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Outcomes with one-bag desensitization protocol for biologic and chemotherapy agents in 451 procedures

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To the Editor,

rapid drug desensitization is an essential procedure to allow the maintenance of first-line treatments in patients suffering from hypersensitivity reactions (HSR) to biological and chemotherapeutic agents (1-6).

Since our first description of the one-bag drug desensitization protocol in 2016 (2), several groups have implemented it in their clinical practice (1-8), demonstrating its good tolerance and efficacy. In addition to the already proven effectiveness and security of the one-bag protocol, throughout these years of clinical practice we have been able to reduce the time of the standard procedure with no further appearance of adverse events, by shortening its initial steps, making it a more convenient option for both physicians and patients.

In this setting, we present the results of the application of the one-bag desensitization in two different hospitals of our region

(Complejo Hospitalario Universitario de Santiago de Compostela and Ferrol), along six years of experience.

From April 2016 to December 2022, a total of 451 rapid desensitization procedures were performed in 86 patients (77% women, mean age 68 years-old [range 19-85]). More than one third of the patients (36%) were diagnosed with ovarian cancer. The remaining patients suffered from breasts (18%), colon (9%), prostate (7%), endometrium (7%), lung (4,5%), lymphoma (4,5%), uterus (3%), gastric (3%), liver (2%), gallbladder (1%), rectum (1%), kidney (1%) and central nervous system (1%) cancers. Platinum salts were the most common drugs involved in HSR (45%), shortly followed by taxanes (34%), biological therapies (18%), and alkylating agents (1%).

Most of the reactions had occurred during the first minutes after the administration of the drug involved in the reaction and had been well documented by the oncologist in charge who shortly after asked for allergic evaluation. Regarding the severity, 56%

of the reactions were moderate while 20% were mild and 24% were severe, according to Brown's classification (10).

Between 15 and 21 days after the reaction, and prior to desensitization, patients underwent allergological assessment and according to the suspected immunological mechanism involved, skin testing was performed, if needed. For this purpose, standardized concentrations and doses approved for each agent were used (3). Only 42% of the patients did react against skin tests (92% of them with immediate positivity), being platinum salts the most frequently drugs responsible for these results. Thus, 87% of patients with platinum salt hypersensitivity showed a positive result. However, 97% of taxanes and 100% of biologics were tested negative, which is consistent with other previously published series (8). Two patients with a suspected non-IgE-mediated reaction to rituximab and temozolamide were not skin tested.

Desensitizations were performed in a short-stay hospital bed under the supervision of a chemotherapy nurse and an allergist. Informed consent was obtained prior to the desensitization procedure. Patients received standard oncologic premedication for their drug and premedication according to the symptoms and type of their initial HSR as previously suggested (8). Dexchlorpheniramine 5 mg IV was administered to every patient 5 minutes before starting the procedure (3).

According to our previously published protocol, once the dose required for each patient had been calculated, it was diluted in 0.9% saline solution for taxanes and biological agents and in 5% dextrose solution for platinum salts to reach a final concentration of 1 mg/mL, 0.5 mg/mL or 0.1 mg/mL, depending on the total amount of the drug so that the volume to be administered differed from patient to patient (an example of the protocol, with a total amount of 650 mg of drug to be administered and a required concentration of 1mg/ml can be found in **table I**). The line (15 Micron Filter in Sight Chamber, polyethylene-lined light-resistant tubing, distal microbore tubing 272 cm/12 mL) was primed with the antineoplastic agent and clamped. The distal line was connected to a 3-way stopcock (BD Connecta, Becton Dickinson Infusion Therapy, Stockholm, Sweden). An infusion pump with automated multistep infusion options (Icumedical Plum360, ICU Medical BV, The Netherlands) was used, but infusion rates were changed manually every 15 minutes until the last two steps when infusion rates were changed after 30 minutes. Using this standard protocol, the duration of the procedure was 4:30 hours for every patient. However, most recently, we have implemented in our daily clinical practice a shortened schedule in those patients who had well tolerated the first desensitization cycle. Thus, in a total of 17 patients and 93 desensitizations, the procedure was shortened, removing a mean of the 4 initial steps from the protocol, and consequently, reducing the time of the procedure to a mean of 3:30 hours.

Using the one-bag procedure, all the patients were able to receive the complete dose of their drug. However, despite desensiti-

Table I - Example for the administration of 650 mg of chemotherapy using one bag at a concentration of 1 mg/ml.

