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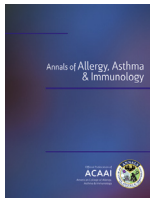

Risk-stratification protocol for carboplatin and oxaliplatin hypersensitivity: repeat skin testing to identify drug allergy

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ABSTRACT

Background: Hypersensitivity reactions (HSRs) to platinum-based chemotherapies are increasingly being recognized. The authors developed a novel risk-stratification protocol that was used successfully in a small number of patients with carboplatin-induced HSRs.

Objective: To describe the utility of this protocol in a large number of patients with carboplatin- or oxaliplatin-induced HSRs.

Methods: A 5-year retrospective review of patients referred to Massachusetts General Hospital with carboplatin- or oxaliplatin-induced HSR was performed. Patients were managed using a risk-stratification protocol using 3 repeat skin tests (STs) with intervening desensitizations. If the repeat ST result remained negative 3 times, patients received subsequent infusions without desensitization.

Results: From 2008 to 2012, 142 patients (92 treated with carboplatin, 50 treated with oxaliplatin) completed 574 desensitizations. Most patients were women (84.5%, mean ± SD 58.1 ± 9.3 years). Patients with carboplatin-induced HSRs were classified as having positive (n = 32, 34.8%), negative (n = 38, 41.3%), or converted (n = 22, 23.9%) ST reactions when the initial negative ST reaction converted to positive at repeat ST. Of those with oxaliplatin-induced HSRs, 22 (44%) had positive, 25 (50%) had negative, and 3 (6%) had converted ST reactions. Of the patients with negative ST reactions, 17 with carboplatin-induced HSRs and 16 with oxaliplatin-induced HSRs safely completed 59 and 95 outpatient infusions, respectively, without desensitizations. For carboplatin and oxaliplatin, ST conversion was associated with an interval of at least 6 months from the HSR to the initial ST (carboplatin, $P = .002$; oxaliplatin, $P = .045$).

Conclusion: This risk-stratification protocol for presumed carboplatin- and oxaliplatin-induced HSRs safely identifies false-negative ST reactions and nonallergic patients who can receive infusions without desensitizations. This leads to fewer unnecessary desensitizations and improved patient care.

Introduction

The incidence of hypersensitivity reactions (HSRs) to carboplatin and oxaliplatin has increased with the increasing use of platinum-based chemotherapies.[1] The incidence of HSR increases with repeat exposure and reaches 27% in patients receiving more than 6 cycles of carboplatin and 24% in patients receiving oxaliplatin.[2,3] Skin testing remains the diagnostic standard for evaluating carboplatin- and oxaliplatin-induced HSRs, and desensitization allows patients who require additional cycles of these agents to receive treatment despite an allergy.[4]

One-time skin testing has a high negative predictive value but is problematic, with up to an 8.5% false-negative rate.[5–8] In addition, chemotherapy desensitization is highly specialized, resource intensive, and available only at a limited number of academic centers with experienced physicians and nurses.[4,9] The authors previously published a novel protocol for patients with a history of carboplatin-induced HSR that used repeat skin testing before each desensitization, and they used this protocol in a small cohort of patients to safely identify those who were not allergic to carboplatin despite presumed HSR.[10]

Accurate identification of nonallergic patients despite presumed HSR allows patients who are referred to tertiary centers for desensitizations to return to outpatient infusion centers, decreases unnecessary desensitizations, and improves patient care. Since the development of the risk-stratification protocol, the allergy and immunology service at Massachusetts General Hospital (Boston, Massachusetts) has expanded this protocol to all patients referred with carboplatin- and oxaliplatin-induced HSR. The authors reviewed the safety, efficacy, and outcomes of this risk-stratification protocol in managing a large group of patients with carboplatin- and oxaliplatin-induced HSRs.

