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Original Article

Characteristics of patients with hypersensitivity reactions to chemotherapeutic and biological agents and desensitization behavior

Características de pacientes com reações de hipersensibilidade a agentes quimioterápicos e biológicos e comportamento de dessensibilização

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ABSTRACT

Introduction: Hypersensitivity to chemotherapeutic and biological agents has increased in recent years due to their frequent use. Avoidance has been the first line of defense, leading to decreased treatment efficacy and increased adverse events. **Objective:** To characterize the sociodemographic and clinical aspects of patients with hypersensitivity reactions to chemotherapeutic agents who underwent desensitization and biological procedures in a Colombian city. **Methods:** This observational, descriptive, retrospective, multicenter study was conducted in patients with hypersensitivity reactions to chemotherapeutic and biological agents who underwent desensitization. **Results:** In the 14 included patients with a history of hypersensitivity reactions to chemotherapeutic and biological agents (57.1% women; median age 42.5 years), 45 desensitization procedures were performed. The most commonly prescribed drug was rituximab (57%). The skin was the most frequent reaction site (78.6%), and systemic corticosteroids were the most common treatment (78.6%). Breakthrough reactions occurred in 31.1% of the patients and only premedication with corticosteroids was associated with less severe reactions. All cases of desensitization were successful. **Conclusions:** Desensitization to chemotherapeutic and biological agents proved to be a useful and safe tool in a Colombian population.

Keywords: Hypersensitivity, chemotherapeutic agent, biological agent, desensitization.

RESUMO

Introdução: A hipersensibilidade aos agentes quimioterápicos e biológicos aumentou nos últimos anos devido ao seu uso frequente. Evitar tem sido a primeira linha de ação, levando à diminuição da eficácia do tratamento e ao aumento de eventos adversos. **Objetivos:** Caracterizar os aspectos sociodemográficos e clínicos de pacientes com reações de hipersensibilidade a agentes quimioterápicos submetidos a dessensibilização e procedimentos biológicos em uma cidade colombiana. **Métodos:** Foi realizado um estudo observacional, descritivo, retrospectivo e multicêntrico em pacientes com reações de hipersensibilidade a agentes quimioterápicos e biológicos submetidos à dessensibilização. **Resultados:** Foram incluídos 45 procedimentos de dessensibilização em 14 pacientes com histórico de reações de hipersensibilidade a agentes quimioterápicos e biológicos (57,1% mulheres, com mediana de idade de 42,5 anos). O medicamento mais relatado foi o rituximabe (57%). O envolvimento cutâneo foi o mais frequente (78,6%) e os corticosteroides sistêmicos foram o tratamento mais utilizado (78,6%). As reações ocorreram em 31,1% e apenas a pré-medicação com corticosteroides foi associada a uma menor gravidade destas. Todos os casos de dessensibilização foram bem-sucedidos. **Conclusões:** A dessensibilização a agentes quimioterápicos e biológicos provou ser uma ferramenta útil e segura em uma população colombiana.

Descritores: Hipersensibilidade, agentes antineoplásicos, terapia biológica, dessensibilização.

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Introduction

Adverse drug reactions are a public health problem,[1] and hypersensitivity reactions comprise 15-20% of these cases.[2] For taxane-based chemotherapeutic agents, a 2%-10% prevalence of hypersensitivity reactions has been reported, while for platinum-based[13] drugs it depends on the number of infusions.[4] The epidemiology of hypersensitivity reactions to biological agents is insufficiently known; the most commonly involved drug is rituximab, for which the prevalence is 5% to 10%.[5]

Chemotherapeutic and biological agents have been increasingly used in recent years, resulting in more hypersensitivity reactions,[6] which can lead to the use of less effective and safer alternatives.[7,8] These patients can benefit from drug desensitization protocols for temporary tolerance.[9]

Although evidence indicates that desensitization is safe, the procedure is not risk-free, and thus should be performed in an appropriate medical environment, with the necessary supplies to manage emergencies, and it should be performed by qualified and trained personnel.[6,10]

