of whom 12 had positive results and 11 had negative results. Skin testing was performed in 16 patients receiving platinum, with 11 (68.8%) positive—2 on oxaliplatin and 9 on carboplatin—and 5 (31.3%) negative. In the taxane group, 7 patients were tested; 6 were negative, and the single positive case was receiving paclitaxel (p=0.027) (Table II). Except for one patient who showed a positive reaction to carboplatin on the SPT, all other positive results were detected through IDT.

Table II: Phenotypic comparison of patients treated with platinum and taxane agents

Variables	Platinum group	Taxane group	p value
Age (Year) †	56.5 (±10.3)	47.5 (±9.6)	**0.028**
Sex*			
Female	16 (88.9)	10 (90.9)	**0.684**
Male	2 (11.1)	1 (9.1)	
Type of Index HSR*			
Type 1 (immediate)	14 (78)	8 (73)	**0.925**
Cytokine Release	1 (5)	1 (9)	
Mixed	3 (17)	2 (18)	
Initial HSR Cycle‡	6 (2-15)	1 (1-3)	**0.001**
Initial HSR Minute‡	30 (7-60)	5 (1-15)	**0.002**
Severity of Initial HSRs*			
Grade 1	4 (22.2)	1 (9.1)	**0.219**
Grade 2	11 (61.1)	5 (45.5)	
Grade 3	3 (16.7)	5 (45.5)	
Skin testing*			
Positive	11 (68.8)	1 (14.3)	**0.027**
Negative	5 (31.3)	6 (85.7)	
BTR during RDD*			**0.065**
Yes	13 (72.2)	4 (36.4)	
No	5 (27.8)	7 (63.6)	
Severity of BTRs*			**0.635**
Grade 1	9 (69.3)	3 (75)	
Grade 3	4 (30.7)	1 (25)	

* Number (%), † Mean (±SD), ‡Median (min-max)

HSR: Hypersensitivity reaction, **RDD:** Rapid drug desensitization, **BTR:** Breakthrough reaction

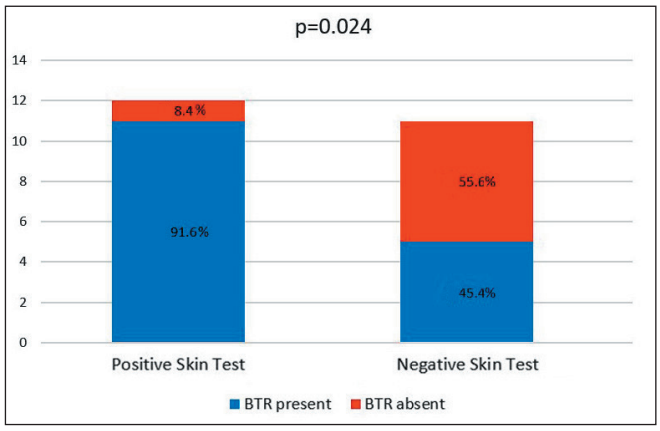


Figure 3: The incidence of BTRs according to skin test results.

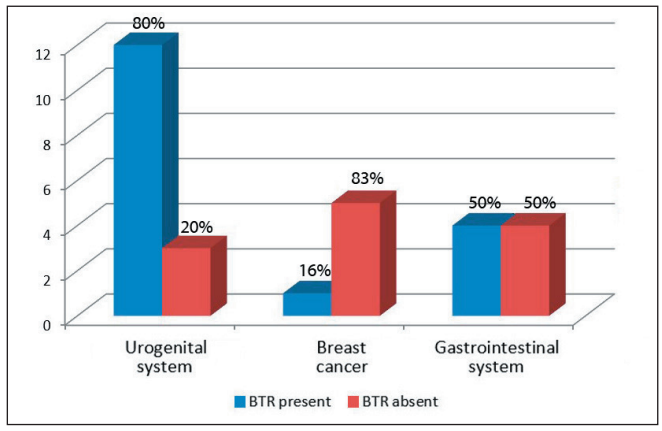


Figure 4: Frequency of BTRs according to malignancy type.

Although skin test results were negative in 5 patients from the platinum group and 6 patients from the taxane group, RDD was still performed, as their clinical histories strongly supported a severe HSR.

