
Letters

USEFULNESS OF SKIN TESTING WITH PLATINUM SALTS TO DEMONSTRATE LACK OF CROSS-REACTIVITY BETWEEN CARBOPLATIN AND CISPLATIN

Hypersensitivity reactions to platinum salts are potentially lethal adverse events in chemotherapy and often require its discontinuation. Because the resumption of treatment may be fatal, several preventive procedures have been proposed, most often successfully: premedication, desensitization regimens, or replacement with different platinum salts.¹

Carboplatin and cisplatin, derivatives of platinum salts, have been used for the treatment of several cancers, being the mainstay therapy for ovarian and testicular carcinoma. Both drugs act in the same phase of the cellular cycle² and, therefore, similar adverse effects could be expected.

Immediate hypersensitivity reactions have been noted as often as up to 5% with carboplatin and cisplatin and were documented by a positive cutaneous test result.³ Nevertheless, there are few studies regarding cross-reactivity between platinum salts.⁴

Herein, we report 2 cases of carboplatin anaphylaxis with good tolerance to cisplatin in 2 patients with ovarian carcinoma.

Case 1 was a 36-year-old woman with ovarian cancer. After surgery, she received treatment with carboplatin and paclitaxel (4 cycles). After 5 courses of treatment, she developed pruritus on her palms and palmar erythema and hypotension during carboplatin administration. She was referred to the allergy division, where a skin prick test (SPT) with carboplatin and cisplatin was performed. The SPT result with carboplatin, 0.1 mg/mL, was positive, whereas the SPT and intradermal test (IDT) results with cisplatin, 0.001, 0.01, and 0.1 mg/mL, were negative.

Case 2 was a 60-year-old woman diagnosed as having bilateral ovarian cancer. She received 6 cycles of carboplatin and paclitaxel, with good response. Two years later, she again needed chemotherapy. During the second cycle with carboplatin, she developed urticaria, hypotension, and loss of consciousness. She was diagnosed as having carboplatin hypersensitivity. An SPT result with carboplatin, 0.1 mg/mL, was positive, and SPT and IDT results with cisplatin were negative. Both patients continued treatment with cisplatin with no adverse reactions.

These 2 systemic reactions seem to be mediated by a type 1 hypersensitivity reaction. To our knowledge, no study has searched for platinum-specific IgE in carboplatin- and cisplatin-treated patients, but early onset of symptoms, the fact that

the adverse reaction occurs only after patients have undergone several courses of treatment, and a positive SPT result suggest that these adverse effects are the result of an IgE-mediated reaction.

An SPT with platinum salts seems safe because no serious systemic reactions have been reported.¹ Previous studies^{1,3,5} have shown that SPT and IDT results with platinum salts have excellent negative predictive value of 92% to 99%, and positive test results are associated with the development of immediate hypersensitivity reactions to carboplatin. Leguy-Seguín and coworkers¹ proposed a standardized protocol of skin testing: SPT with pure injectable drugs. Nevertheless, the positive results of the carboplatin SPT with lower concentrations obtained in the present study are similar to those obtained with pure injectable carboplatin¹ and perhaps with less irritative effect. Furthermore, these SPT-positive results performed before IDT should be recommended because SPT is much safer than proceeding with IDT alone, as performed by Markman³ and Zanotti⁵ and coworkers.

The frequency of cross-reactions among cisplatin and carboplatin has not been clearly established. Cross-reactivity can be detected by SPT, suggesting that chemotherapeutic regimens could be modified based on the results of skin testing, thus rendering interruption of effective platinum-based chemotherapy unnecessary. Nevertheless, larger studies are required to validate this observation.

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Disclosures: Authors have nothing to disclose.

A SUCCESSFUL PROTOCOL FOR DAPTOMYCIN DESENSITIZATION

To the Editor:

Daptomycin is a lipopeptide antibiotic that interferes with the bacterial membrane of gram-positive organisms and has important clinical indications not only for skin and soft tissue infections but also for serious gram-positive infections, including methicillin-resistant *Staphylococcus aureus* (MRSA).^{1,2} Despite the increasing use of daptomycin, to our knowledge, there are no publications in the literature describing an effective desensitization protocol for patients with severe allergic reactions to the drug. This letter describes a successful protocol that was applied to a patient with suspected daptomycin allergy and MRSA infection.

A 33-year-old man with a history of acute lymphoblastic leukemia after chemotherapy, radiation, and autologous bone marrow transplantation with known vancomycin allergy presented with fevers, chills, and lancinating right groin pain of 7 days' duration. His initial laboratory evaluation included a white blood cell count of $17.8 \times 10^9/L$, a erythrocyte sedimentation rate of 86 mm/h, and blood cultures that ultimately yielded MRSA. Imaging included a pelvic magnetic resonance image that revealed a large iliopsoas abscess that also yielded MRSA. In addition to surgical drainage, he was prescribed broad-spectrum antibiotics, including daptomycin, because he previously did not tolerate vancomycin because of a diffuse urticarial eruption or linezolid secondary to leukopenia. He was prescribed daptomycin dosed at 350 mg/d. However, within 30 minutes after the third administration, he developed a progressively worsening generalized urticarial rash that was not associated with lip or tongue swelling, wheezing, shortness of breath, or mucosal lesions. His symptoms improved with diphenhydramine, but the urticaria returned within 30 minutes after each subsequent dose. Given the acute onset of urticaria after antibiotic administration, the primary team was concerned about an IgE-mediated reaction to daptomycin and subsequently consulted the allergy service to attempt daptomycin desensitization. Although vancomycin desensitization was also considered, the patient declined this option because he believed his previous reaction to vancomycin was more severe than his current symptoms attributed to daptomycin.

The desired final dose of daptomycin was 350 mg/d intravenously. The patient was transferred to an intermediate care unit, which provided one-to-one nursing care and emer-

gency medications, including epinephrine, diphenhydramine, and albuterol, which were available at the bedside. He did not receive any premedications. As described in Table 1, serial

Table 1. Desensitization Protocol

Dilution No.	Time, min	Concentration, mg
1	0	Desired dose $\times 10^{-6}$
2	30	Desired dose $\times 10^{-5}$
3	60	Desired dose $\times 10^{-4}$
4	90	Desired dose $\times 10^{-3}$
5	120	Desired dose $\times 10^{-2}$
6	150	Desired dose $\times 10^{-1}$
7	180	Desired dose (full strength)

10-fold dilutions were administered starting with $350 \text{ mg} \times 10^{-6}$. Each dilution was administered during 15 minutes, and the patient was closely observed for any signs of urticaria, angioedema, shortness of breath, or hemodynamic instability. If no reaction occurred within 30 minutes, the next dose was administered. The patient tolerated all dilutions and achieved the target dose without any allergic symptoms. He was ultimately discharged on a prolonged course of antibiotics, including daptomycin.

As the proportion of MRSA continues to increase, daptomycin provides an important therapeutic option in the antistaphylococcal armamentarium for those who cannot tolerate traditional therapies.^{3,4} Additionally, no reports have been made of cross-reactivity between daptomycin and other classes of antibiotics. This case describes a successful protocol used for daptomycin desensitization.

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Disclosure: Authors have nothing to disclose.