Desensitization schedule for 1 mg/ml concentration			
Step	Time (min)	Rate (mL/h)	Dose (mg)
1	15	0.2	0.05
2	15	0.3	0.075
3	15	0.7	0.175
4	15	1.3	0.325
5	15	1.6	0.4
6	15	3.25	0.8125
7	15	6.5	1.625
8	15	13	3.25
9	15	16	4
10	15	33	8.25
11	15	65	16.25
12	15	130	32.5
13	15	144	36
14	15	289	72.25
15	15	361	180.5
16	30	578	Remaining: 293.5375

zation, 7 patients (57.4% of them with a severe initial HSR), experimented a HSR during the drug administration. In 43% of them, the HSR appeared in the first desensitization cycle and 43% continued experiencing HSR in two or more cycles. The percentage of patients suffering from HSR using our procedure (8.1%) was fewer than in other multiple-bag and one-bag desensitization protocols (1, 11). Most of the reactions were moderate (57.4%) and were successfully treated. None of the patients who underwent the shortened protocol experienced any adverse events. The clinical characteristics of these patients, including the number of previous tolerated cycles, description of the reaction and results of skin tests with the drug involved in the reaction, are shown in **table II**.

In conclusion, we present an extension of our previously published protocol (2), increasing the number of patients in our series, proving its safety and well-tolerability. We also propose a quicker version of the protocol, shortening its initial steps with no further appearance of hypersensitivity reactions. Thus, we consider the one-bag procedure to be the best and more convenient option for both clinicians and patients for the management of HSR in either low, moderate or high-risk patients in daily clinical practice.

Table II - Clinical characteristics of patients with HSR during desensitization.

Age (Gender)	Cancer	Drug	HSR's cycle (Severity) [Latency]	Skin test result	Number of procedures	Number of HSR during desensitization (description)
36 (F)	Cervix	Paclitaxel	1 st (moderate) [immediate]	Negative	3	1 1 st cycle, step 1: five minutes after starting the infusion, two self-limited hives which resolved with no treatment.
44 (F)	Ovary	Paclitaxel	1 st (moderate) [immediate]	Negative	3	3 1 st cycle, step 14: warmth sensation in the scalp, face, chest erythema, and palmar itching. Cycle was completed without requiring further medication. 2 nd cycle, last step: retroauricular itching with mild erythema. Treated with dexchlorpheniramine with recovery in 15 minutes. 3 rd cycle, step 15: face, ear and chest warmth with erythema. Treated with hydrocortisone, being able to continue the procedure after 10 minutes with no further complications.
78 (F)	Linfoma	Rituximab	1 st (moderate) [immediate]	Negative	4	1 1 st cycle step 15: chills and hypotension. Paracetamol and methylprednisolone were administered after stopping the procedure. Desensitization completed afterwards.
70 (M)	Lung	Oxaliplatin	10 th (severe) [immediate]	Negative	4	2 3 rd cycle, step 15: shivering followed by dizziness and sweating, dyspnea, desaturation and chest oppression at step 16. 4 th cycle, step 13: face erythema treated with dexchlorpheniramine. At step 15, chills, tachycardia and desaturation treated with salbutamol, IV corticosteroids and ipratropium bromide, being able to continue with the procedure.
68 (F)	Breast	Trastuzumab	1 st (severe) [immediate]	Negative	12	1 5 th cycle, step 15: facial erythema, dyspnea and headache treated with antihistamines and corticosteroids, completing the cycle.
52 (F)	Ovary	Carboplatin	2 nd (moderate) [immediate]	Positive	10	1 10 th cycle, step 16: eyelid, mandibular, neck, chest and palms of hands erythema and itching.
69 (F)	Ovary	Carboplatin	2 nd (severe) [immediate]	Positive	7	3 1 st cycle, step 9: erythema in forearms treated with antihistamines and corticosteroids. 2 nd cycle, step 12 generalized erythema, requiring adrenaline. Cycle was completed afterwards. 3 rd cycle, step 14: generalized erythema treated with antihistamines and corticosteroids.

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Contributions

PMB, SLF, MAG, VRV, CVP: conceptualization, methodology.
 IRV, PMB, CVP: formal analysis, writing – original draft. IRV,

PMB, MCM, MGR, PIS, RLA, SCM, TGF, SLF, MAG, VRV,
 CVP: investigation, validation, writing – review & editing.

Conflict of interests

SLF: Expert Witness for ALK, ALLERGY THERAPEUTICS.
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