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Clinical Experience with a One-Bag Rapid Drug Desensitization Protocol in Patients with Chemotherapy-Induced Hypersensitivity Reactions

Kemoterapiye Bağlı Aşırı Duyarlılık Reaksiyonları Olan Hastalarda Tek Torba Hızlı İlaç Desensitizasyon Protokolü ile Klinik Deneyim

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ÖZET

Amaç: Kemoterapötik ajanlara bağlı aşırı duyarlılık reaksiyonları (ADR), hastaların birinci basamak ve vazgeçilmez onkolojik tedavilerini almalarını engelleyebilen önemli bir klinik sorundur. Bu çalışmanın amacı, kemoterapiye bağlı ADR öyküsü olan hastalarda uygulanan tek torba (one-bag) hızlı ilaç desensitizasyon (HİD) protokolü ile elde edilen klinik deneyimi, güvenlilik ve uygulanabilirlik açısından değerlendirmektir.

Materyal ve Metod: Bu çalışma, Aralık 2020–Aralık 2023 tarihleri arasında kemoterapötik ajanlara bağlı ADR öyküsü nedeniyle tek torba HİD uygulanan hastaları içeren tek merkezli, retrospektif, gözlemsel bir kohort çalışmasıdır. Hastaların demografik özellikleri, kullanılan kemoterapötik ajanlar, ADR tip ve şiddeti, desensitizasyon sırasında gelişen breakthrough reaksiyonlar (BTR) ve klinik sonuçlar kaydedildi.

Bulgular: Toplam 21 hastada 87 tek torba HİD işlemi gerçekleştirildi. Hastaların %71,4'ü kadındı ve ortalama yaş 55,8±8,5 yıl idi. ADR'lerin %90,5'i tip I reaksiyonlardı; hastaların %33,3'ünde desensitizasyon öncesi ağır (evre 3) reaksiyon öyküsü mevcuttu. Desensitizasyon işlemlerinin %90,5'i BTR gelişmeden başarıyla tamamlandı. İki hastada (%9,5) hafif (evre 1) BTR gözlendi ve tüm işlemler tedavi kesintisi olmaksızın tamamlandı.

Tartışma ve Sonuç: Tek torba hızlı ilaç desensitizasyon protokolü, kemoterapiye bağlı ADR öyküsü olan hastalarda güvenli, etkili ve uygulanabilir bir yaklaşımdır ve klinik pratikte değerli bir alternatif sunmaktadır.

Anahtar Kelimeler: Aşırı Duyarlılık Reaksiyonları, Desensitizasyon, Tip1 Hipersensitivite

ABSTRACT

Objective: Hypersensitivity reactions (HSRs) to chemotherapeutic agents represent a major clinical challenge, as they may prevent patients from receiving first-line and indispensable oncologic treatments. The aim of this study was to evaluate the clinical experience with a one-bag rapid drug desensitization (RDD) protocol in patients with chemotherapy-induced HSRs, focusing on safety and feasibility.

Materials and Methods: This single-center, retrospective, observational cohort study included patients who underwent one-bag RDD for chemotherapy-induced HSRs between December 2020 and December 2023. Demographic characteristics, culprit drugs, type and severity of HSRs, occurrence of breakthrough reactions (BTRs), and desensitization outcomes were analyzed.

Results: A total of 87 one-bag RDD procedures were performed in 21 patients. The majority of patients were female (71.4%), with a mean age of 55.8±8.5 years. Most index reactions were classified as type I HSRs (90.5%), and 33.3% of patients had a history of severe (grade 3) reactions prior to desensitization. Desensitization was successfully completed without BTRs in 90.5% of patients. Mild BTRs (grade 1) occurred in two patients and were managed without interruption of chemotherapy.

Conclusion: The one-bag rapid drug desensitization protocol is a safe, effective, and feasible approach for managing chemotherapy-induced hypersensitivity reactions and represents a practical alternative for maintaining essential oncologic treatments in real-life clinical settings.

Keywords: Hypersensitivity Reactions, Desensitization, Type I Hypersensitivity

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INTRODUCTION

Antineoplastic chemotherapeutic agents and biologic therapies significantly improve survival and quality of life in patients with a wide range of malignancies. However, hypersensitivity reactions (HSRs) to these agents represent a major challenge in clinical practice, as they may prevent the administration of first-line and indispensable treatments (1). Severe or recurrent HSRs may lead to discontinuation of the culprit drug or switching to less effective alternative therapies, resulting in treatment failure, disease progression, increased healthcare costs, and worsening of patient prognosis (2).

Rapid drug desensitization (RDD) is a well-established and evidence-based approach in the management of drug hypersensitivity reactions, allowing the safe administration of the culprit drug through controlled and stepwise dose escalation. RDD is indicated in IgE-mediated type I reactions, cytokine release reactions, mixed reactions, and selected benign delayed-type hypersensitivity reactions (3). By enabling patients to tolerate medications to which they have previously experienced severe hypersensitivity reactions, RDD allows continuation of first-line and indispensable therapies without interruption, thereby preventing treatment failure and disease progression (4).