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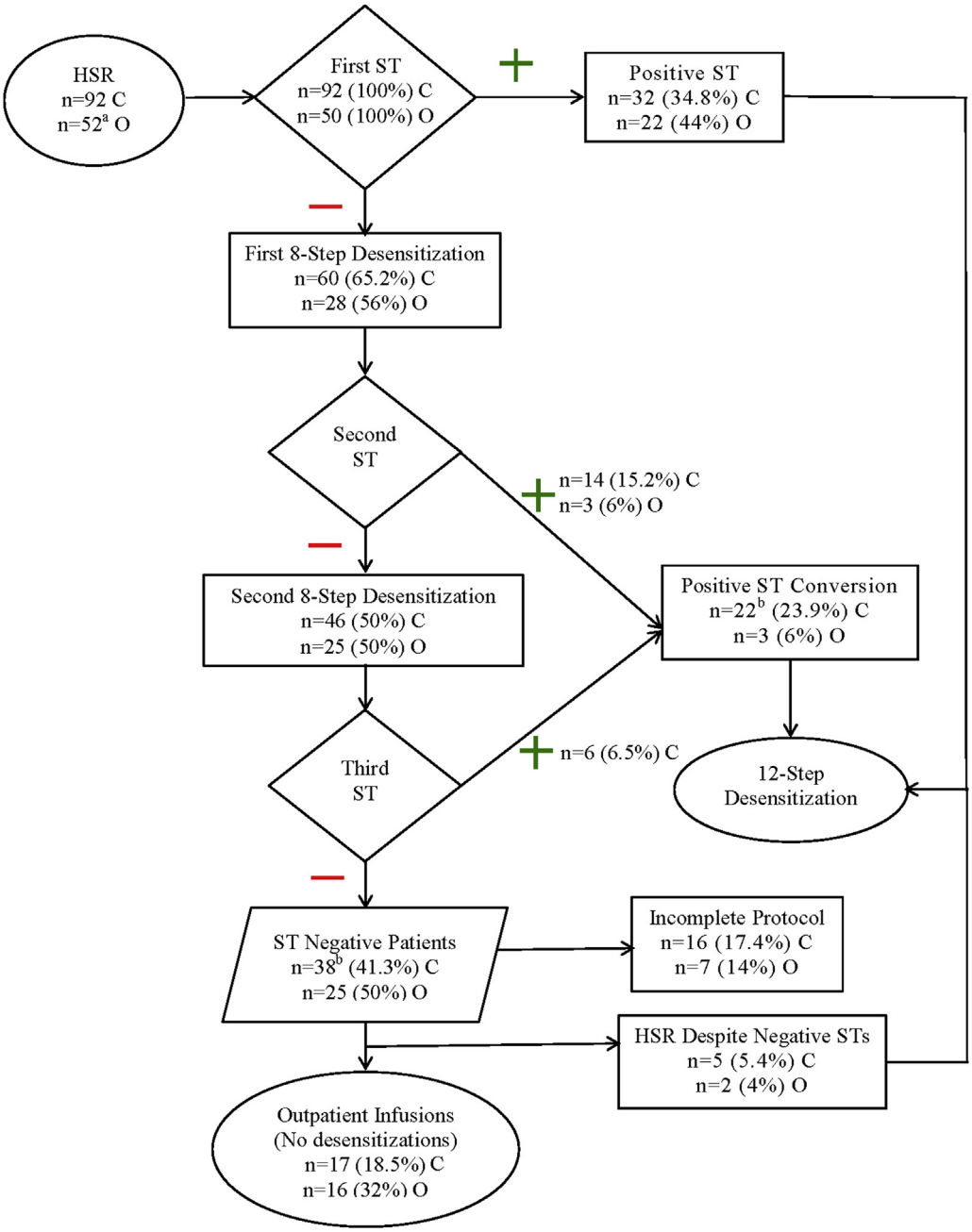

Figure 1. Risk-stratification protocol for carboplatin (C) and oxaliplatin (O) hypersensitivity reactions (HSRs). [a]Two patients received emergency desensitization without initial skin testing (ST) and were excluded from subsequent analysis. [b]Two carboplatin-treated patients had positive ST conversion at the fourth and fifth STs, respectively, that were performed outside the standard protocol owing to symptoms of HSR during desensitizations despite negative ST results.

Methods

A 5-year retrospective review was performed of all patients referred to the allergy and immunology service at Massachusetts General Hospital with carboplatin- or oxaliplatin-induced HSR. Patients were included if they (1) were older than 18 years, (2) had a history of HSR to carboplatin or oxaliplatin, (3) could provide informed consent, and (4) underwent desensitization to carboplatin or oxaliplatin from January 1, 2008 through December 31, 2012. Patients were excluded if skin testing to carboplatin or oxaliplatin was not performed. Patient demographics and clinical characteristics, including history of atopy, cancer diagnosis, chemotherapy cycle number, initial HSR severity grade, and initial HSR symptoms, were reviewed. Approval was obtained from the Massachusetts General Hospital institutional review board.

Evaluation of Initial HSRs

Initial HSRs were graded on a previously reported 4-point scale.[11] Reactions were grade 0 (absent) if there was no reaction; grade 1 (mild) if less than 50% of the skin was involved in a cutaneous reaction (flushing, hives, or pruritus); grade 2 (moderate) if there was generalized cutaneous involvement or angioedema, excluding laryngeal angioedema; and grade 3 (severe) if there was laryngeal angioedema or when respiratory, gastrointestinal, or cardiovascular symptoms were associated with cutaneous symptoms.[11] Symptoms of initial HSR were recorded and classified by organ system.