Characteristics of RDDs and BTRs

In this study, a total of 104 RDD procedures were performed in 29 patients with malignancies. All procedures, except for one, were successfully completed (99% success rate). The median number of RDDs per patient was 3, with the number ranging from 1 (n=9) to 10 (n=1). Twelve patients completed the RDD process without any HSR symptoms. Of the 104 RDD procedures performed, 38 (36.5%) were complicated by BTRs. BTRs occurred in 17 out of 29 patients (58.6%); of these, 12 (41.3%) experienced grade 1 HSRs, while 5 (17.2%) had grade 3 HSRs. In 7 patients, a BTR was observed only during the first RDD.

The BTRs were observed in the majority of patients receiving platinum-based therapy (n=13, 72.2%), whereas they occurred in only 4 patients (36.4%) in the taxane group (p=0.065). Of the 13 patients who experienced BTRs in the platinum group, 10 were receiving carboplatin and 3 were receiving oxaliplatin. In the taxane group, all 4 patients who experienced BTRs were receiving paclitaxel and no BTRs were observed in patients receiving docetaxel. The majority of patients in both the platinum group (n=9, 69.3%) and the taxane group (n=3, 75%) developed grade 1 reactions. Grade 3 reactions occurred in 4 (30.7%) patients in the platinum group and in 1 (25%) patient in the taxane group (p=0.635). The phenotypic comparison of patients receiving platinum and taxane therapies is summarized in Table II.

Among patients with a positive skin test, BTRs occurred in 11 of 12 patients (91.7%), whereas 1 patient (8.3%) did not experience BTR. In patients with a negative skin test, BTRs occurred in 5 of 11 patients (45.5%), while 6 patients (54.5%) did not experience BTR (p = 0.024) (Figure 3).

The BTRs were observed in 12 of 15 patients with urogenital system malignancies, 1 of 6 with breast cancer, and 4 of 8 with gastrointestinal system malignancies (p=0.024). Of the 12 patients with urogenital system malignancies who developed BTRs, 9 (75%) were treated with carboplatin and 3 (25%) with paclitaxel (Figure 4).

Failed RDD

In our study, one RDD procedure could not be completed. The patient, diagnosed with colon cancer and undergoing first-time RDD with oxaliplatin, tolerated 1/100 and 1/10 dilutions without symptoms. However, at the 1/1 dilution (40 mL/h), dyspnea, chills, and back pain developed, requiring medical treatment and oxygen support due to desaturation. After symptom resolution, the infusion was restarted but similar complaints recurred at 80 mL/h, leading to termination of the desensitization due to repeated BTRs.

DISCUSSION

In this retrospective study covering a 5-year period, we analyzed the timing, severity, and type of index HSRs, as well as the results of skin testing. Also, the potential impact of patients' clinical characteristics, the type of chemotherapeutic agent, malignancy type, and the nature and severity of the index HSR on the occurrence and severity of BTRs was evaluated. Among 104 RDD procedures, 38

BTRs were recorded, with all but one procedure successfully completed.

The majority of our study group consisted of women and the mean age was 53.1 years. In a similar study involving 58 cancer patients and 234 RDD procedures, 42 of the patients were women, and the mean age was reported as 54.7±11.0 years (16). In another study including 98 patients with a history of HSR to chemotherapy who underwent RDD, only one was male while the remaining were female, with a mean age of 55 years (range: 30–78) (17). Similar to our findings, it was also reported in a previous study that patients receiving taxane-based chemotherapy were significantly younger than those treated with platinum-based regimens (18).

The most common malignancy was urogenital followed by gastrointestinal and breast cancer in our study. In another study, the most common malignancies were gynecologic (44.8%) and gastrointestinal cancers (39.7%), followed by hematologic (8.6%), breast (5.2%), and lung cancers (1.7%) (16). Similarly, in the study by Castells and colleagues, the most common malignancies were ovarian, breast, and peritoneal cancers (17).

Similar to findings in the literature, patients in our cohort who experienced HSR with platinum agents developed initial HSRs during later cycles, whereas those receiving taxanes tended to react during the first or second cycle (6,14,17,19,20). In a previous study, among the 55 carboplatin-treated patients, the majority (73%, n=40) developed HSRs between the seventh and tenth administrations. In contrast, nearly all paclitaxel-treated patients (96%, 27 out of 28) experienced HSRs during their initial exposure (17). According to the data reported by Boulanger et al., the onset of HSRs to platinum agents may occur minutes to days after infusion, whereas taxane-related reactions typically arise within the first minutes (21). Our results demonstrated that the time to reaction onset was significantly shorter in patients receiving taxanes compared with those receiving platinum agents.

