Cimetidine: A useful drug for treatment of anaphylaxis
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This case report describes an anaphylactic reaction to intravenous contrast media in which the administration of cimetidine appeared to be beneficial. The presumed mechanism of the action of cimetidine is discussed and recommendations for its use are made.

Anaphylaxis is a mild or severe symptom complex which may involve any organ system and has a variable course. IgE-mediated release of vasoactive substances which precipitate the clinical manifestations is the presumed mechanism. Of these vasoactive substances, histamine is felt to play a primary role. Traditional therapy of anaphylaxis has involved the use of adrenergic agents, methylxanthines, corticosteroids, and antihistamines.

Case report
A 42-year-old male patient with a history of urinary outflow tract obstruction was scheduled for an intravenous pyelogram (IVP) examination. There had been no adverse reaction to an IVP performed several years earlier. A history of seafood intolerance as denoted by nausea and vomiting was obtained at this time.

Immediately following the injection of 21 cc of iothalamate meglumine (Conray® 60) the patient complained of nausea, shortness of breath and back pain. Labored respirations were also evident and peripheral cyanosis developed over a two minute period. There was no evidence of wheezing. A cardiac monitor was applied and showed a sinus tachycardia at a rate of 134/min. A brachial pulse was barely palpable and blood pressure was unobtainable.

The patient quickly developed an erythematous coloration and became combative. He was placed in a Trendelenburg position and resuscitation was begun with 100% oxygen administered via an Ambu® bag and mask. A subclavian line was inserted, through which 100 mg diphenhydramine, 500 mg cortisol and 2 ampules (88 mEq) sodium bicarbonate were given. Epinephrine (2 mg in 250 cc N/S) was begun per IVAC mini-drip. Pulse remained 130-140/min and a blood pressure of 70/40 mm Hg was obtained. The cyanotic coloration, dyspnea, nausea and combative behavior persisted.

For the next 15 minutes ventilation was assisted and blood pressure remained 70/40 mm Hg. As no significant response to this pharmacological regimen was apparent, cimetidine, 600 mg was given via the subclavian line. Over the next 3.5 minutes the cyanosis completely resolved. Blood pressure increased to 110/70 mm Hg, pulse rate decreased to 110/min, and the epinephrine infusion was discontinued. The dyspnea, nausea and back pain had resolved, and the patient was alert.

The patient was admitted to the recovery room for a period of observation, during which time his pulse and blood pressure remained stable.
Two days later he underwent a transurethral resection of the prostate under spinal anesthesia without difficulty.

Discussion

Systemic anaphylaxis is a presumed hypersensitivity reaction which, when severe, can cause death within minutes. The syndrome consists of a highly variable symptom complex including at least some of the following: conjunctivitis, vasoconstriction, rhinitis, pilomotor erection, pruritic urticaria, angioedema, gastrointestinal disturbances, laryngeal edema, bronchospasm, hypotension, and cardiac arrhythmias. In fatal anaphylaxis the disturbances of the cardiovascular and respiratory systems predominate and occur rapidly.\(^1\)

An immunologic mechanism has been proposed as the basis for anaphylactic reactions.\(^2,3\) It is felt that an individual exposed to an antigen forms specific IgE antibodies that fix to the surface of most cells and basophils. Subsequent exposure to the antigen, which results in the bridging of two IgE molecules on the surface of the mast cell, results in loss of histamine from mast cell granules and slow reacting substance of anaphylaxis (SRS-A) from unknown sources. Release of other vasoactive substances, such as bradykinin and serotonin, probably plays a role as well. The physiologic effects of bradykinin and serotonin result in the variable clinical manifestations just described. The traditional pharmacologic treatment of anaphylaxis has involved the use of (1) adrenergic agents, (2) methyldxanthines, (3) corticosteroids, and (4) antihistamines. Detailed reviews of their use can be found in several sources.\(^2,3\)

Since histamine is thought to be a major mediator of anaphylaxis in man, knowledge of its actions is important in treating this syndrome. The predominant effect of endogenous histamine release in man is a generalized dilatation of terminal arterioles which may lead to profound hypotension.\(^4\) Other important effects include bronchial constriction and increased capillary permeability.

The effects of histamine are believed to be due to its effects on two types of receptors, H\(^1\) and H\(^2\).\(^5\) Although these receptors have not been identified by physical or chemical methods, they can be pharmacologically classified by means of antagonists. Antihistamines such as diphenhydramine have been shown to be antagonists to the contractions of the gut and bronchi produced by histamine; thus these contractions are said to be produced by the action of histamine on H\(^1\) receptor sites.

Cimetidine has been shown to antagonize the production of gastric acid produced by histamine; the acid production is said to be due to the action of histamine on the H\(^2\) receptor sites. The contribution of the H\(^1\) and H\(^2\) receptors to terminal arterioles and the hemodynamic effects of histamine is not precisely known. However, there is experimental work that indicates that both receptors are involved.\(^6\)

Philbin et al.\(^7\) have recently studied the use of H\(^1\) and H\(^2\) blocking drugs in attenuating the hemodynamic effects of morphine, a drug that causes the release of histamine. They found that the administration of high doses of morphine to cardiac surgical patients resulted in significant increases in histamine levels and lowering of systemic vascular resistance and diastolic blood pressure. The prior administration of either diphenhydramine or cimetidine provided minimal hemodynamic protection. Patients who received morphine and both antagonists demonstrated significant attenuation of hemodynamic responses, although plasma histamine levels showed a comparable increase. The researchers concluded that the adverse hemodynamic effects of histamine release caused by morphine could be protected against by the use of the combination of H\(^1\) and H\(^2\) antagonists.

The previously recommended use of antihistamines in the treatment of anaphylaxis has involved only H\(^1\) antagonists.\(^2,3\) Theoretically, and based upon Philbin's study,\(^7\) H\(^2\) antagonists would be beneficial as well. The patient in the case study received a dose of steroids, diphenhydramine, and epinephrine: anaphylactic treatment that is well accepted.\(^2,3\) Methylxanthines were not given because wheezing did not occur and gas exchange appeared to be adequate. However, hypotension and other signs of histamine effect (erythema, flushing) persisted. The administration of cimetidine, an H\(^2\) blocker, resulted in the prompt resolution of erythema and hypotension and allowed discontinuation of epinephrine. Thus it appeared to be beneficial in reversing the effects of a contrast media-induced allergic reaction.

In summary, the case study presented in this article describes an anaphylactic reaction in which the use of conventional agents was only partially successful in restoring hemodynamic stability. The addition of cimetidine, an H\(^2\) antagonist, appeared to restore a normal blood pressure and allow discontinuation of pharmacologic pressor support. It is suggested that cimetidine be available for use in areas where anaphylactic reactions might be encountered and used when conventional therapy is not successful. Finally, the use of cimetidine in treating anaphylaxis clearly deserves further study.
REFERENCES

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ACKNOWLEDGEMENT
The author gratefully acknowledges Dr. David Alfery for his advice, help, and inspiration in the preparation of this article and in the practice of anesthesia.