Traditionally, rapid drug desensitization (RDD) protocols have been based on multibag systems. The most widely used approach, the three-bag (3-bag) protocol, involves preparation of serial drug dilutions and administration through approximately 12–16 incremental steps with progressively increasing infusion rates. Although these protocols are well established and generally safe, they are associated with significant logistical and operational challenges, including prolonged administration time, increased pharmacy and nursing workload, multiple bag changes, and concerns regarding the stability of chemotherapeutic agents at very low concentrations. These complexities can limit feasibility and efficiency, particularly in high-volume centers and in healthcare systems with constrained resources (5).

In recent years, advances in infusion technologies—particularly the widespread use of high-precision programmable infusion pumps—have facilitated the development of single-bag (one-bag, 1-bag) rapid drug desensitization protocols. In one-bag protocols, the drug is prepared in a single infusion bag at the full therapeutic concentration, and desensitization is achieved by initiating the infusion at extremely low rates followed by controlled, stepwise increases in the infusion rate. This strategy preserves the pharmacodynamic principles underlying traditional

multibag desensitization protocols while significantly reducing administration time, simplifying procedural steps, and decreasing pharmacy and nursing workload (6)

A growing body of evidence from observational studies, cohort analyses, and systematic reviews indicates that one-bag desensitization protocols are associated with high completion rates, ranging from approximately 97% to 99%, while breakthrough reactions (BTRs) occurring during desensitization are predominantly mild to moderate in severity (7). Severe reactions are uncommon, and in most cases, BTRs can be effectively managed with temporary interruption of the infusion and symptomatic treatment, allowing successful completion of desensitization without permanent discontinuation of therapy. These findings collectively support the safety and clinical feasibility of one-bag desensitization protocols in patients with prior drug hypersensitivity reactions (8).

The main advantages of one-bag desensitization protocols include shorter administration time, reduced pharmacy preparation requirements, lower overall costs, a decreased risk of medication errors, and a structure that is more suitable for outpatient administration. These features are particularly important in real-world clinical settings, as they enhance patient access and facilitate the delivery of desensitization services across a broader range of centers, including high-volume institutions and healthcare systems with limited resources (7)

The aim of this study was to present our clinical experience with the one-bag rapid drug desensitization protocol in patients who experienced hypersensitivity reactions to chemotherapeutic agents.

MATERIALS AND METHODS

Study Design

This study was designed as a single-center, retrospective, observational cohort study evaluating patients referred from various oncology outpatient clinics between December 2020 and December 2023 who had a history of hypersensitivity reactions (HSRs) to chemotherapeutic agents and subsequently underwent desensitization using a one-bag rapid drug desensitization protocol. The one-bag desensitization protocol applied to the patients is presented in Table 1 (9).

Table 1. Example of a 1-bag 12-step desensitization protocol for oxaliplatin 100 mg (9)

Step	Rate (mL/hr)	Time (min)	Dose (mg)	Volume (mL)
1	0.1	15	0.0114	0.025
2	0.2	15	0.0227	0.05
3	0.5	15	0.0568	0.1
4	1.2	15	0.1364	0.2
5	2.5	15	0.2841	0.4
6	5	15	0.5682	0.75
7	12.5	15	1.4205	1.5
8	25	15	2.8409	3.125
9	50	15	5.6818	6.25
10	90	15	10.2273	12.5
11	150	15	17.0455	25
12	250	32.6	61.7045	160.1

Oxaliplatin 100 mg/20 mL was reconstituted with 200 mL of 5% dextrose water. The concentration of the solution was 0.45455 mg/mL.

Dose (mg) = Rate (mL/hr) × time/60 (hr) × concentration (mg/mL)

Patient Population

Patients aged 18 years and older with a documented history of hypersensitivity reactions (HSRs) to chemotherapeutic agents, including taxanes, platinum compounds, or monoclonal antibodies, were eligible for inclusion. Patients were included if the hypersensitivity reaction occurred during maintenance therapy and no clinically appropriate alternative to the implicated chemotherapeutic agent was available.

Patients with concomitant mast cell disorders, such as systemic mastocytosis, who underwent multistep, multidilution rapid drug desensitization (RDD) protocols (12- or 16-step protocols) were excluded from the study.

Clinical and Laboratory Assessment

Demographic characteristics of the patients, including age and gender, the type of underlying malignancy, and the class of the administered chemotherapeutic agent (e.g., platinum compounds, taxanes, monoclonal antibodies), were retrieved from the hospital database. Laboratory parameters, including serum tryptase levels and peripheral blood eosinophil counts (PBEC), were also collected from electronic medical records.

