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EDITORIAL

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Could Single-Bag Protocols Serve as An Alternative to Multiple-Bag Protocols for Desensitization?

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Desensitization is a crucial tool in allergy practice, ensuring that patients with documented hypersensitivity reactions (HSRs) can continue their treatment when suitable alternatives are not available. Especially in situations such as cancer, where alternatives may already be limited, less effective, or more toxic, desensitization is pivotal for overcoming the hypersensitivity barrier and allowing the patient to continue treatment with first-line chemotherapeutic or biologic agents (1,2).

Traditional desensitization protocols typically involve multiple bags and multistep infusion schemes, where patients are gradually exposed to increasing doses of the culprit drug. A classic and widely accepted and validated protocol is the three-bag, 12-step protocol developed by Brigham and Women's Hospital (BWH), Massachusetts General Hospital, and Ramon y Cajal University Hospital, which takes approximately 6 hours (3). While these and similar multi-bag protocols have a proven safety record, including high completion rates and the extreme rarity of serious breakthrough reactions (BTRs), administrative complexity, increased workload for pharmacy and nursing services, drug stability issues, long infusion times, and the potential for dilution errors remain significant drawbacks (4-6).

However, in recent decades, with the convenience of advancing technology (e.g., programmable infusion pumps), there has been a shift in interest towards single-bag (single-bag or single-dilution) rapid desensitization protocols, spurred by the desire to simplify logistics, shorten infusion times, reduce the possibility of errors, and enable outpatient administration without compromising safety or effectiveness.

In this context, a review published in The Journal of Asthma, Allergy & Immunology highlighted that single-bag rapid drug desensitization (RDD) protocols may represent a safe and effective alternative in carefully selected patients, with substantial time and labor savings (5). The studies reviewed, especially those comparing single-bag and multibag protocols, provided valuable and insightful information (7,8). For example, Lee et al. researched RDD procedures using paclitaxel in patients with comparable initial reaction severities. They reported similar success rates, with single-bag protocols completed in 4.4 ± 2.5 hours, compared to 8.1 ± 3.0 hours for three-bag protocols (7). Similarly, Sala-Cunill et al. compared desensitizations performed with three-bag protocols (2014–2016) versus single-bag protocols (2017–2019) for various chemotherapeutic and biologic agents. BTR rates and severity were comparable in both groups, while single-bag protocols achieved successful completion in 3.3–4.8 hours versus 4.3–5.8 hours for the multibag group (8).

Since 2020, we have used a single-bag protocol for desensitization in our clinic and documented our initial experience, consisting of 163 desensitization procedures completed in 46 patients, with a success rate of 99.3% (9). Further we conducted a recent comparative study

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with 582 desensitization procedures performed in 153 patients between 2020 and 2024, using both single- and three-bag RDD protocols. Completion rates were nearly identical (~99.8%), and BTRs were evenly distributed in both groups. Notably, single-bag protocols demonstrated a time-saving of approximately 90 minutes per infusion, confirming both their safety and operational advantages (10). A summary of studies comparing single- and multi-bag desensitization protocols is shown in Table I.

Another study, currently in press and incorporating a meta-analysis of 16 studies involving 975 patients

