

IgE-Mediated Hypersensitivity in Two Pediatric Patients After Intraoperative Bacitracin Irrigation

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Case report

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Abstract

Background: Bacitracin is a common topical antibiotic that is also used for tissue irrigation in the operative setting. While bacitracin is generally well tolerated, Twelve reports of anaphylaxis to intraoperative applications have been published, all in adults.

Case presentation: Here, we present the first reported cases of intraoperative Immunoglobulin E-mediated hypersensitivity to bacitracin irrigation in the pediatric population. Both cases were corroborated by allergy testing. Case 1 is a 10 year old male who had surgery to remove an infected tissue expander placed in setting of trauma from motor vehicle accident. Case 2 is a 6 year old female with history of spina bifida who underwent vesicostomy recreation.

Conclusions: Bacitracin should be considered a potential occult allergen in the perioperative setting in both adult and pediatric populations.

Background

The incidence of perioperative anaphylaxis is poorly defined, however it is likely in the range of 1 in 10,000 to 1 in 20,000 procedures.¹ Neuromuscular blocking agents, latex, and antibiotics are the most frequently identified etiologies, though approximately 30–40% of cases have no identified trigger.^{1–3} In these scenarios with no clear culprit, other perioperative exposures must be considered.

Bacitracin, a cyclic polypeptide antibiotic, is frequently administered both intraoperatively via wound irrigation as well topically over-the-counter.⁴ Bacitracin was first identified in 1943 from *Bacillus subtilis* culture obtained from the wound of a patient named Tracy—hence the name bacitracin.⁵ Due to systemic toxicity, bacitracin is predominantly used in topical preparations either alone or in combination with other antibiotics such as neomycin and polymyxin. While bacitracin is generally well tolerated, reports of anaphylaxis to both topical and intraoperative applications have been published. Twelve cases of intraoperative bacitracin IgE-mediated hypersensitivity have been reported in the medical literature (Table 1). Reactions thus far have been limited to the adult population in a variety of operative settings.^{6–9} Of the 12 published cases, 6 reported results of allergy testing (Table 1). IgE mediated reactions to topical bacitracin have also been reported, including in one pediatric patient.¹⁰

Table 1

Pertinent details of previously reported cases of intraoperative IgE-mediated bacitracin hypersensitivity.
SPT: skin prick test

Reference	Age	Sex	Procedure	Clinical Findings	Allergy Testing
Burnett, GW and Meisner, J. ⁹	28	Female	Breast implant exchange	Tachycardia, hypotension, and low end tidal carbon dioxide following bacitracin irrigation	Positive SPT to bacitracin, concentration not reported
Damm, S. ⁶	88	Female	Cardiac pacemaker implantation	Hypotension, apnea, loss of consciousness, and erythema of torso and legs following bacitracin irrigation	None reported
Damm, S. ⁶	69	Male	Cardiac defibrillator insertion	Hypotension, cardiac arrest, pallor, diaphoresis, erythema, and maculopapular rash after bacitracin irrigation	None reported
Damm, S. ⁶	83	Female	Cardiac pacemaker battery change	Hypotension, flushing, anxiety, and agitation following bacitracin irrigation	None reported
Freiler, JF, et al. ⁵	72	Female	Cardiac pacemaker revision after pocket infection	Hypotension, wheeze, and urticaria following bacitracin irrigation	Positive SPT to bacitracin 500 U/g and 150 U/mL
Greenberg, SB, et al. ¹⁰	62	Female	Thoracic laminectomy and spinal fusion	Hypotension, cardiac arrest, hypoxia, and decreased somatosensory evoked potentials following bacitracin irrigation	Positive SPT to bacitracin, concentration not reported
Gall, R, et al. ¹¹	48	Male	Septorhinoplasty	Hypotension, cardiac arrest, oxygen desaturation, diffuse erythema, and facial edema following nasal packing with bacitracin-soaked latex glove	Positive SPT to bacitracin, concentration not reported
Blas, M, Briesacher, KS, and Lobato, EB. ¹²	65	Male	Sternal debridement and rewiring	Hypotension, low end tidal carbon dioxide, face and upper extremity erythema following bacitracin irrigation	None reported
Netland, PA, Baumgartner, JE, and Andrews, BT. ¹³	67	Male	Lumbar laminectomy and foraminotomies	Hypotension, cardiac arrest, decreased end tidal carbon dioxide, and facial swelling following bacitracin irrigation	None reported