Studies have described the results and safety of desensitization to chemotherapeutic agents in 413, 609, and 122 patients.[11-13] An Australian study described 25 procedures with chemotherapeutic and biological agents,[14] and a more recent study reported the results of 69 desensitization procedures.[15] In Latin America, Villarreal et al.[16] described a cohort of patients with reactions to paclitaxel who underwent successful desensitization. However, we could find no information on other therapeutic agents, except as case reports. In Colombia, we found no studies evaluating hypersensitivity reactions to chemotherapeutic and biological agents or desensitization protocols for these drugs.

The primary objective of this study was to characterize the sociodemographic and clinical aspects of patients with hypersensitivity reactions to chemotherapeutic and biological agents who underwent desensitization and treatment in a Colombian city.

Methodology

An observational, multicenter, descriptive study was conducted at the Hospital San Vicente Fundación and the IPS Universitaria, both of which are in Medellín. The secondary objectives were to describe the sociodemographic aspects of the study population; to describe the clinical and paraclinical history of this population; to determine aspects of desensitization, adverse reactions, and the final outcome of the procedure, and finally; to explore the relationship between demographic, clinical and paraclinical aspects according to desensitization, adverse reactions, and procedure outcome.

Data were collected from the medical records of patients with a history of hypersensitivity reaction to chemotherapeutic or biological agents who underwent a desensitization protocol between 2015 and 2020. We assessed the demographic and clinical characteristics of the patients, as well as clinical aspects of the index reaction and desensitization procedure.

For this study, hypersensitivity reactions were considered signs or symptoms produced by an agent normally tolerated by the general population, in this case chemotherapeutic and biological agents, that are unrelated to drug's action and are, thus, unpredictable.[1] Hypersensitivity was not diagnosed by the researchers; the sample included patients who had already been diagnosed by an allergist. The type of hypersensitivity reaction was not differentiated. The Ring-Messmer scale[6] was used to determine reaction severity: mild reactions were considered grade I (affecting only the skin), while all other were considered moderate to severe (grades II-IV).

The index reaction was considered the patient's predictable response to the drug, ie, that for which hypersensitivity was diagnosed. Reactions that occurred during desensitization were considered breakthrough reactions.

Statistical analysis

For descriptive analysis of the sociodemographic, clinical, and paraclinical variables, absolute and relative frequencies and summary indicators, such as median, quartiles, interquartile range, and minimum and maximum values were used. The standard criterion for quantitative variables was determined with the Shapiro-Wilk test.

The likelihood ratio chi-square test and Fisher's exact test were applied to determine the relationship between demographic, clinical, and paraclinical aspects according to desensitization, adverse reactions, and outcome. Cramer's V was used as a measure of effect size. P-values < 0.05 were considered statistically significant.

Ethical aspects

This investigation was based on international ethical principles in accordance with the Declaration of Helsinki and the Nuremberg Code and was approved by the ethics committee of the participating institutions.

Results

Sociodemographic aspects and clinical history

The sample included 14 patients with hypersensitivity reactions to chemotherapeutic and biological agents who underwent desensitization procedures for these drugs. Most patients were women (57.1%) and the median age was 42.5 years.

The drugs that caused the reactions were prescribed for hematological diseases (42%), solid organ neoplasms (28.5%), or autoimmune diseases (28.5%). The majority (64%) of the patients had previously used a chemotherapeutic or biological agent (Table 1).

Characteristics of the index hypersensitivity reaction

The most commonly reported drug reactions were to rituximab (57.1%) and oxaliplatin (28.6%). The median number of reactions per patient was 1, and most (85.7%) were immediate. The skin was the most commonly affected site (78.6%). No patient had a fever or liver or renal involvement. The most commonly used drugs for these reactions were corticosteroids (78.6%) and antihistamines (64.3%).

Serum tryptase measurement was not performed for any patients at the time of the reaction, and a skin test was only performed in 1 patient (Table 2).

