

# Antibiotic prophylaxis in beta-lactam allergic patients undergoing cesarean and vaginal delivery: An opportunity for stewardship

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*To the Editor*—It is now known that the R1 group side chain is the predominant allergenic determinant in patients with a  $\beta$ -lactam allergy and that patients with a confirmed IgE-mediated  $\beta$ -lactam allergy can safely receive other  $\beta$ -lactams that do not share similar R1 side-chain structures.<sup>1,2</sup> Cefazolin in particular has a distinct R1 structure and is thought to be safe to administer even in patients with a history of anaphylaxis to other  $\beta$ -lactams.<sup>1,2</sup> Based on this knowledge, multiple studies have successfully increased rates of cefazolin use for perioperative prophylaxis in patients with a  $\beta$ -lactam allergy.<sup>3,4</sup>

No studies have specifically applied this knowledge to obstetrics and gynecology. Cefazolin is the antibiotic of choice for cesarean section prophylaxis and is also the recommended alternative to penicillin for patients with a “low risk” penicillin allergy who require peripartum group B *Streptococcus* (GBS) prophylaxis.<sup>5,6</sup> We conducted a retrospective study to identify opportunities for stewardship in  $\beta$ -lactam allergic patients undergoing cesarean and vaginal delivery based on our knowledge of  $\beta$ -lactam cross reactivity.

## Methods

Medical records of patients who delivered at 1 of 2 academic medical centers in Los Angeles from January 1, 2017, to November 30, 2020, were retrospectively reviewed. Patient allergy, type of allergic reaction, delivery type (vaginal vs cesarean), GBS screening status, and antibiotics administered during the hospitalization were electronically abstracted. A descriptive analysis of patients' allergies and prophylactic antibiotics administered were performed on 2 specific subgroups: (1) patients with a  $\beta$ -lactam allergy label who underwent cesarean section and (2) patients with a  $\beta$ -lactam allergy label with a positive GBS screen who underwent vaginal delivery. Patients with suspected active peri-partum infection were excluded. This study was conducted as a quality improvement initiative.

## Results

In total, 8,749 patients underwent cesarean or vaginal delivery. Of these, 827 patients (9.5%) had a  $\beta$ -lactam allergy label. A list of antibiotics to which patients were allergic can be found in Supplementary Table 1 (online). Of these 827 patients, 360 met our prespecified subgroups: 260 patients who underwent cesarean delivery and 100 patients who were GBS positive and delivered

vaginally. Of the 260 patients that underwent cesarean delivery, 165 (63.5%) received a non- $\beta$ -lactam alternative (vancomycin or clindamycin) for perioperative prophylaxis. Of the 100 patients who underwent vaginal delivery, 64 (64.0%) received a non- $\beta$ -lactam alternative for GBS prophylaxis.

The documented allergic reactions are listed in Table 1 for patients who received a non- $\beta$ -lactam alternative. Rash (n = 60, 38.0%) and hives (n = 27, 43.5%) were the most common documented reactions for patients that underwent cesarean and vaginal delivery, respectively. Only 5 patients (2.3% of total) reported an allergic reaction whereby cefazolin would not have been recommended, and conversely, 215 (97.7%) patients reported reactions whereby cefazolin likely could have been safely administered.

## Discussion

History of  $\beta$ -lactam allergy was common in our cohort, seen in 9.5% of patients that underwent Cesarean or vaginal delivery. Additionally, we found that many patients in our cohort who received a non- $\beta$ -lactam alternative had documented reactions that were unknown or suggestive of an intolerance rather than a true allergy. These findings are consistent with studies in the literature, which have demonstrated that most patients with an allergy label do not actually have a true allergy.<sup>7</sup> Our study highlights an important opportunity for antibiotic allergy de-labeling initiatives in the obstetrics population.