In our study, the majority of initial HSRs in the platinum group were grade 2 HSRs, whereas in the taxane group, grade 2 and grade 3 reactions were observed with equal frequency. In a study involving 72 patients with a history of HSR to platinum agents, initial HSRs were classified as grade 2 in 40 patients (55.6%), grade 3 in 27 patients (37.5%), and grade 1 in 5 patients (6.9%) (22). In a separate study of 75 patients treated with taxane-based chemotherapy, grade 2 HSRs were observed approximately twice as often as grade 3 reactions, with 50 and 22 cases reported, respectively (23).

In a prospective observational study published on April 2025, platinum-based agents were found to have a significantly higher proportion of type I (immediate) HSRs compared to other therapeutic classes, including taxanes, biologics, and checkpoint inhibitors (12). In our study, however, no significant difference was observed in the distribution of reaction phenotypes between patients receiving platinum agents and those treated with taxanes. The absence of a significant difference may be explained by insufficient statistical power, variability among drug subclasses (such as oxaliplatin vs. carboplatin or paclitaxel vs. docetaxel), and incomplete assessment of biomarkers like tryptase and IL-6.

Kang et al., in their analysis of BTRs occurring during RDD, noted that the reported incidence of BTRs ranged from 10% to 40% across different studies. In our study, BTRs were observed in more than half of the patients, with a total of 38 events, most of which were grade 1, whereas a smaller proportion were grade 3. No significant difference in the severity of BTRs was observed between the platinum and taxane groups, consistent with the previously mentioned study (16).

Previous studies have demonstrated that a positive skin test to the culprit drug is a risk factor for the development of BTRs during RDD (22,24-26). In a study of platinum-sensitive patients, 87.5% (28/32) of individuals who developed BTRs during RDD exhibited strong positive reactions on skin testing with platinum agents (22). In another study, patients with BTRs were significantly more likely to have a positive skin test (50% vs. 20%, $p < 0.05$). In addition, skin test positivity correlated with the severity of BTRs, as all grade III cases occurred in the positive skin test group ($p = 0.023$) (24). Our data also demonstrated that patients with a positive skin test to the culprit chemotherapeutic agent had a significantly higher incidence of BTRs during RDD compared to those with a negative result.

In a study investigating the risk factors for BTRs, logistic regression analysis demonstrated that the severity of the initial HSR, a history of drug allergy, and increased frequency of exposure to the chemotherapeutic agents were independent predictors of moderate to severe BTR (16). In a large study including a total of 1471 RDD procedures in

272 patients involving platinum, taxane, and monoclonal antibodies, BTRs were more frequently observed in platinum-reactive patients, those who had received 10 or more prior infusions, and patients with total IgE levels ≥100 U/mL (27). Consistent with the literature, our study also observed that cancer patients receiving platinum-based chemotherapy experienced BTRs more frequently than those receiving taxane-based chemotherapy; however, this difference was not statistically significant (24,28).

Our study demonstrated that patients with gynecologic malignancies had higher rates of BTRs compared to those with other malignancies. A review of the literature revealed no studies specifically investigating the risk of BTRs during RDD according to cancer type; however, one study reported a higher rate of immediate-type HSRs in gynecologic cancers compared to other malignancies, a finding attributed to repeated exposure in this patient group (12). The finding that a diagnosis of urogenital malignancy is a risk factor for BTR may be explained by the fact that platinum agents are the primary treatment option for ovarian cancer, and since ovarian cancer is characterized by relapses, patients are repeatedly exposed to platinum at different time points, thereby increasing the likelihood of sensitization.