Characteristics of the desensitization procedure

A total of 45 desensitization procedures were performed for the 14 included patients, averaging 2.5 procedures per patient. Of the desensitization procedures, 28 (65.1%) were administered using a 3-bag, 12-step protocol, and 9 (20.9%) used a 4-bag, 16-step protocol. All protocols involved solutions with different drug dilutions, beginning with the most dilute solution. Four protocol steps were administered for each bag, increasing the infusion rate every 15 minutes in each step. Premedication was administered in all procedures, the most common of which were antihistamines (97.8%) and corticosteroids (82.2%).

Breakthrough reactions occurred during 14 (31.1%) procedures, in which the skin was the main affected site (92.9%). More than a third (35.7%) of these reactions occurred during step 12. The reactions were treated with antihistamines (85.7%) and systemic corticosteroids (35.7%). All procedures were completed at the full dose and were thus considered successful (Table 3).

Demographic and clinical characteristics according to index reaction

All patients ≥ 45 years of age presented systemic symptoms, compared to 50% of those < 45 years of age (medium effect size; Cramer's V = 0.548). Likewise, among patients with a solid organ neoplasm, 50% of those with a hematologic neoplasm and 75% of those with autoimmune diseases presented systemic reactions (medium effect size; Cramer's V = 0.487). There was no difference in the systemic reaction rate between patients with a history of atopic disease and those with other diseases (Table 4).

All of the patients who had an index reaction to cytarabine and 87.5% of those who had an index reaction to rituximab did so with ≤ 3 doses of the drug , while all of those who had an index reaction to methotrexate or oxaliplatin did so after the third dose. This difference was significant (p = 0.006) and had a large effect size (Cramer's V = 0.863).

Demographic and clinical characteristics according to breakthrough reaction

Among cytarabine desensitization procedures, 83.3% involved a breakthrough reaction, compared to 50% for oxaliplatin and 16.7% for rituximab. These differences were significant and had a moderate effect size (p = 0.007, Cramer's V = 0.524). There was no relationship between systemic symptoms in the index reaction and the occurrence of a breakthrough reaction.

Breakthrough reactions occurred in 75% of the procedures in which corticosteroids were not administered, which was a significant difference with a moderate effect size (p = 0.04; Cramer's V = 0.441). There was also a significant association between breakthrough reactions and desensitization protocols > 6 hours in length (p = < 0.001) (Table 5).

Table 1
Sociodemographic and clinical characteristics of the included patients

		Relative frequency
Sex	Female	57.1% (8)
	Male	42.9% (6)
Age groups	Age < 45	40% (18)
	Age ≥ 45	60% (27)
Residential area	Rural	7.1% (1)
	Urban	92.9% (13)
Race	Mestizo (Mixed race)	100% (14)
Asthma	Yes	14.3% (2)
Rhinitis	Yes	14.3% (2)
Conjunctivitis	Yes	7.1% (1)
Dermatitis	Yes	0
HBP	Yes	14.3% (2)
Diabetes mellitus	Yes	7.1% (1)
Cardiovascular disease	Yes	7.1% (1)
Pulmonary disease	Yes	14.3% (2)
Liver disease	Yes	7.1% (1)
Renal disease	Yes	21.4%
Endocrine disease	Yes	7.1% (1)
Psychiatric disease		7.1% (1)
Underlying disease	Hematologic neoplasm [a]	42.8% (6)
	Solid organ neoplasm [b]	28.5% (4)
	Autoimmune disease [c]	28.5% (4)

[a] Burkitt's leukemia, acute myeloid leukemia, B-cell lymphoma, non-Hodgkin's lymphoma, Waldeström macroglobulinemia.
[b] Colon cancer, cholangiocarcinoma, gastric cancer.
[c] Dermatomyositis, SLE, optic neuritis, primary immune thrombocytopenia.