Table I: Studies Comparing Single Bag and Multiple Bag Protocols

Authors, (year) (Ref no), N: patients (RDDs)	Agents	Protocol	Patients-Initial rx characteristics	BTR characteristics	Completion rate	Duration
Lee et al. (2020) (7)		1BP-13S	1BP initial HSR (Brown) Grade I: 1 (4%) Grade II: 14 (58%) Grade III: 9 (38%)	1BP BTR rate: 16% Grade I: 7% Grade II: 8% Grade III: 1%	98% (121/124)	4.4 ± 2.5 h (4.1 ± 1.3 h for desensitizations without BTR)
1BP:24(124) 3BP: 25(87)	Paclitaxel	3BP-12S	3BP initial HSR (Brown) Grade I: 1 (4%) Grade II: 15 (60%) Grade III: 9 (36%)	3BP BTR rate: 27% Grade I: 7% Grade II: 17% Grade III: 3%	99% (86/87)	8.1 ± 3.0 h (7.3 ± 1.9 h for desensitizations without BTR)
Kim et al. (2020) (15)		1BP-12S	1BP initial HSR Grade I: 7 (14%) Grade II: 18 (37%) Grade III: 24 (49%)	1BP BTR rate: 15.6%*	97.3(143/147)	~258 min.
1BP:35(147) 3BP:14(43)	Rituximab	3BP-12S	3BP initial HSR Grade I: 1 (7%) Grade II: 3 (21%) Grade III: 10 (71%)	3BP BTR rate: 20.9%*	93 (40/43)	~329 min.
Sala-Cunill et al. (2021) (8)	Oxaliplatin:22 Carboplatin:50 Cisplatin:3 Paclitaxel:33 Docetaxel:6	1BP-11S	Initial HSR (Brown) for 1BP and 3BP combined: Grade I: 56 (36%) Grade II: 67 (43%) Grade III: 34 (21%)	1BP BTR rate:49% Grade I: 40% Grade II: 7% Grade III: 2%	99.5 (432/434)	3.3-4.8 h.
1BP:109(434) 3BP:48(205)	Cetuximab:7 Rituximab:14 Other: 22	3BP-10S		3BP BTR rate:48% Grade I: 31% Grade II: 17% Grade III: 0%	99.5 (204/205)	4.3-5.8 h
Gul et al. (2025) (10)	Oxaliplatin:65 Carboplatin:38 Cisplatin:6 Paclitaxel:19 Docetaxel:17 Rituximab:3	1BP-12S	1BP initial HSR (Brown) Grade 1: 13 (17.1%) Grade 2: 44 (57.9%) Grade 3: 19 (25.0%)	1 BP BTR rate:7.7% Grade 1: 8 (36.4%) Grade 2: 12 (54.5%) Grade 3: 2 (9.1%)	99.6 (283/284)	273±42 min.
1BP:76(284) 3BP:77(298)	Trastuzumab:3 Other:2	3BP-12S	3BP initial HSR (Brown) Grade 1: 6 (7.8%) Grade 2: 40 (51.9%) Grade 3: 31 (40.3%)	3BP BTR rate:7.3% Grade 1: 10 (45.4%) Grade 2: 8 (36.4%) Grade 3: 4 (18.2%)	100 (298/298)	367±33 min.

Rx: Reaction, **1BP:** Single-bag protocol, **3BP:** Three-bag protocol, **S:** Step, **HSR:** Hypersensitivity reaction, **ST:** Skin test, **BTR:** Breakthrough reaction.

* A statistically significant reduction in the severity of the hypersensitivity reaction compared to the initial reaction was observed with both protocols.

and 4,473 RDD procedures, reported a consistently high completion rate with single-bag protocols across various drug classes. The pooled completion rate for single-bag protocols was 99.7%. Also, no significant difference was observed between single-bag and multibag protocols in terms of completion rates; the risk difference was 0.00; p=0.966 (11).

Taken together, these studies indicate that single-bag desensitization protocols—representing a paradigm shift in the field—offer multiple advantages to both clinical allergy practice and appropriately selected patients undergoing desensitization:

- Completion rates of approximately 99%
- Comparable incidence and severity of breakthrough reactions (BTRs)
- Shorter infusion and preparation times (~90–200 minutes saved)
- Reduced logistical burden and lower risk of dilution-related errors
- Potential for safe implementation in outpatient settings

In summary, while multibag protocols continue to be the preferred option for high-risk patients, single-bag protocols offer significant benefits for a larger population with drug hypersensitivities, allowing faster administration without compromising safety or efficacy.

Several crucial questions and requirements remain despite the increasing amount of comparative data:

- Although published single-bag protocols vary in the number of steps (usually ranging from 9 to 17) (7-9,12,13), a universally accepted standardized protocol has not yet been established. Multicenter standardization efforts are needed.
- While retrospective comparative studies offer important insights, prospective randomized controlled trials comparing single-bag and multibag protocols across various drug classes are limited.
- Preliminary data on outpatient implementation are promising (12-15); however, larger studies are necessary to validate safety, cost-effectiveness, and broader applicability in real-world outpatient settings.

In conclusion, especially considering the increasing amount of comparative data, we believe that the RDD procedure with single-bag protocols for chemotherapeutic and biologic agents can become the new standard of care with the satisfaction of the above-mentioned questions and requirements, reduce the barriers to effective first-line treatments, and improve the quality of life of patients with drug hypersensitivity.

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