Reference	Age	Sex	Procedure	Clinical Findings	Allergy Testing
Sprung, J, Schedewie, HK, and Kampine, JP. ⁷	36	Male	Nephrectomy	Hypotension, cardiac arrest, decreased end tidal carbon dioxide, rash, and facial swelling following bacitracin irrigation	None reported
Caraballo, J, et al. ⁸	63	Male	Scleral buckle	Hypotension, hypoxia, decreased end tidal carbon dioxide, wheeze, and urticaria following placement of scleral buckle soaked in bacitracin	Positive SPT to bacitracin 150 U/mL
Antevil, J, et al. ¹⁴	62	Female	Knee arthroplasty revision	Hypotension, tachycardia, and flushing following bacitracin irrigation	Positive SPT to bacitracin, concentration not reported

We have seen two cases of IgE-mediated bacitracin hypersensitivity corroborated by allergy testing in pediatric patients.

Case Presentation

Case 1

A 10-year-old male underwent abdominal surgery for removal of an infected tissue expander placed in preparation for repair of a large fascial defect as a result of a motor vehicle accident. Sevoflurane, midazolam, propofol, rocuronium, fentanyl, and cefazolin were given at induction. Dissection to the tissue expander in the right flank was performed and the pocket was irrigated with bacitracin (200,000 units in 500 mL lactated ringers). This procedure was repeated for the left flank. Acetaminophen, hydromorphone, and phenylephrine were also given. The reaction was noted 150 minutes into the case—2 hours following bacitracin irrigation—as the team was preparing to extubate. The drapes were removed revealing full body urticaria without hemodynamic instability, respiratory symptoms, or gastrointestinal symptoms. Diphenhydramine and cetirizine were administered. Serologic testing obtained 10 minutes after the urticaria were noted showed an elevated plasma histamine at 14 nmol/L (normal 0–8 nmol/L) and normal tryptase at 7.5 mcg/L (normal < 11 mcg/L). The patient was admitted for monitoring and had no further allergic symptoms. Table 2 contains details of allergy testing. Skin prick testing was positive to bacitracin 500 units/ml resulting in a 5 mm wheal and 34 mm flare. Negative skin prick testing was noted to cefazolin 20 mg/mL, chlorhexidine 4%, cisatracurium 2 mg/mL, fentanyl 50 mcg/mL, midazolam 5 mg/mL, propofol 10 mg/mL, rocuronium 10 mg/mL, sugammadex 100 mg/mL, and mixture of rocuronium 10 mg/mL and sugammadex 100 mg/mL. Intradermal testing was negative to cefazolin 2 mg/mL, cisatracurium 0.02 mg/ml, fentanyl 5 mcg/mL, midazolam 0.5 mg/mL, propofol 1 mg/mL,

rocuronium 0.05 mg/mL, sugammadex 1 mg/mL, and mixture of rocuronium 0.2 mg/mL and sugammadex 2 mg/mL.

Case 2

A 6-year-old female with a medical history of spina bifida with multiple sequelae and egg allergy underwent vesicostomy recreation. Lidocaine, propofol, fentanyl, morphine, cisatracurium, midazolam, sevoflurane, and nitrous oxide were given at induction. Cystoscopy was performed followed by ureteral reimplantation with subsequent laparotomy for vesicostomy recreation. Bacitracin irrigation (50 units/mL in normal saline) occurred at 165 minutes. At 255 minutes, shortly after the patient received both cefoxitin and metronidazole, the patient became hypotensive and tachycardic without rash, change in airway pressure, or gastrointestinal symptoms. Hypotension and tachycardia were refractory to both crystalloid fluid resuscitation and ephedrine but improved after epinephrine. The case was aborted before vesicostomy revision, and the patient was admitted to the Pediatric Intensive Care Unit on an epinephrine continuous infusion. Serum histamine and tryptase obtained 2.5 hours after the reaction were both normal (< 8.0 nmol/L and 3.9 mcg/L respectively). The patient was weaned from epinephrine infusion and extubated later that day with no further reaction. Notably, testing was negative to cefoxitin (100 mg/mL skin prick test, 10 mg/mL intradermal), and the patient had subsequently tolerated metronidazole without reaction. Bacitracin gave a negative reaction to skin prick test, but intradermal testing to 50 units/ml bacitracin was positive with a 10 mm wheal and 25 mm flare. Testing was negative to cisatracurium (2 mg/mL skin prick test, 0.2 mg/mL intradermal). Additional testing to lidocaine, propofol, midazolam, and fentanyl were deferred as the patient had subsequently tolerated these medications. Table 2 contains details of allergy testing.

