

## Cimetidine Treatment of Recalcitrant Acute Allergic Urticaria

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Received for publication November 11,  
1985. Accepted for publication  
January 15, 1986.

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*Cimetidine, an H-2-receptor-blocking antihistamine, was used in the treatment of five consecutive patients who developed acute allergic urticaria in response to insect stings. All five had persistent hives after treatment with at least epinephrine and diphenhydramine (Benadryl®, an H-1 receptor blocker). All also had been given corticosteroids. Each patient responded dramatically within 15 minutes to one IV infusion of 300 mg cimetidine. All were discharged on oral cimetidine (300 mg every six hours) and reported no recurrences or exacerbations of urticaria on follow up. There were no complications. Cimetidine may be effective in patients with recalcitrant acute allergic urticaria who are already being treated with H-1-receptor-blocking antihistamines. Controlled clinical trials should be done to confirm the efficacy of cimetidine for treatment of acute allergic reactions. [Rusli M: Cimetidine treatment of recalcitrant acute allergic urticaria. Ann Emerg Med November 1986;15:1363-1365.]*

### INTRODUCTION

H-1-receptor-blocking antihistamines have been commonly used for treating acute allergic urticaria. However, it is now widely accepted that human skin vasculature contains both H-1 and H-2 receptors.<sup>1-5</sup> H-2 receptor blockers such as cimetidine have been studied extensively in chronic idiopathic urticaria,<sup>6-12</sup> and also have been used for dermographism, systemic mastocytosis, eosinophilic fasciitis, psoriasis, cold-induced urticaria, atopic dermatitis, and the blocking of the cutaneous flushing response to IV histamine infusion.<sup>13-19</sup> There have been isolated case reports of cimetidine dramatically reversing anaphylactic reactions to radiographic contrast media in patients already pretreated with corticosteroids and diphenhydramine (H-1 blocker).<sup>20,21</sup>

There are no known studies of cimetidine in the treatment of acute allergic urticaria, a condition commonly seen in the emergency department. We present the cases of five consecutive patients with acute allergic urticaria (from insect stings) recalcitrant to treatment by epinephrine, diphenhydramine and, in some cases, corticosteroids, who were then treated with cimetidine. All had dramatic responses typified by rapid disappearance of hives within minutes of cimetidine infusion. None showed any recurrence or exacerbation of hives after discharge on oral cimetidine.

### CASE REPORTS

#### Case One

A 32-year-old woman presented for the third time since being stung by a bee 32 hours earlier. She had developed persistent generalized urticaria since the bee sting. On her previous two visits, she had been given diphenhydramine, epinephrine, and dexamethasone with only marginal improvement. After discharge, she had taken diphenhydramine 50 mg every six hours without further improvement.

On this visit, she had pruritic urticarial lesions to both arms, thighs, low back, and anterior neck and abdomen. Her vital signs were as follows: blood pressure, 110/60 mm Hg; pulse, 72; temperature, 37.3 C; and respirations, 18. Cimetidine 300 mg was given IV over 15 minutes. The urticarial rash and itching virtually disappeared within 15 minutes after the infusion. No other medications were given and there were no complications. The patient was

discharged on cimetidine 300 mg orally every six hours for three days and no other medications. On follow up six weeks later she reported no further recurrence of rash or symptoms.

#### Case Two

A 25-year-old man presented for the second time five hours after he suffered multiple bee stings. He had been stung on the thighs and arms, and within five minutes developed generalized erythema and itching. He presented for the first time with these findings. His blood pressure was 144/96 mm Hg and the pulse was 140. There was no respiratory problem or angioedema. He was treated with epinephrine 0.4 mg subcutaneously, plus diphenhydramine 25 mg and dexamethasone 8 mg, both intramuscularly. After 30 minutes, he had shown marked improvement of symptoms, fading of the erythema, and normalization of vital signs.

Four and a half hours after discharge the patient developed a pruritic urticarial rash and returned to the ED. On this visit, he had clear-cut, generalized urticarial lesions concentrated mostly on the extremities. Vital signs were as follows: blood pressure, 150/80 mm Hg; pulse, 100; temperature, 37.4 C; and respirations, 24. Cimetidine 300 mg was given IV over ten minutes. The urticarial rash and itching disappeared completely within 15 minutes after the infusion was completed. There were no complications. The patient was discharged on oral cimetidine 300 mg every six hours and oral diphenhydramine 50 mg every six hours for four days. On follow up three weeks later, the patient reported no further recurrence of rash or symptoms.

#### Case Three

A 16-year-old boy presented with acute generalized pruritic urticaria

that developed 20 minutes after he received multiple bee stings to his right cheek. His blood pressure was 128/86 mm Hg, the pulse was 116, and respirations were 24. He had local swelling at the sting site and generalized pruritic urticaria mainly above the waist. There was no respiratory problem. The patient received two subcutaneous injections of epinephrine 0.4 mg 30 minutes apart. He also received diphenhydramine 50 mg and dexamethasone 8 mg, both IM.