Hypersensitivity reactions (HSRs) were classified based on the clinical manifestations observed during the reaction. Accordingly, reactions were categorized as follows:

- **Type I (IgE-mediated or non–IgE-mediated):** flushing, pruritus, urticaria, dyspnea, back pain, nausea, vomiting, diarrhea, and cardiovascular collapse
- **Type II (cytokine-release reactions):** fever with chills/rigors, headache, nausea, hypotension, and decreased oxygen saturation
- **Type III (mixed reactions):** fever with chills/rigors, pain, headache, flushing, pruritus, rash, urticaria, chest pain, dyspnea, nausea, vomiting, diarrhea, and cardiovascular collapse
- **Type IV (complement-mediated reactions):** hypotension and oxygen desaturation (10)

The severity of HSRs was assessed according to the Brown classification (11). Based on this classification:

- **Grade 1 (mild):** Symptoms limited to the skin (e.g., flushing) or involving a single organ/system with mild manifestations (e.g., mild cough)
- **Grade 2 (moderate):** Involvement of at least two organs/systems (e.g., nausea/vomiting and dyspnea) without a significant decrease in blood pressure or oxygen saturation
- **Grade 3 (severe):** Severe symptoms involving at least two organs/systems, accompanied by a significant decrease in blood pressure (systolic <90 mmHg and/or syncope) and/or oxygen saturation (<92%)

All patients received premedication approximately one hour prior to desensitization, consisting of oral fexofenadine 180 mg and intravenous methylprednisolone 40 mg. During desensitization, the occurrence of breakthrough reactions (BTRs) and the infusion step at which they developed were prospectively recorded. The distribution of the administered chemotherapeutic agents is summarized in Figure 1.

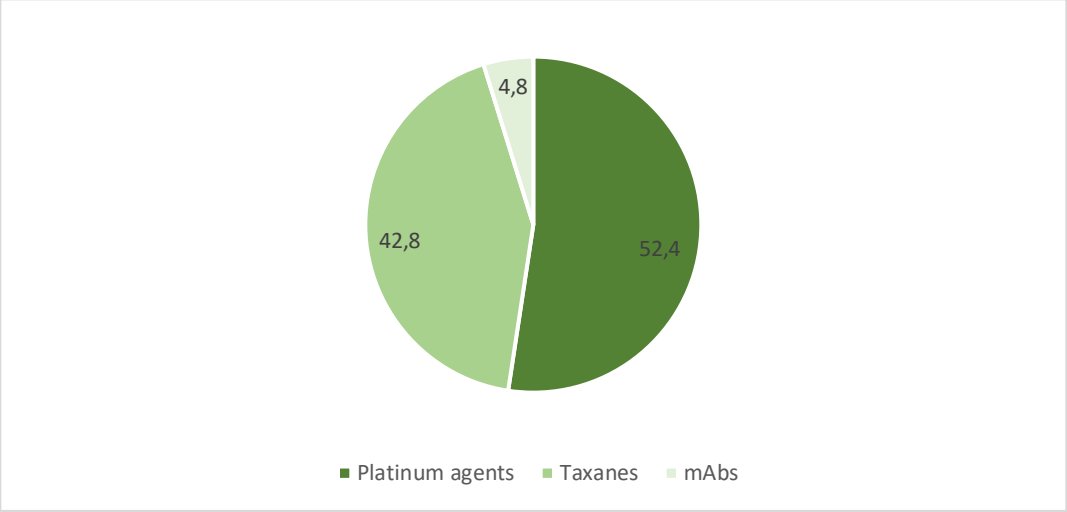

Figure 1. Distribution of chemotherapeutic agents administered to the patients

mAbs: Monoclonal Antibodies

Breakthrough reactions occurred in two patients; in both cases, the severity of the BTR was classified as Grade 1. Desensitization was successfully completed following temporary interruption of the infusion and symptomatic treatment. A detailed evaluation of these two patients revealed that carboplatin was the culprit chemotherapeutic agent, and the initial HSR prior to desensitization had been classified as Grade 3.

None of the patients included in the study underwent skin prick testing or intradermal testing with the culprit chemotherapeutic agents prior to desensitization. This approach was primarily driven by the fact that all patients were receiving active chemotherapy, and the recommended minimum waiting period of at least six weeks after a hypersensitivity reaction—required for reliable skin test performance—was not clinically feasible. Considering the potential negative impact of delaying oncologic treatment on disease course and prognosis, the decision was made to proceed directly with the desensitization protocol without performing diagnostic skin testing.

Statistical Analysis of Data

Two-tailed distribution and two-sample t-test analysis were used for data analysis. The statistical significance of the results obtained was evaluated over a p-value of 0.05, and values with a p-value of ≤ 0.05 were considered reliable.