Table 2
Characteristics of the index hypersensitivity reactions

		Relative frequency
Drug	Cytarabine	7.1% (1)
	Methotrexate	7.1% (1)
	Oxaliplatin	28.6% (4)
	Rituximab	57.1% (8)
No. of reactions [a]	1 (1) [1; 3]	
Latency time	< 1 hour	85.7% (12)
	> 6 hours	14.3% (2)
Dose at which the reaction occurred [a]	3 (2) [1; 9]	
Clinical manifestations	Skin	78.6% (11)
	Respiratory	57.1% (8)
	Gastrointestinal	14.3% (2)
	Cardiovascular	28.6% (4)
	Neurological	7.1% (1)
Tryptase measurement	No	100%
Skin test	Positive	0
	Negative	7.1% (1)
	Not performed	92.9% (13)
Reaction treatment	Adrenaline	35.7% (5)
	Antihistamine	64.3% (9)
	Corticosteroid	78.6% (11)
	Anti-H2	4.4% (2)
	LTRA	0
	EVF	28.6% (4)
	Analgesics or antipyretics	7.1% (1)
	Beta-2 agonists	0
	Oxygen	28.6% (4)

[a] Results are presented as median (interquartile range) [minimum value; maximum value].
LTRA = Leukotriene receptor antagonist, EVF = Endovenous fluids.

Table 3
Aspects of desensitization, breakthrough reactions, and final outcome of the procedure

		Relative frequency
Number of desensitization procedures per patient [a]	2.5 (3) [1; 6]	
Regimen used	3-bag, 12-step	65.1% (28)
	4-bag, 16-step	20.9% (9)
	Other	14% (6)
Site of procedure	Inhospital	82.2% (37)
	Emergency services	2.2% (1)
	SCU	4.4% (2)
	Outpatient department	11.1% (5)
Procedure duration (hours) [a]	6.5 (2) [4.5; 10]	
Premedication	Yes	100% (45)
Used premedication	Corticosteroid	82.2% (37)
	Antihistamine	97.8% (44)
	LTRA	8.9% (4)
	Analgesics	24.4% (11)
	Anxiolytic	4.4% (2)
	LEV	0
Breakthrough reaction	Yes	31.1% (14)
	No	68.9% (14)
Step in which the reaction occurred	4	7.1% (1)
	12	35.7% (5)
	15	7.1% (1)
	>24 hours	35.7% (5)
	No information	14.2 (2)
Clinical manifestations of the breakthrough reaction	Skin	92.9% (13)
	Respiratory	0
	Cardiovascular	7.1% (1)
	Gastrointestinal	14.3% (2)
	Renal	0
	Liver	0
	Neurological	0
	Fever	7.1% (1)
Breakthrough reaction treatment	Adrenaline	0
	Antihistamine	85.7% (12)
	Corticosteroid	35.7% (5)
	LTRA	7.1% (1)
	Analgesics or antipyretics	14.3% (2)
	Oxygen	0
	EVF	21.4% (3)
	Beta-2 agonist	0
Procedure results	Successful	100% (45)

[a] Results presented as median (interquartile range) [minimum value; maximum value].
LTRA = Leukotriene receptor antagonist, EVF = Endovenous fluids, SCU = Special care unit.