Both patients had bacitracin labeled as an allergy and have since undergone subsequent procedures with general anesthesia without further reactions.

Table 2

Allergy testing results for cases 1 and 2. *Equal volumes of the reported concentrations were mixed prior to skin testing.

Drug	Skin Prick Testing		Intradermal Testing	
	Concentration	Result (wheal diameter/ flare diameter)	Concentration	Result (wheal diameter/ flare diameter)
Case 1				
Histamine		5mm/42mm	-	-
Diluent		Negative	-	-
Bacitracin	500 units/mL	5mm/34mm	-	-
Cefazolin	20mg/mL	Negative	2mg/mL	Negative
Chlorhexidine	4%	Negative	-	-
Cisatracurium	2mg/mL	Negative	0.02mg/mL	Negative
Fentanyl	50mcg/mL	Negative	5mcg/mL	Negative
Midazolam	5mg/mL	Negative	0.5mg/mL	Negative
Propofol	10mg/mL	Negative	1mg/mL	Negative
Rocuronium	10mg/mL	Negative	0.05mg/mL	Negative
Sugammadex	100mg/mL	Negative	1mg/mL	Negative
Rocuronium/ Sugammadex mixture	10mg/mL*	Negative	0.2mg/mL*	Negative
	100mg/mL*		2mg/mL*	
Case 2				
Histamine		5mm/10mm	-	-
Diluent		Negative	-	-
Bacitracin	5000 units/mL	Negative	50 units/mL	10mm/25mm
Cefoxitin	100mg/mL	Negative	10mg/mL	Negative
Cisatracurium	2mg/mL	Negative	0.2mg/mL	Negative

Discussion And Conclusions

We believe these are the first reported cases of intraoperative IgE-mediated bacitracin hypersensitivity in the pediatric population. While contact dermatitis reactions¹⁷ to bacitracin are well recognized¹⁷, IgE-

mediated allergic reactions to this antibiotic are rare. It can affect pediatric patients and should be considered as a potential occult allergen. This is especially true in the operative setting as irrigants are not administered by anesthesia teams and therefore may not be reported in the anesthesia documentation. In each case, the bacitracin reaction occurred with the first intraoperative exposure to the medication. However, both patients had previously received topical bacitracin prior to their surgeries and may have become sensitized via this exposure. Patients who have had an allergic reaction to bacitracin may be at risk for subsequent reactions to topical preparations including products intended for use in the eyes, nose, ears and skin⁶. Patients should be instructed to read labels of topical antibiotic products and to avoid using products containing bacitracin. Over-the-counter, bacitracin is combined with polymyxin B (brand name: Double antibiotic, Polysporin), polymyxin B and neomycin (Triple antibiotic, Neosporin), polymyxin B, neomycin, and pramoxine (Neosporin + Pain Relief, Tri Biozene), and polymyxin B, neomycin, and hydrocortisone (Corticosporin). In ophthalmic formulation by prescription, bacitracin is combined with polymyxin B (brand name: AK Poly-Bac, Polycin), polymyxin B and neomycin (Neo-Polycin), and polymyxin B, neomycin, and hydrocortisone (Neo-Polycin HC)¹⁸. These formulations are summarized in Table 3. There are no reports of bacitracin cross-reactivity to other antibiotics, so use of alternative antibiotics should be feasible for patients with history of allergy to bacitracin.

Table 3

Commonly used formulations containing bacitracin available in the United States. *Denotes formulations available over-the-counter.

Generic Medications	Brand: Topical	Brand: Ophthalmic
Bacitracin and polymyxin B	Double Antibiotic*, Polysporin*	AK-Poly-Bac, Polycin
Bacitracin, polymyxin B, and neomycin	Triple Antibiotic*, Neosporin*	Neo-Polycin
Bacitracin, polymyxin B, neomycin, and pramoxine	Neosporin + Pain Relief*, Tri Biozene*	None
Bacitracin, polymyxin B, neomycin, and hydrocortisone	Cortisporin	Neo-Polycin HC

List Of Abbreviations

Immunoglobulin E (IgE), Skin Prick Testing (SPT), Intradermal (ID)

Declarations

Ethics approval and consent to participate

not applicable

Consent for publication

written consent from parents was completed for both cases.

Availability of data and materials

not applicable

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none

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Authors' contributions

HD helped perform manuscript writing and literature review. IF helped perform manuscript writing and literature review. ML was the Allergy consultant for the patients whose cases are reported and helped with manuscript

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Not applicable

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