Previous studies have evaluated inappropriate or guideline discordant antibiotic use for penicillin allergic patients in the obstetrics population.<sup>8,9</sup> However, to our knowledge, our study is the first to evaluate appropriateness of antibiotics based on side-chain cross reactivity, and we found that most patients who received a non- $\beta$ -lactam prophylaxis likely could have safely received cefazolin. Given the inferior outcomes and greater side-effect profile of non- $\beta$ -lactam alternatives,<sup>10</sup> it is imperative that efforts be made to maximize  $\beta$ -lactam utilization in patients with a  $\beta$ -lactam allergy label.

Based on these data, we devised an algorithm (Supplementary Fig. 1a and b online) to help providers make appropriate antibiotic selections for patients with a  $\beta$ -lactam allergy label at our institution. Notably, this approach, based on side-chain cross reactivity, is not reflected in the recent American College of Obstetrics and Gynecology (ACOG) guidelines.<sup>5,6</sup> For example, in the ACOG guidelines, cefazolin is not recommended for GBS prophylaxis in patients with a history of severe IgE-mediated penicillin allergy, whereas cefazolin is considered safe in our algorithm. Despite this deviation from guidelines, feedback from obstetrics and gynecology colleagues at our institution have been favorable with no

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**Table 1.** Recorded Allergic Reactions to  $\beta$ -Lactams for Patients Who Received a Non- $\beta$ -Lactam Alternative

Reaction	Cesarean Delivery (n = 158 <sup>a,b</sup> )	GBS + Vaginal Delivery (n = 62 <sup>a,b</sup> )
<b>Cefazolin recommended</b>		
<b>IgE mediated, no. (%)</b>		
Anaphylaxis	12 (7.6)	3 (4.8)
Angioedema	1 (0.6)	0 (0.0)
Rash	60 (38.0)	20 (32.3)
Hives	55 (34.8)	27 (43.5)
Throat swelling	8 (5.1)	2 (3.2)
Shortness of breath	7 (4.4)	1 (1.6)
Wheezing	1 (0.6)	1 (1.6)
<b>Intolerance or unknown, no. (%)</b>		
Itching	11 (7.0)	8 (12.9)
Diarrhea	1 (0.6)	1 (1.6)
Dizziness	2 (1.3)	0 (0.0)
Nausea	6 (3.8)	2 (3.2)
Unknown	32 (20.3)	10 (17.7)
<b>Cefazolin not recommended<sup>c</sup></b>		
<b>Severe non-IgE reaction, no. (%)</b>		
Fever	3 (1.9)	1 (1.6)
Hemolysis	1 (0.6)	0 (0.0)

Note. GBS, group B *Streptococcus*.

<sup>a</sup>Patients with cefazolin or "cephalosporin" allergy were excluded from this table.

<sup>b</sup>Sum of number of patients experiencing each reaction is greater than total number of patients as one patient can endorse >1 reaction.

<sup>c</sup>Cefazolin was not recommended only when patients reported an allergic reaction suggestive of a severe non-IgE mediated reaction such as Stevens-Johnson syndrome, DRESS syndrome, hemolytic anemia, drug fever, serum sickness, etc.

reported safety concerns to date. We recommend that other institutions take similar actions to engage obstetrics and gynecology colleagues to improve prophylactic antibiotic selection in patients with a  $\beta$ -lactam allergy.

Our study has limitations. First, the retrospective study design limited our analysis of allergy history to what was recorded in the medical records. Thus, we may have overestimated the number of patients with an unknown reaction. However, even if we had conservatively concluded that patients with unknown allergy reaction were not suitable for cefazolin use, cefazolin would have still been

acceptable in most patients and our conclusions would have remained unchanged. Second, the study was conducted in a single institution and generalizability may be limited.

In conclusion, we demonstrated that  $\beta$ -lactam allergy is common in pregnant patients, but most patients who received a non- $\beta$ -lactam alternative for cesarean or GBS prophylaxis likely could have safely received cefazolin based on our knowledge of  $\beta$ -lactam cross reactivity.  $\beta$ -lactam allergy in pregnancy is a prime opportunity for future stewardship interventions.

**Supplementary material.** To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2021.315>

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