Table 4
Demographic and clinical characteristics according to index reaction

		Systemic involvement in index reaction		p-value[a]	Difference in proportions (95%CI)	Cramer's V
		Yes	No			
Sex	Female	6 (75.0%)	2 (25.0%)	0.999	0.0833 (-0.399 to 0.565)	0
	Male	4 (66.7%)	2 (33.3%)			
Age groups	Age < 45	4 (50.0%)	4 (50.0%)	0.085	0.500 (0.154-0.846)	0.548
	Age ≥ 45	6 (100%)	0 (0%)			
Involved drug	Cytarabine	0 (0.0%)	1 (100.0%)	0.043	NA	0.689
	Methotrexate	0 (0.0%)	1 (100.0%)			
	Oxaliplatin	4 (100.0%)	0 (0.0%)			
	Rituximab	6 (75.0 %)	2 (25.0%)			
Treated with adrenaline	Yes	4 (80.0%)	1 (20.0%)	0.999	0.133 (-0.133 to 0.600)	0.141
	No	6 (66.7%)	3 (33.3%)			
Treated with antihistamines	Yes	1 (50.0%)	1 (50.0%)	0.505	-0.250 (-0.985 to 0.485)	0.194
	No	9 (75.0%)	3 (25.0%)			
Treated with corticosteroids	Yes	9 (81.8%)	2 (18.2%)	0.176	0.485 (-0.0952 to 1.00)	0.440
	No	1 (33.3%)	2 (66.7%)			
Treated with anti-H2	Yes	1 (50.0%)	1 (50.0%)	0.505	-0.250 (-0.985 to 0.485)	0.194
	No	9 (75.0%)	3 (75.0%)			
Treated with analgesics and/or antipyretics	Yes	1 (100.0%)	0 (0.0%)	0.999	0.308 (0.0568-0.559)	0.175
	No	9 (62.0%)	4 (30.8%)			
Treated with oxygen	Yes	4 (100.0%)	0 (0.0%)	0.251	0.400 (0.0964-0.704)	0.400
	No	6 (60.0%)	4 (40.0%)			
Treated with EVF	Yes	4 (100.0%)	0 (0.0%)	0.251	0.400 (0.0964-0.704)	0.400
	No	6 (60.0%)	4 (40.0%)			

[a] Fisher's exact test.
EVF = Endovenous fluids; NA = Not applicable.

Table 5
Demographic and clinical characteristics according to breakthrough reaction

		Breakthrough reaction				
		Yes	No	p-value[a]	Difference in proportions (95%CI)	Cramer's V
Sex	Female	8 (30.8%)	18 (69.2%)	0.954	-0.00810 (-0.282 to 0.266)	0.00864
	Male	6 (31.6%)	13 (68.4%)			
Age group	Age < 45	6 (33.3%)	12 (66.7%)	0.793	-0.0370 (-0.315 to 0.241)	0.0392
	Age ≥ 45	8 (29.6%)	19 (70.4%)			
Previous use of chemotherapeutic or biological agents	Yes	7 (28.0%)	18 (72.0%)	0.615	-0.0700 (-0.343 to 0.203)	0.0751
	No	7 (35.0%)	13 (65.0%)			
Site of procedure	Inhospital	13 (35.1%)	24 (64.9%)	0.050	NA	0.354
	Emergency services	1 (100.0%)	0 (0.0%)			
	SCU	0 (0.0%)	2 (100.0%)			
	Outpatient department	0 (0.0%)	5 (100.0%)			
Corticosteroid	Yes	8 (21.6%)	29 (78.4%)	0.004	-0.534 (-0.862 to -0.206)	0.441
	No	6 (75.0%)	2 (25.0%)			
Antihistamine	Yes	14 (31.8%)	30 (68.2%)	0.385	0.318 (-0.181 to -0.456)	0.101
	No	0 (0.0%)	1 (100.0%)			
LTRA	Yes	2 (50.0%)	2 (50.0%)	0.409	0.207 (-0.302 to -0.717)	0.127
	No	12 (29.3%)	29 (70.7%)			
Analgesic	Yes	2 (18.2%)	9 (81.8%)	0.270	-0.171 (-0.450 to 0.108)	0.159
	No	12 (35.3%)	31 (64.7%)			
Anxiolytic	Yes	0 (0.0%)	2 (100.0%)	0.216	-0.326 (-0.466 to -0.186)	0.145
	No	14 (32.6%)	29 (67.4%)			
Duration	≤ 6 hours	1 (7.1%)	17 (58.6%)	< 0.001	-0.515 (-0.739 to -0.290)	0.489
	> 6 hours	13 (92.9%)	12 (41.4%)			

[a] Likelihood ratio.
LTRA = Leukotriene receptor antagonist; NA = Not applicable; SCU = Special care unit.

