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# Clindamycin hypersensitivity appears to be rare

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**Background:** A patient developed a generalized confluent erythematous papular rash after a single injection of clindamycin preoperatively. The literature from two small studies suggested a 10% incidence of cutaneous eruptions to clindamycin which seemed too high.

**Objective:** Describe a patient with clindamycin hypersensitivity and determine the incidence of hospital-wide adverse drug reactions from clindamycin from 1995–1997.

**Methods:** At a tertiary care center, utilizing the Department of Pharmacy records, the incidence of adverse drug reactions was determined with (1) voluntary physician reporting, (2) Health Information Management chart reviews and adverse drug reaction coding, and (3) chart reviews by the Pharmacy and Therapeutics Committee of adverse drug reactions.

**Results:** (1) A 50-year-old patient developed a generalized raised, erythematous rash that worsened over 3.5 days until hydrocortisone was administered. Immediate skin tests with clindamycin were negative. (2) From 3,896 administrations of clindamycin from April 1995 to October 1997, 14 (0.47%) adverse drug reactions occurred but 7 were confounded by other medications also being administered.

**Conclusion:** (1) Adverse drug reactions to clindamycin are much lower than reported 25 years ago with an incidence <1%. (2) A patient who previously had experienced facial edema and a generalized rash after receiving clindamycin and a cephalosporin 6 years ago and who was considered allergic to cephalosporins, was found to be clindamycin allergic when she received a preoperative dose of clindamycin.

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## INTRODUCTION

Clindamycin was first synthesized in 1966. It is a chemical derivative of lincomycin with activity against aerobic gram positive and anaerobic gram positive and gram negative bacteria.<sup>1</sup> Clindamycin binds exclusively to the 50s subunit of bacterial ribosomes and suppresses intracellular protein synthesis.<sup>2</sup> Side effects include diarrhea, pseudomembranous colitis, metallic taste in mouth, transient elevation of

transaminases, granulocytopenia, thrombocytopenia and a rash.<sup>2</sup>

The incidence of maculopapular skin rashes has been reported to be approximately 10%.<sup>2</sup> In 1970, Geddes et al attributed the rash to residual impurities from the manufacturing process.<sup>3</sup> They reported that the maculopapular and pruritic eruptions appeared at the end of the first or during the second week of therapy in 5 of 50 (10%) patients.<sup>3</sup> In a series in 1973, 2 of 19 (10.5%) patients treated with clindamycin developed generalized but not specified rashes.<sup>4</sup> The reactions were not considered serious but did necessitate stopping clindamycin.

We report a case of a severe erythematous rash developing within 24 hours after clindamycin administration that responded to intravenous steroids.

## CASE REPORT

A 50-year-old woman had an rhytidectomy and was treated preoperatively

with clindamycin for endocarditis prophylaxis because of mitral regurgitation. Approximately 12 hours after the clindamycin administration, she noted a mildly pruritic, erythematous, macular, papular rash on her abdomen with a few red lesions on her arms. She had not received other medications preoperatively. The following day despite administration of diphenhydramine, the rash progressed to the back and arms and became intensely pruritic. Four days after clindamycin had been administered and 3½ days after onset of the cutaneous eruption, the patient had diffuse confluent erythema on her abdomen, breasts, arms, neck, face, and back. There were no bullae or urticarial lesions. No evidence of mucosal involvement or organomegaly was evident. She received intravenous hydrocortisone 100 mg daily for 2 days, then prednisone 40 mg orally for 2 days followed by a tapering dose. The diffuse intense erythema began subsiding only after 2 days of intravenous hydrocortisone.

One month later she underwent skin prick and intradermal tests with clindamycin, which were found to be negative with 1 mg/mL for the prick testing and 0.1 mg intradermal dosage. Her previous medical history was significant for mitral regurgitation. As a child the patient had a “rash” following penicillin administration. Following a cholecystectomy 6 years ago she was treated with clindamycin and a cephalosporin which resulted in facial swelling and a severe rash. Our service had conducted penicillin skin prick and intradermal testing to Prepen (Schwarz Pharma, Milwaukee, WI) and the minor determinants, benzylpenicilloate, benzylpenicilloyl-n-propylamine, and penicillin G (6,000 units/mL). These skin tests were negative and the patient tolerated a test challenge of amoxicillin 3 mg and full dose 250 mg without any allergic manifestations.

