

Successful rapid oral clindamycin desensitization in a pediatric patient

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Clinical Implications

- Rapid oral desensitization to clindamycin was safely achieved in a pediatric patient with clindamycin clinical hypersensitivity and positive skin testing.

TO THE EDITOR:

Clindamycin is a lincosamide antibiotic commonly used as an alternative to beta-lactams for preoperative prophylaxis and to treat a variety of infections.¹ Hypersensitivity to clindamycin is rare, with an incidence of 0.4% of 3462 patients in one review.² Three cases of anaphylaxis to clindamycin,³ but no cases of rapid desensitization to clindamycin have been reported. We describe a successful rapid oral desensitization to clindamycin in a pediatric patient.

An 8-year-old girl presented with recurrent distal humeral osteomyelitis. She was empirically treated with intravenous (IV) ceftriaxone and vancomycin. After bone cultures grew methicillin-sensitive *Staphylococcus aureus*, her antimicrobial therapy was changed to IV cefazolin. Although she had no prior history of urticaria, 8 days later, she developed diffuse urticarial rash, vaginal itching, labial swelling, and extremity swelling. Cefazolin was discontinued; her symptoms improved but did not resolve completely. Thirty-five hours after her last cefazolin dose, she was started on oral clindamycin, which was considered a safe choice given no prior history of use. One hour after the first dose, she developed subjective throat tightness and worsening urticarial rash, possibly secondary to the clindamycin-induced anaphylactoid reaction versus worsening cefazolin reaction. Clindamycin was discontinued immediately. Over the next 48 hours, she developed lip swelling, urticarial rash, joint pain, and extremity swelling. Her rash had no vasculitic qualities; she had no joint effusions or renal symptoms. Seventy-two hours after clindamycin was discontinued, her symptoms improved. Antimicrobial therapy with doxycycline was initiated. Four days later, she developed nausea, emesis, and maculopapular rash. Doxycycline was discontinued, and she was referred for urgent allergy evaluation.

Because of recent antihistamine use, skin testing could not be performed immediately. As clindamycin was the preferred oral agent and clinical history alone was insufficient to establish hypersensitivity, the patient underwent a 3-step graded, oral challenge to clindamycin. She tolerated the first dose (1/100th full therapeutic dose [FTD]). Three minutes after the second dose (1/10th FTD), she developed diffuse urticaria consistent with immediate-type hypersensitivity that developed after the initial dose of clindamycin. Given the urgent need to restart therapy, the decision was made to pursue rapid clindamycin

TABLE I. Skin testing protocol for clindamycin

Skin prick testing (SPT)*	Testing results (wheal/flare)
Clindamycin 15 mg/mL	Negative
Histamine 10 mg/mL	9 mm/30 mm
Normal saline	Negative
Intradermal testing (IDT)†	Testing results (wheal/flare)
Step 1: Clindamycin 0.15 mg/mL‡	N/A
Normal saline	Negative
Step 2: Clindamycin 1.5 mg/mL	Negative
Step 3: Clindamycin 15 mg/mL	7 mm/20 mm

*If negative for SPT, proceed to IDT.

†If negative for each step, proceed to the successive step.

‡Optional step depending on severity of reaction history.

desensitization. The patient later underwent skin testing (Table I) 8 weeks after completing desensitization to clindamycin. Skin prick testing (SPT) was negative, but intradermal testing (IDT) at a nonirritating concentration⁴ (15 mg/mL) was positive (7 mm wheal, 20 mm flare), consistent with clindamycin hypersensitivity.

As shown in Table II, we performed a 9-step rapid oral desensitization to clindamycin. The goal dose was 33 mg/kg/day divided Q8hours (300 mg/dose). Cetirizine 10 mg premedication was given orally 1 hour before desensitization. She tolerated the desensitization and received multiple doses of clindamycin under inpatient observation. She was discharged home on clindamycin, cetirizine daily, and ranitidine Q12hours. At home, she developed urticarial rash and throat tightness 15 minutes after taking the next clindamycin dose. The following dose was observed in a local emergency department. Despite premedication with cetirizine and montelukast, she developed urticaria and throat tightness within 15 minutes. She was readmitted to our institution for adjustments to her premedication regimen. She subsequently tolerated clindamycin without symptoms on the following premedication regimen: cetirizine 10 mg Q8hours (60 minutes before each dose), montelukast 5 mg daily (60 minutes before evening dose), and ranitidine 60 mg Q12hours (4 hours before afternoon dose, 60 minutes before evening dose). After discharge home, she completed 4 weeks of oral clindamycin therapy with no further allergic symptoms and resolution of her osteomyelitis.