Demographic and clinical characteristics according to systemic symptoms in breakthrough reactions

Systemic symptoms and baseline disease were significantly associated, having a large effect size. Among patients with solid organ neoplasms, 75% had a systemic breakthrough reaction, compared to 15% of those with hematologic neoplasms and 0% of those with an autoimmune disease (p = 0.039; Cramer's V = 0.661).

Breakthrough reactions with systemic symptoms occurred in 75% of the procedures for oxaliplatin, compared to 0% for rituximab. This difference was significant and had a large effect size (p = 0.008; Cramer's V = 0.791).

Breakthrough reactions with systemic symptoms occurred in 44% of the first 2 procedures and none occurred after the third procedure. This difference was significant and had a moderate effect size (p = 0.036; Cramer's V = 0.471) (Table 6).

Table 6
Distribution of clinical aspects according to systemic involvement in the breakthrough reaction

		Systemic involvement in the breakthrough reaction		p-value[a]	Difference in proportions (95%CI)	Cramer's V
		Yes	No			
Underlying disease	Solid organ neoplasm	3 (75.0%)	1 (25.0%)	0.039	NA	0.661
	Hematologic neoplasm	1 (14.3%)	6 (85.7%)			
	Autoimmune disease	0 (0.0%)	3 (100.0%)			
Drug	Cytarabine	1 (20.0%)	4 (80.0%)	0.064	NA	0.474
	Methotrexate	0 (0.0%)	0 (0.0%)			
	Oxaliplatin	3 (75.0%)	1 (25.0%)			
	Rituximab	0 (0.0%)	5 (100%)			
Regimen	3-bag, 12-step	0 (0.0%)	3 (100.0%)	0.059	NA	0.548
	4-bag, 16-step	4 (50.0%)	4 (50.0%)			
	Other	0 (0.0%)	3 (100%)			
Systemic involvement in index reaction	Yes	3 (37.5%)	5 (62.5%)	0.383	-0.208 (-0.657 to 0.241)	0.228
	No	1 (16.7%)	5 (83.3%)			
Number of desensitization procedures	≤ 2	4 (44.4%)	5 (55.6%)	0.036	-0.444 (-0.769 to -0.120)	0.471
	> 2	0 (0.0%)	5 (100%)			

[a] Likelihood ratio.
NA = Not applicable.

Discussion

The present sample included 45 desensitization procedures with chemotherapeutic and biological agents. Like other studies, our patients were mostly women, possibly due to the large number of patients with gynecologic malignancies. In addition, biological agents are an important treatment for rheumatological and autoimmune diseases, which are more frequent in women.[11,19]

The median patient age was also similar to other studies, although we found that all patients > 45 years had systemic symptoms in the index reaction, unlike in other studies, where none described a relationship between age and index reaction severity.[11,15]

The youngest patient in our sample (6 years), had a hypersensitivity reaction to rituximab and underwent 4 desensitization procedures with a 12-step protocol. No breakthrough reactions occurred in any of these procedures. Diley et al. described 17 desensitization procedures with rituximab, also using a 12-step protocol in 3 children (aged 14 years, 7 years, and 23 months). Because the younger 2 had breakthrough reactions, a modified protocol was used with an infusion rate ≤ 2 mg/kg/h.[20]

Similar to our findings, other authors have reported that these drugs were mainly prescribed (70-94%) for neoplastic diseases.[15,21] The most frequently reported neoplasms in similar studies are ovarian and breast cancer,[13] in contrast to hematological neoplasms in our study.