During the next hour, his truncal urticaria improved, but he had persistent facial urticaria. His pulse normalized to 80. Cimetidine 300 mg was given IV over 20 minutes. By the end of the infusion, there was complete resolution of rash and symptoms. The patient was discharged on oral cimetidine 300 mg every 12 hours and Decadron Dose Pack.<sup>®</sup> On follow up one week later, the patient reported no recurrence of rash or symptoms.

#### Case Four

A 30-year-old man presented for the third time in 25 hours with recurrent urticaria after being stung by a wasp. He had developed acute allergic urticaria five to ten minutes after being stung once on the leg. On the first visit, he had manifested generalized, sparse, pruritic urticarial lesions. His vital signs were as follows: blood pressure, 122/80 mm Hg; pulse, 80; respirations, 24; and temperature, 35.4 C. He was given epinephrine 0.3 mg subcutaneously twice; diphenhydramine, 25 mg IM; and dexamethasone, 8 mg IM. His symptoms and rash improved significantly and he was discharged on diphenhydramine 25 mg every six hours orally.

The patient returned for a second visit 12 hours later with recurrence of urticaria. Generalized, sparse, small lesions were noted. The patient was given dexamethasone 8 mg IM and

discharged on Medrol Dose Pack<sup>®</sup> and diphenhydramine 25 mg every six hours orally.

Twenty-five hours after the first visit, he returned with worsening generalized urticaria and pruritis while taking the prescribed medications. The rash and itching had worsened 30 minutes after each dose of diphenhydramine despite having doubled the dosage to 50 mg every six hours. The patient's hives had appeared much worse than on his previous two visits. Epinephrine 0.3 mg SQ and hydroxyzine 50 mg IM were given. There was no appreciable response after 30 minutes. Cimetidine 300 mg IV was administered over 15 minutes. There was dramatic disappearance of the hives and pruritis within minutes after the infusion. There were no complications from the cimetidine. The patient was discharged on cimetidine 400 mg by mouth every eight hours for ten days. On follow up three weeks later he reported that he developed urticarial lesions to his hands and feet only, which have gradually cleared while on oral corticosteroids.

#### Case Five

A 16-year-old man presented with recurrent generalized urticaria after being stung by bees the day before. Shortly after being stung, he was treated by his family physician with epinephrine, diphenhydramine, and dexamethasone (dosage and route uncertain). He presented one day later with pruritic urticaria to his groin, legs, arms, and chest while taking oral diphenhydramine and dexamethasone. He had the following vital signs: blood pressure, 144/62 mm Hg; pulse, 60; temperature, 37 C; and respirations, 16.

Cimetidine 300 mg was given IV over 20 minutes. The urticaria and pruritis disappeared completely within minutes after the infusion ended.

No other medications were given. There were no complications. The patient was discharged on cimetidine 300 mg three times daily by mouth for seven days. On follow up two weeks later no recurrence of urticaria or pruritis was reported.

## DISCUSSION

The use of H-2 receptor blockers in treating chronic idiopathic urticaria has been reported.<sup>6-12</sup> The results of double-blind trials comparing H-1 and H-2 receptor blockers combined and H-1 receptor blockers alone<sup>6,7,10,12</sup> have favored the former. There also have been case reports showing dramatic improvement in patients with chronic idiopathic urticaria given the H-1 plus H-2 blocker regimen over those given H-1 blockers alone.<sup>8,9,11</sup>

With a growing body of evidence<sup>1-5</sup> pointing to the presence of H-2 as well as H-1 histamine receptors in skin blood vessels, it is surprising to find such a lack of reports in the medical literature concerning the use of H-2 receptor blockers in the treatment of acute allergic urticaria and acute allergic reactions in general. Myers<sup>20</sup> reported the case of a patient with a known previous severe reaction to radiologic contrast material who developed an acute generalized allergic reaction to dye despite having been premedicated for four days with prednisone and diphenhydramine. The reaction, characterized by generalized urticaria, wheezing, and laryngeal edema, was reversed rapidly by cimetidine 300 mg IV.

Similar findings have been reported by others.<sup>21</sup> Tryba<sup>19</sup> reported, in a double-blind placebo-controlled study, that H-1 and H-2 receptor blockers combined blocked completely the cardiovascular and cutaneous flushing reactions from IV histamine infusion, whereas an H-1 receptor blocker alone only partially blunted these responses.

## SUMMARY

With this background in mind, cimetidine seems to be the natural therapeutic agent to try in patients with acute allergic urticaria recalcitrant to conventional therapy (epinephrine, H-1 receptor blockers, and corticosteroids). The low complication

rate of short-term cimetidine therapy<sup>22</sup> adds to the attractiveness of this drug. Each of the five patients responded dramatically to an IV infusion of 300 mg cimetidine. Given the probable commonality of mechanism in acute allergic urticaria from all precipitating causes, it is reasonable to assume that cimetidine may have therapeutic value in all types of acute allergic urticarial reactions. In addition, for patients with significant cardiovascular diseases who develop severe allergic reactions, cimetidine might be used (in conjunction with an H-1 receptor blocker) in place of epinephrine. Controlled studies should be carried out to validate scientifically the preliminary conclusions suggested by this case series.

The author thanks the emergency physicians of the Chester County Hospital for their kind cooperation.

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