Drug desensitization induces temporary tolerance to a drug and can enable patients with hypersensitivity reactions to receive potentially life-saving therapies.⁵ Two successful multiday desensitizations for oral clindamycin in adults have been reported.^{6,7} Marcos et al⁶ described a 35-year-old woman who developed delayed generalized cutaneous eruption with clindamycin, and successfully underwent a 7-day desensitization to oral clindamycin. Martin et al⁷ reported a patient who developed rash after 5 days of clindamycin treatment, who also tolerated oral clindamycin after dose escalation over 7 days. Our patient's urgent clinical status necessitated rapid desensitization over hours rather than days; thus, we developed a rapid oral desensitization protocol for clindamycin for a cumulative dose of 11 mg/kg/dose

TABLE II. Rapid oral desensitization protocol for clindamycin

Step	Total time (min)	Concentration (mg/mL)	Volume (mL)	Dose (mg)	Cumulative dose (mg)
1	0	0.02	0.25	0.005	0.005
2	30	0.02	2.5	0.05	0.055
3	60	0.2	2.5	0.5	0.56
4	90	2.0	2.5	5.0	5.56
5	120	20.0	0.5	10.0	15.6
6	150	20.0	1.0	20.0	35.6
7	180	20.0	2.0	40.0	75.6
8	210	20.0	4.0	80.0	156.0
9	240	Capsule	N/A	150.0	306.0

(=300 mg/dose). After initial desensitization, the same dose was subsequently administered every 8 hours. This dosing regimen could be extrapolated to other pediatric patients requiring weight-based dosing, or to standard adult dosing dependent on clinical indication. We preferred oral desensitization for our patient, but because oral and IV bioavailability of clindamycin approach near-equivalence, this protocol could potentially be adapted for desensitization to IV clindamycin.

Ultimately, our patient required a premedication regimen including cetirizine, montelukast, and ranitidine, to complete her clindamycin therapy. Future patients requiring rapid clindamycin desensitization may benefit from initiation of this extensive premedication regimen before desensitization.

In our patient's case, both skin testing and oral challenge confirmed her clindamycin hypersensitivity, likely occurring after her first exposure to clindamycin. In one study, 31 patients with a history of possible clindamycin reactions had negative SPT and IDT to clindamycin; yet 10 patients (32%) reacted to oral challenge.⁸ In another study, 33 patients evaluated for clindamycin allergy had negative SPT on initial read; 15% had positive skin prick/patch testing after 2 to 4 days.⁹ Of those with negative testing, 6 of the 26 patients who underwent oral challenge to clindamycin had convincing reactions.⁹ Thus, cutaneous reactions to clindamycin with negative SPT and IDT may represent a more common delayed-type of clindamycin reaction or histamine-releasing activity in an anaphylactoid nature.

Seitz et al⁹ discussed that skin testing alone for evaluation of clindamycin hypersensitivity is not sufficient and that oral challenge testing should be considered. Based on these reports and on our experience, even in cases of immediate-type hypersensitivity, negative SPT does not exclude clinical reactivity to clindamycin. Complete evaluation of immediate-type clindamycin hypersensitivity may require both SPT and IDT at 15 mg/mL followed by oral challenge.

In summary, we present a patient with hypersensitivity reaction to clindamycin with positive intradermal skin testing and symptoms of immediate-type reaction during a graded oral challenge, who successfully tolerated rapid oral desensitization and a full therapeutic course with oral premedications. Our experience provides a platform for future rapid oral desensitizations to clindamycin.

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REFERENCES

- Smieja M. Current indications for the use of clindamycin: a critical review. *Can J Infect Dis* 1998;9:22-8.
- Mazur N, Greenberger PA, Regalado J. Clindamycin hypersensitivity appears to be rare. *Ann Allergy Asthma Immunol* 1999;82:443-5.
- Bullock MN, Baccas JT, Arnold S. Clindamycin-induced hypersensitivity reaction. *Infection* 2016;44:357-9.
- Empedrad R, Darter AL, Earl HS, Gruchalla RS. Nonirritating intradermal skin test concentrations for commonly prescribed antibiotics. *J Allergy Clin Immunol* 2003;112:629-30.
- del Carmen Sancho M, Breslow R, Sloane D, Castells M. Desensitization for hypersensitivity reactions to medications. *Chem Immunol Allergy* 2012;97:217-33.
- Marcos C, Sopena B, Luna I, Gonzalez R, de la Fuente J, Martinez-Vazquez C. Clindamycin desensitization in an AIDS patient. *Aids* 1995;9:1201-2.
- Martin JA, Alonso MD, Navas E, Antela A. Clindamycin desensitization in a patient with the acquired immunodeficiency syndrome [in Spanish]. *Med Clin (Barc)* 1992;98:478-9.
- Notman MJ, Phillips EJ, Knowles SR, Weber EA, Shear NH. Clindamycin skin testing has limited diagnostic potential. *Contact Dermatitis* 2005;53:335-8.
- Seitz CS, Brocker EB, Trautmann A. Allergy diagnostic testing in clindamycin-induced skin reactions. *Int Arch Allergy Immunol* 2009;149:246-50.