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## METHODS

Hospital-wide adverse reactions were found through the Adverse Drug Reaction Review Program that is conducted through the Pharmacy and Therapeutic Drug Committee in conjunction with the Department of Pharmacy. In addition to voluntary reporting of adverse drug reactions, the Adverse Drug Reaction Review Program includes all cases that are identified by the Health Information Management staff and coded with adverse reactions. All charts coded with adverse drug reactions were reviewed by members of the Pharmacy and Therapeutic Subcommittee. Specific charts were reviewed for the temporal relationship between the clindamycin and the adverse reaction by designated pharmacists with assistance from physicians on the Pharmacy and Therapeutic Drug Committee.

## RESULTS

Utilizing Department of Pharmacy records at Northwestern Memorial Hospital, 3,462 patients were treated

with clindamycin consisting of 3,896 administrations from April 1995 until October 1997. During this time period, 14 (0.4%) adverse reactions were found but 7 were confounded by concurrent administration of other medications. In Table 1, the specific reactions listed with clindamycin are presented. There were no cases of toxic epidermal necrolysis or Stevens-Johnson Syndrome.

## DISCUSSION

A literature review for hypersensitivity reactions to clindamycin over the years 1969 to 1997 was carried out. In 1973, a case of Stevens-Johnson syndrome associated with clindamycin occurred on day 14 of therapy.<sup>5</sup> The patient developed multiple cutaneous round, raised lesions covering the trunk and extremities with oropharyngeal and ocular involvement. The conjunctivae were edematous and hemorrhagic. The oropharynx had multiple white areas on the mucosa and striking erythema of the surrounding mucous membrane.<sup>5</sup> The patient was treated with

prednisone 60 mg daily for 6 days and then weaned over 3 weeks.<sup>5</sup> In a series of 90 consecutive cases of toxic epidermal necrolysis accumulated from 1985–1991, clindamycin was suspected in 3 cases.<sup>6</sup> In 1991, Vidal et al reported a patient who developed a generalized maculopapular pruritic eruption accompanied by palpebral and lip edema following treatment with clindamycin 600 mg intravenously four times a day for 27 days.<sup>7</sup> After discontinuation of clindamycin, the patient was treated with high dose corticosteroids with resolution of the rash in 7 days. Two months later immediate prick tests to clindamycin were negative. Six hours after challenge with clindamycin 300 mg intravenously, the patient developed facial edema, generalized erythema and a maculopapular rash.<sup>7</sup> Corticosteroids and antihistamines were required to control the reaction.

In 1993, Segars et al reported a patient without a previous exposure to clindamycin, who within five minutes of receiving clindamycin 600 mg intra-

Table 1. Tabulation of Adverse Drug Reactions Probably or Possibly Related to Clindamycin Administration, 1995–1997

| Patient                                        | Effects to Skin                                                                                                                                                                 | GI Upset/Nausea         |
|------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Probable adverse drug reactions to clindamycin |                                                                                                                                                                                 |                         |
| 1                                              | Drug rash-unknown improvement due to drug change                                                                                                                                |                         |
| 2                                              | Erythematous macules/papules-resolved after clindamycin discontinued                                                                                                            |                         |
| 3                                              | Blanching erythema                                                                                                                                                              |                         |
| 4                                              | Rash and elevated temperature                                                                                                                                                   |                         |
| 5                                              | Erythema on chest, arms, and back with shaking; chills and elevated temperature                                                                                                 |                         |
| 6                                              |                                                                                                                                                                                 | Diarrhea                |
| 7                                              |                                                                                                                                                                                 | Constipation and nausea |
| Possible adverse drug reactions to clindamycin |                                                                                                                                                                                 |                         |
| 8                                              | Ciprofloxacin-Rash on trunk, improvement unknown after both drugs were discontinued                                                                                             |                         |
| 9                                              | Ciprofloxacin and gentamicin-Skin rash. Rash resolved after discontinuation of all drugs                                                                                        |                         |
| 10                                             | Primaquine-Rash within 24 hours. Rash resolved after discontinuation of both drugs                                                                                              |                         |
| 11                                             | Hydrocodone and aztreonam-Erythematous, maculopapular rash on trunk and extremities                                                                                             |                         |
| 12                                             | Trimethoprim-sulfamethoxazole-Diffuse skin rash. Symptom improvement after both drugs were discontinued                                                                         |                         |
| 13*                                            | Allopurinol-Red macular rash on neck, back, arms, thighs, chest and multiple follicle based white papules at nape of neck. Symptoms resolved after both drugs were discontinued |                         |
| 14                                             | Phenytoin-Skin rash. Symptoms resolved after both drugs were discontinued                                                                                                       |                         |