Our study had certain limitations. Given its retrospective, single-center design and relatively small sample size, this study was not powered to fully evaluate the risk factors for BTRs. For example, although information on patients' allergic history and baseline tryptase levels was collected, these variables were excluded from the analysis due to substantial missing data. Additionally, since only platinum and taxane agents were evaluated, the results of this study may not be generalizable to other chemotherapeutic regimens. Secondly, although skin testing was performed in the majority of patients, the fact that it was not conducted in all participants can be considered another limitation of the study. Some studies have emphasized the importance of performing drug provocation tests at the final stage of the diagnostic work-up for antineoplastic agents, similar to the approach used for other drugs (29). The lack of drug provocation testing in our clinic represents another limitation of our study. Although drug provocation tests could not be performed due to clinical circumstances, the decision to proceed with RDD in the patients was made according to their risk classification. Of the five patients with grade 1 reactions, three underwent RDD due to positive skin test results. Skin tests could not be performed in the remaining two because antihistamines could not be discontinued; however, given their unstable cardiac status, RDD was performed for these patients as a precaution.

In conclusion, this study highlights several key messages that may guide clinical practice. First, skin test positivity emerged as the most consistent predictor of BTRs during RDD, underscoring the importance of incorporating skin testing into risk stratification when feasible. Second, the timing and severity patterns of platinum- and taxane-induced HSRs in our study were largely aligned with the prior literature, reinforcing known class-specific HSR characteristics. Third, patients with urogenital malignancies demonstrated higher BTR rates, likely reflecting repeated platinum exposure; this subgroup may warrant closer monitoring during RDD. Collectively, these findings emphasize the need for individualized risk assessment and tailored management strategies to optimize the safety of RDD protocols in oncology patients.

Conflict of Interest

The authors declare no conflicts of interest related to this work.

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REFERENCES

1. Chabner BA, Roberts TG Jr. Timeline: Chemotherapy and the war on cancer. Nat Rev Cancer 2005;5(1):65-72.
2. Martin V. Overview of paclitaxel (TAXOL). Semin Oncol Nurs 1993;9(4 Suppl 2):2-5.
3. Kelland L. The resurgence of platinum-based cancer chemotherapy. Nat Rev Cancer 2007;7(8):573-84.
4. Castells M. Rapid desensitization of hypersensitivity reactions to chemotherapy agents. Curr Drug Saf 2006;1(3):243-51.

