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Screening for Beta-Lactam Allergy in Joint Arthroplasty Patients to Improve Surgical Prophylaxis Practice

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ABSTRACT

Background: The reliability of patient-reported penicillin allergies has been disputed. A Drug Allergy Clinic (DAC) was established at our institution in combination with an electronic best practice alert (BPA) in the Orthopedic Clinic. Joint arthroplasty patients with a reported history of beta-lactam allergy (HOBA) were preoperatively referred via the BPA to the DAC. The purpose of this study was to determine the effectiveness of beta-lactam allergy screening in enabling the surgical team to optimize antimicrobial prophylaxis.

Methods: Between February 2013 and May 2015, 161 patients with a HOBA were referred to the DAC where they underwent penicillin skin testing (PST), a drug challenge to a beta-lactam antibiotic, and/or had no intervention depending on the history obtained.

Results: PST was performed on 140 of 161 (87%) patients. A negative PST was noted in 139 (99%) patients, indicating no penicillin allergy. Cefazolin was safe to use in 145 (90%) patients evaluated. Significantly more patients evaluated in the DAC vs those not seen got cefazolin in any surgical prophylaxis regimen (90% vs 77%) without any adverse perioperative reactions. Concurrently, the use of non-beta-lactam antibiotics was significantly less in the patients evaluated vs not evaluated (16% vs 27%). The overall use of cefazolin in orthopedic surgeries in patients with HOBA was >84% over the course of the study period.

Conclusion: Beta-lactam allergy screening using a BPA and a DAC promotes the use of standard surgical prophylaxis with cefazolin. Joint arthroplasty surgeons should consider implementing allergy screening programs to promote antimicrobial stewardship.

The American Society of Health-System Pharmacists, the Infectious Diseases Society of American, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America Clinical Practice Guidelines for antimicrobial prophylaxis in surgery recommend the first-generation cephalosporin, cefazolin, for patients undergoing orthopedic spinal or joint procedures [1]. Beta-lactam antibiotics, such as penicillins and cephalosporins, are amongst the most common drugs to cause allergic reactions with prevalence rates between 1% and 10% of the general population

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[2,3]. Although cefazolin is not a penicillin derivative, it shares a similar chemical group with the beta-lactam ring. Due to this common structure, patients who are allergic to penicillin may also be allergic to cephalosporins [2]. However, the incidence of cross-reactive allergic reactions to cephalosporins among penicillin-allergic patients varies with the chemical side chain similarity of the cephalosporin to penicillin, amoxicillin, or ampicillin. For first-generation cephalosporins, the increased attributable risk is thought to be 0.4% [3]. A true, IgE-mediated allergic reaction often presents rapidly with symptoms of hives, difficulty breathing, facial or lip swelling, or low blood pressure. Yet, many patients may be inappropriately labeled as having a history of a beta-lactam allergy (HOBA) when their reaction may, in fact, have only been an adverse drug effect (ie, nausea, vomiting, or diarrhea), may have been delayed in onset and therefore not fulfilling the definition of an immediate IgE-mediated reaction, or may have occurred many years prior. Furthermore, it has been previously reported that more than 80% of patients could have diminished penicillin-specific IgE antibody over 8-10 years and that most of the reported reactions are frequently on a patient's allergy list for more than 10 years [2].

Due to time or training constraints within the medical community, medical personnel are frequently unable to obtain a detailed patient allergy history. Thus, if a patient has a reported allergy to a beta-lactam antibiotic, they are typically not prescribed this antibiotic class even when it may be medically indicated. The surgical prophylaxis recommended for total joint replacement in a patient with HOBA in place of cephalosporins is clindamycin or vancomycin with or without gentamicin depending on the need for gram-negative coverage [4]. In lieu of rising antibacterial resistance and the cost and potential adverse effects of alternative antibiotics (primarily gentamicin-associated nephrotoxicity, clindamycin-associated *Clostridium difficile* infection, and vancomycin-resistant enterococci emergence), it has become increasingly important to confirm whether a true IgE-mediated beta-lactam antibiotic allergy does indeed exist in surgical patients who report a history of such allergy.