\* Patient was admitted twice with two ADRs. During the second admission, patient was treated with clindamycin only.

venously developed lip and nasal passage swelling. After approximately 20 minutes his lips were extremely swollen and nasal passages closed off secondary to swelling. He was not re-challenged nor skin tested with clindamycin.<sup>8</sup>

In 1995 Marcos et al reported a patient who experienced a generalized cutaneous eruption during day 12 of clindamycin administration which resolved after its discontinuation.<sup>9</sup> The patient underwent single-blind placebo controlled oral challenge with progressively increasing doses of clindamycin. The starting dose was 60 mg which was increased twofold at 3-hour intervals until the therapeutic dose 600 mg was reached. Four hours after the second dose of 600 mg the patient developed a morbilliform-pruritic rash on the trunk and thighs. Skin prick tests as well as intradermal skin testing with clindamycin 150 mg/mL were negative. The patient was subsequently desensitized successfully with clindamycin.<sup>9</sup>

Our case is similar to two of the cases in the literature in that the patients had negative immediate skin tests to clindamycin. Further, the cutaneous eruption and facial swelling that had occurred 6 years previously after receiving a cephalosporin and

clindamycin likely was attributable to clindamycin.

Early reports suggested that patients treated with clindamycin have a 10% risk for developing a rash.<sup>2</sup> The experience during a 2½-year period at this institution determined that the incidence of adverse drug reactions to clindamycin was only 0.4% or perhaps lower. We conclude that severe hypersensitivity reactions to clindamycin appear to be rare but do occur. Despite earlier reports of skin rashes, the mechanism is not known. We were not able to find any cases in the literature where IgE antibodies were detected or immediate skin tests were positive.

In summary, this case involved a patient with a previous diagnosis of cephalosporin allergy but readministration of clindamycin elicited the hypersensitivity reaction that occurred in the absence of other medications and with absence of immediate skin reactivity. It is likely that the earlier facial edema and generalized rash was attributable to clindamycin and not the cephalosporin. Nevertheless, adverse drug reactions to clindamycin appear to be uncommon.

## REFERENCES

1. Dhawan VK, Thadepalli H. Clindamycin: a review of fifteen years of experience. *Rev Infect Dis* 1982;4: 1133–1143.
2. Klainer A. Clindamycin. *Med Clin North Am* 1987;71:1169–1174.
3. Geddes AM, Bridgwater FA, Williams DN, et al. Clinical and bacteriological studies with clindamycin. *Br Med J* 1970;2:703–704.
4. Fass RJ, Scholand JF, Hodges GR, et al. Clindamycin in the treatment of serious anaerobic infections. *Ann Intern Med* 1973;78:853–859.
5. Fulghum DD, Catalano PM. Stevens-Johnson syndrome from clindamycin. *JAMA* 1973;223:318–319.
6. Correia O, Chosidow O, Saiag P, et al. Evolving pattern of drug induced toxic epidermal necrolysis. *Dermatol* 1993; 186:32–37.
7. Vidal C, Iglesias A, Saez A, et al. Hypersensitivity to clindamycin. (letter) *DICP Ann Pharmacother* 1991;25: 317.
8. Segars LW, Threlkeld KR. Clindamycin induced lip and nasal passage swelling. *Ann Pharmacother* 1993;27: 885–886.
9. Marcos C, Sopena B, Luna I, et al. Clindamycin desensitization in an AIDS patient. *AIDS* 1995;9: 1201–1202.

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