Most of the rituximab hypersensitivity reactions in our sample occurred in the first treatment cycles, which is consistent with the literature.[15] Up to 50% of the reactions to this drug occur during the first exposure, which suggests a cytokine-releasing endotype.[22] Moreover, reactions to oxaliplatin occurred after the fourth exposure, which has been reported in other studies.[13] This can be explained by the fact that most hypersensitivity reactions to platinum-based drugs are IgE-mediated.[23,24]

Most reactions were immediate; only 2 patients had delayed reactions: one with a maculopapular rash due to cytarabine and another with a fixed drug eruption due to methotrexate. Skin lesions 6 to 12 hours after administration are typical of hypersensitivity to cytarabine.[25,26] On the other hand, hypersensitivity reactions to methotrexate are rare, and the most common are IgE-mediated.[27]

Regarding reaction severity, in our results, as well as the literature, most index reactions are moderate or severe (64.3 to 87.9%),[19,21] with skin and respiratory symptoms being the most common symptoms. However, another study found that respiratory (80.5%) and cardiovascular (58.8%) symptoms were the most common types.[15]

None of our patients were tested for biomarkers, such as serum tryptase and IL-6, and only 1 patient, who reacted to methotrexate, was given had a patch test (the results of which were negative). Measuring these biomarkers and performing skin tests is important for phenotyping patients. Elevated tryptase levels during the reaction are associated with an IgE-mediated phenotype,[28] and IL-6 values above the upper threshold are related to cytokine-release.[30] Skin testing, however, has been proposed as a way to stratify risk and guide treatment.[31]

The most widely applied desensitization protocol for chemotherapeutic and biological agents was developed at the Brigham and Women's Hospital (Boston, MA, USA) and involves 3 bags and 12 steps.[11] In our study, 28 procedures were of this type, while 9 were 4-bag, 16-step protocols. The latter type was also described by the Brigham and Women's Hospital group in that they recommended adding steps and modifying the final rate to the original protocol to increase safety.[23] Recently, a 1-bag, 11-step desensitization protocol was tested in 434 procedures, with an efficacy of 99.5% and a breakthrough reaction rate of 49%.[21]

All desensitization procedures in our study involved premedication. Only corticosteroid use was associated with a lower breakthrough reaction rate. We could find no comparable data in the literature about this phenomenon. Current recommendations suggest selecting the premedication according to the symptoms presented in the index reaction.[10]

Breakthrough reactions occurred in 31% of the procedures in our sample. In the literature, breakthrough reactions have been reported in 13% to 39% of desensitization procedures[11,114,15] Reactions generally occur during the final steps of the protocol,[11] which corroborates our finding that most reactions occurred in step 12.

Breakthrough reaction severity was associated with drug type. There was a high percentage of moderate to severe reactions to oxaliplatin, whereas there were only mild reactions to rituximab. Accordingly, the literature reports more severe breakthrough reactions to platinum-based drugs than to biological agents.[19] We also found a relationship between protocol type

and breakthrough reaction severity. In the 16-step protocol, 50% of the reactions were moderate to severe, while in the 12-step protocol the reactions were mild. This may be because patients indicated for the longer protocol had a higher risk in baseline stratification.

In patients who underwent multiple desensitization procedures, although the frequency of breakthrough reactions did not decrease as more procedures were performed, the severity did. Other studies have reported that in addition to severity, the frequency of reactions also decreases.[11,13]

All desensitization procedures in our study were successful. In some cohorts, lower success rates have been obtained (84%[14] and 98%[19]), while others report complete success.[11]

The retrospective nature of this study can be considered a limitation, as can the small sample and number of desensitization protocols. This is due to the fact that these procedures are still little known in our work environment and are only performed at certain institutions. Finally, none of the patients were tested for biomarkers and only 1 underwent skin testing, which are important diagnostic and therapeutic tools.

The study's main advantage is that it is the first, to the best of our knowledge, in Latin America to describe the characteristics of desensitization procedures in patients with hypersensitivity reactions to chemotherapeutic and biological agents. We hope that it leads to further research on the topic.

Conclusion

Desensitization protocols are an effective alternative in patients with hypersensitivity reactions to chemotherapeutic and biological agents and, although they are not risk-free procedures, they are safe if performed under adequate conditions by trained personnel. We found that corticosteroid administration was associated with fewer reactions during the procedure, which would be an interesting topic for future research.

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