5. Brianna, Lee SH. Chemotherapy: how to reduce its adverse effects while maintaining the potency? Med Oncol 2023;40(3):88.
6. Lee C, Gianos M, Klaustermeyer WB. Diagnosis and management of hypersensitivity reactions related to common cancer chemotherapy agents. Ann Allergy Asthma Immunol 2009;102(3):179-87; quiz 87-9, 222.
7. Rosello S, Blasco I, Garcia Fabregat L, Cervantes A, Jordan K, Committee EG. Management of infusion reactions to systemic anticancer therapy: ESMO Clinical Practice Guidelines. Ann Oncol 2017;28(suppl_4):iv100-iv18.
8. Pagani M, Bavbek S, Alvarez-Cuesta E, Berna Dursun A, Bonadonna P, Castells M, et al. Hypersensitivity reactions to chemotherapy: an EAACI Position Paper. Allergy 2022;77(2):388-403.
9. Castells M, Sancho-Serra Mdel C, Simarro M. Hypersensitivity to antineoplastic agents: mechanisms and treatment with rapid desensitization. Cancer Immunol Immunother 2012;61(9):1575-84.
10. Brown SG. Clinical features and severity grading of anaphylaxis. J Allergy Clin Immunol 2004;114(2):371-6.
11. Jimenez-Rodriguez TW, de Las Vecillas L, Labella M, Lynch DM, Besz KM, Marquis K, et al. Differential presentation of hypersensitivity reactions to carboplatin and oxaliplatin: Phenotypes, endotypes, and management with desensitization. Allergy 2024;79(3):679-89.
12. Rasmussen TH, Mortz CG, Pfeiffer P, Andersen N, Bindslev-Jensen C. Prevalence and management of immediate drug hypersensitivity observed during antineoplastic drug therapy. Acta Oncol 2025;64:574-84.
13. Brockow K, Garvey LH, Aberer W, Atanaskovic-Markovic M, Barbaud A, Bilo MB, et al. Skin test concentrations for systemically administered drugs -- an ENDA/EAACI Drug Allergy Interest Group position paper. Allergy 2013;68(6):702-12.
14. Tsao LR, Young FD, Otani IM, Castells MC. Hypersensitivity Reactions to Platinum Agents and Taxanes. Clin Rev Allergy Immunol 2022;62(3):432-48.
15. Breslow RG, Caiado J, Castells MC. Acetylsalicylic acid and montelukast block mast cell mediator-related symptoms during rapid desensitization. Ann Allergy Asthma Immunol 2009;102(2):155-60.
16. Kang Y, Kwon OY, Jung H, Kang M, An J, Lee JH, et al. Breakthrough reactions during rapid drug desensitization: Clinical outcome and risk factors. Ann Allergy Asthma Immunol 2019;123(1):48-56 e1.
17. Castells MC, Tennant NM, Sloane DE, Hsu FI, Barrett NA, Hong DI, et al. Hypersensitivity reactions to chemotherapy: outcomes and safety of rapid desensitization in 413 cases. J Allergy Clin Immunol 2008;122(3):574-80.
18. Zwimpfer TA, Scherer K, Schotzau A, Heinzelmann-Schwarz V, Hartmann K, Vetter M, et al. Desensitization in patients with hypersensitivity to platinum and taxane in gynecological cancers. Cancer Med 2024;13(1):e6840.
19. Banerji A, Lax T, Guyer A, Hurwitz S, Camargo CA, Jr., Long AA. Management of hypersensitivity reactions to Carboplatin and Paclitaxel in an outpatient oncology infusion center: a 5-year review. J Allergy Clin Immunol Pract 2014;2(4):428-33.
20. Queiros Gomes J, Pereira Dias LP, Barreira P, Barradas Lopes J, Sousa MJ, Cadinha S, et al. Relevance of the diagnosis of hypersensitivity reactions to antineoplastic and biological agents: experience with drug provocation test. Eur Ann Allergy Clin Immunol 2025;57(1):12-22.
21. Boulanger J, Boursiquot JN, Cournoyer G, Lemieux J, Masse MS, Almanric K, et al. Management of hypersensitivity to platinum- and taxane-based chemotherapy: cepo review and clinical recommendations. Curr Oncol 2014;21(4):e630-41.
22. Gorgulu Akin B, Erkoc M, Korkmaz ET, Ozdel Ozturk B, Colak S, Ozalp Ates FS, et al. Rapid drug desensitization with platin-based chemotherapy: Analysis of risk factors for breakthrough reactions. World Allergy Organ J 2021;15(1):100619.
23. Bayrak Durmaz MS, Unutmaz DG, Demir M, Goksel O, Dursun AB, Bavbek S. Hypersensitivity Reactions to Taxanes: A Multicenter Study for Outcomes and Safety of Rapid Drug Desensitization. Allergy Asthma Immunol Res 2024;16(2):142-53.
24. Kendirlinan R, Gumusburun R, Cerci P, Ozbek E, Altiner S, Celebi Sozener Z, et al. Rapid Drug Desensitization with Chemotherapeutics (Platins, Taxanes, and Others): A Single-Center Retrospective Study. Int Arch Allergy Immunol 2019;179(2):114-22.
25. Wong JT, Ling M, Patil S, Banerji A, Long A. Oxaliplatin hypersensitivity: evaluation, implications of skin testing, and desensitization. J Allergy Clin Immunol Pract 2014;2(1):40-5.
26. Buhari GK, Kalkan IK, Ates H, Bahcecioglu SN, Demir S, Yesilkaya S, et al. Platin desensitizations in thoracic malignancies and risk factors for breakthrough reactions. Allergol Immunopathol (Madr) 2023;51(2):130-6.
27. Caiado J, Bras R, Paulino M, Costa L, Castells M. Rapid desensitization to antineoplastic drugs in an outpatient immunoallergology clinic: Outcomes and risk factors. Ann Allergy Asthma Immunol 2020;125(3):325-33 e1.
28. Kim HH, Seo J, Ahn YH, Kim H, Yoon JE, Suh JH, et al. Analysis of Breakthrough Reactions in 1,143 Desensitization Procedures in a Single Tertiary Hospital Using a One-Bag Desensitization Protocol. Front Allergy 2022;3:786822.
29. Vazquez-Revuelta P, Marti-Garrido J, Lleonart R, Ali FR, Alvarez-Cuesta E. Importance of Diagnostics Prior to Desensitization in New Drug Hypersensitivity: Chemotherapeutics and Biologicals. Current Treatment Options in Allergy 2020;7(1):1-13.