RESULTS

A total of 21 patients underwent 87 one-bag rapid drug desensitization procedures. Of these patients, 15 (71.4%) were female, and the mean age was 55.81 ± 8.5 years. Evaluation of

laboratory parameters revealed a median PBEC of 90 cells/µL (range: 0–1810) and a mean serum tryptase level of 6.48 ± 4.25 ng/mL.

Nineteen patients (90.5%) had a history of type I hypersensitivity reactions, while the remaining patients had a history of mixed-type reactions. When classified according to reaction severity, 2 patients (9.5%) experienced grade 1 reactions, 12 patients (57.1%) grade 2 reactions, and 7 patients (33.3%) grade 3 reactions prior to desensitization.

Desensitization was successfully completed without any breakthrough reactions (BTRs) in 19 patients. Breakthrough reactions occurred in 2 patients during desensitization; however, in both cases, the severity of the BTR was classified as grade 1. Following temporary interruption of the infusion and symptomatic treatment, desensitization was successfully completed in these patients. A detailed evaluation of the two patients who developed BTRs revealed that carboplatin was the implicated chemotherapeutic agent, and the initial hypersensitivity reactions prior to desensitization had been classified as grade 3 (Table 2).

Table 2. A detailed analysis of the two patients who developed breakthrough reactions during desensitization

	Prior HSR Grade	**KT agent**	**BTR grade**	**Desensitization step of BTR occurrence**
Patient 1	3	Carboplatin	1	8
Patient 2	3	Carboplatin	1	11

DISCUSSION

In larger one-bag chemotherapy desensitization cohorts (n ≥ 36), patients typically undergo multiple desensitization procedures, with reported mean values ranging from 3.5 to 7.6 and most cohorts clustering around 4–5 procedures per patient (12,13). In line with these data, the mean number of desensitization procedures per patient in our cohort was 4.14, further supporting the feasibility of repeated one-bag desensitization in routine oncology practice.

Across published one-bag chemotherapy desensitization cohorts, the mean age of patients generally ranges from the mid-50s to early-60s, with a consistent female predominance that has been largely attributed to the high prevalence of ovarian and breast cancers in these populations (7,14). The demographic characteristics of our cohort closely mirror these observations, with a mean age of 55.81 ± 8.5 years and a female predominance (71.4%). Correspondingly, gynecologic and breast malignancies constituted nearly half of our study

population, supporting previously reported demographic trends in one-bag chemotherapy desensitization cohorts.

Our findings further confirm the favorable safety profile of the one-bag rapid drug desensitization protocol. The majority of patients completed desensitization without breakthrough reactions, and BTRs were observed in only two patients, both of which were mild (grade 1), promptly managed with temporary infusion interruption and symptomatic treatment, and did not prevent completion of the protocol. These results are consistent with larger one-bag chemotherapy cohorts reporting BTR rates between 5% and 27%, with severe reactions occurring in only a small proportion of procedures (7,12,14). Notably, both BTRs in our cohort occurred in patients receiving carboplatin, in agreement with previous studies identifying platinum agents—particularly carboplatin—as being associated with a higher likelihood of hypersensitivity reactions and BTRs during desensitization (15,16). Importantly, despite a considerable proportion of patients having experienced grade 2–3 index reactions prior to desensitization, no moderate or severe BTRs were observed, underscoring the robustness of the one-bag protocol even in higher-risk patients.

The distribution of chemotherapeutic agents in our cohort is also highly consistent with previously published one-bag desensitization studies. Prior reports indicate that platinum-based agents account for approximately 50–60% of desensitized patients, followed by taxanes (25–35%) and monoclonal antibodies (5–15%) (7,12). Similarly, platinum agents represented the majority of desensitizations in our cohort (52.4%), followed by taxanes (42.8%), while monoclonal antibodies accounted for a smaller proportion (4.8%). Minor differences in agent distribution likely reflect center-specific oncology referral patterns and underlying cancer epidemiology. Overall, this concordance supports the external validity and real-world applicability of our findings.

CONCLUSION

Collectively, these findings support the safety, feasibility, and clinical reliability of the one-bag desensitization approach and demonstrate strong concordance between our real-world experience and both reported outcomes from one-bag cohorts and mechanistic insights from the broader desensitization literature.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Ethics Approval and Consent

Ethical approval was obtained from the Ethical Committee of the Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital (approval number: 116.2017.R-349, date: November 11, 2023). All patients participating in the study were informed and an informed consent form was filled.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author Contributions

Şeyma Özden: Conceptualization and study design; data collection; data analysis and interpretation; drafting of the manuscript; literature review; critical revision of the manuscript for important intellectual content; and approval of the final version of the manuscript.

Fatma Merve Tepetam: Contribution to data collection; validation and interpretation of clinical data; participation in manuscript writing; critical review of the scientific content; and approval of the final version of the manuscript.

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