In light of the above, the Infectious Diseases and Immunology Divisions at our institution established a Drug Allergy Clinic (DAC) in February 2013 in collaboration with the Orthopedics Department. The DAC also has a pharmacist who helps to see patients in the clinic. The role of the DAC is to evaluate patients with an upcoming joint surgery and a suspected HOBA for the presence of a true IgE-mediated hypersensitivity. Appropriate patients were identified by means of an electronic best practice alert (BPA) in orthopedic preoperative clinics. The purpose of our study was to determine the effectiveness of this new initiative at our institution in enabling the surgical team to optimize antimicrobial prophylaxis and promote antimicrobial stewardship.

Materials and Methods

Study Patients

We undertook a retrospective observational study of adult orthopedic patients (18 years and older) with a HOBA that were seen in the orthopedic total joint arthroplasty preoperative clinics at the University of Iowa Hospitals and Clinics between February 1, 2013, and March 1, 2015. This project was undertaken as a practice improvement measure at our institution. Before the start of the study, approval for database review through an expedited process was obtained from our institutional review board.

Patients were identified through an electronic BPA that triggered electronically at the time that a patient with a listed beta-lactam allergy was checked in by ancillary clinic staff (registered nurse or medical assistant) to the orthopedic clinic for determination of surgical candidacy. The BPA was designed in collaboration between the Divisions of Immunology and Infectious Diseases at our institution. The list of beta-lactam antibiotics that would trigger the BPA in a patient's allergy profile included 119 possible entries for penicillin derivatives and 116 for cephalosporins. The BPA comprised the following 2 simple questions aimed at the patient's reported HOBA: (1) the patient's initial reaction consisted only of nausea, vomiting, and/or diarrhea or (2) if the patient had taken the same beta-lactam medication uneventfully since the reaction. Orthopedic clinic staff could override the BPA for patients with HOBA who answered yes to either of the 2 questions or if the allergy had been entered in error. They were required to update a patient's allergy record if during the screening the HOBA was deemed to be non-IgE-mediated. If, however, the BPA indicated a possibility of an IgE-mediated beta-lactam allergy, the patient was referred for formal evaluation in the DAC via an electronic consult order. The supervising orthopedic practitioner for that patient was required to sign the consult order.

DAC Evaluation

Patients who were referred to the DAC were evaluated by a detailed history regarding their reported reaction(s) to beta-lactam medications, including the time that lapsed since the reaction, reason for the medication having been prescribed, nature of, time into onset and duration of the reaction, associated systemic effects, treatments given, and use of the same or similar class of medication since the reaction. If the evaluation of a penicillin allergy was suggestive of an IgE-mediated allergy, patients underwent penicillin skin testing (PST) using prick and intradermal tests to Pre-Pen (benzylpenicilloyl polylysine injection) and a penicillin G solution (by diluting to a concentration of 10,000 units/mL by taking 5 million units diluted with 500 mL of 0.9% sodium chloride injection), along with positive and negative controls [5]. If a patient had a negative PST, the standardized testing has been reported to have a 97%-99% negative predictive value for determining a penicillin IgE-mediated hypersensitivity. However, if the reaction was very suspicious for a recent IgE-mediated reaction or if the reaction was to amoxicillin or ampicillin only, the negative PST was sometimes followed by a supervised oral drug challenge to amoxicillin, as this has been shown to increase the negative predictive value of testing closer to 100% [6]. For patients, in whom the suspicion for a true IgE-mediated reaction was low, in cases where skin testing was not available (ie, some cephalosporins), if the patient refused a skin test, or would have unreliable skin testing results (due to use of antihistamines or lack of adequate response to the positive histamine control skin test), a graded supervised oral or intravenous (IV) drug challenge to a beta-lactam was performed instead of skin testing. Patients who were referred for evaluation of a history of cephalosporin allergy underwent either (1) a supervised drug challenge to IV cefazolin or the oral cephalosporin they had reacted to in the past or (2) no further testing or intervention if their reported reaction was very suggestive of a true IgE-mediated reaction. If the patient had a negative PST and/or tolerated a supervised drug challenge, the penicillin-based allergy was removed from the patient's medical record. Similarly, if skin testing was negative or supervised oral or IV drug challenge to a cephalosporin was well tolerated, the patient's allergy history was updated to reflect either the absence of a cephalosporin allergy or the specific cephalosporin that was tolerated in the drug challenge. The allergy team notified the referring orthopedic provider of the DAC outcome. Where a beta-lactam allergy was ruled out, the orthopedic provider was advised to administer cefazolin for perioperative prophylaxis for any future surgeries.