

Paracetamol (acetaminophen) hypersensitivity

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Background: Paracetamol (acetaminophen) intolerance can occur in less than 5% of aspirin-sensitive subjects as a result of inhibition of prostaglandin synthesis but hypersensitivity to paracetamol without aspirin sensitivity is rare.

Methods: We report a case of an acute life-threatening hypersensitivity reaction to paracetamol.

Results: An oral challenge with 125 mg of paracetamol was carried out and followed by generalized anaphylactic reaction. An oral provocation test with 500 mg aspirin was well tolerated in the patient.

Conclusion: An acute hypersensitivity reaction to paracetamol is described in this study. The results of the study suggest a real allergic mechanism rather than inhibition of prostaglandin synthesis as responsible.

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INTRODUCTION

Paracetamol (acetaminophen) and aspirin are probably the most commonly used analgesic-antipyretic drugs. Aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs) may induce urticaria and angioedema, rhinitis, bronchial asthma, and anaphylactoid reactions in susceptible subjects.¹ The mechanism of this aspirin sensitivity is not completely understood but inhibition of prostaglandin synthesis has been proposed since both aspirin and NSAIDs shared this pharmacologic effect.² Paracetamol is a weak inhibitor of cyclooxygenase and as a result less than 5% of aspirin-sensitive subjects react to paracetamol on provocation tests.³ For that reason, paracetamol is generally considered a safe drug for NSAID-intolerant patients.

Anaphylaxis due to paracetamol in patients without aspirin intolerance is rare and it has been demonstrated in only two patients to date.^{4,5}

The present article reports one case of paracetamol hypersensitivity with good tolerance of NSAIDs.

CASE REPORT

A 40-year-old woman experienced pruritus on her palms followed by generalized urticaria, dyspnea, chest tightness, and loss of consciousness one hour after receiving paracetamol (500 mg) plus codeine (15 mg). She had also used 500 mg of aspirin 30 minutes earlier. At the casualty service, objective signs included hypotension (blood pressure, 70/40 mmHg) and generalized hives. The patient was treated with parenteral corticosteroids and antihistamines with improvement in five hours. A few days later, she received methamizole (575 mg) without any problems.

Two months later, the patient was studied in our Allergy Unit. She had no personal or family history of atopy and had taken paracetamol, codeine, and aspirin with good tolerance in the past.

Inasmuch as clinical data indicated aspirin sensitivity was the most probable diagnosis, an oral challenge with paracetamol was carried out. Forty minutes after 125 mg of paracetamol was given, generalized pruritus occurred followed by erythema, urticaria, conjunctival edema, and facial and finger angioedema. She was treated with epinephrine and prednisone with recovery in 30 minutes. Serum-specific IgE antibody to paracetamol was investigated using commercial discs (Pasteur-Sanofi Lab, France) with a

negative result. Oral challenge with aspirin doses of 50, 100, 250, and 500 mg given at 60-minute intervals (cumulative dose: 900 mg) was done with no reaction. Oral provocation test with 15 mg of oral codeine was also negative.

DISCUSSION

An acute hypersensitivity reaction to paracetamol has been described here. The immediate response obtained with low doses of paracetamol (125 mg) on challenge suggests an allergic mechanism even in the presence of negative specific serum IgE antibody. Clinical data initially suggested aspirin sensitivity, especially since paracetamol anaphylaxis is uncommon. That is the reason why the choice was made to first undertake oral provocation with paracetamol.

Reactions developing after the ingestion of paracetamol are reported by doctors quite often in the context of aspirin sensitivity associated with paracetamol intolerance⁶; however, previously confirmed acute hypersensitivity reactions to paracetamol are few. Le Van Diem reported one case of anaphylactic shock induced by paracetamol, proven on rechallenge but no data on the patient's aspirin tolerance was given.⁷ Leung et al described clinical anaphylactic reactions in five patients but formal paracetamol challenge was performed in only two. Further, one of them reacted only to high doses of paracetamol (750 mg) and also to aspirin (600 mg) suggesting inhibition of prostaglandin synthesis as the mechanism. The other patient with provocation required 500 mg of paracetamol to induce erythema and pruritus.⁴ As it has been stated above, the patient reported here only required 125 mg of paracetamol to provoke the reaction so that an allergic mechanism seems more likely although specific IgE antibodies were not detected.

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A positive specific IgE determination by RAST to a protein conjugate of paracetamol was detected in one patient by Martin et al. The authors reported a case of an acute cutaneous reaction to paracetamol in which a skin test was also positive, indicating the possible existence of specific IgE antibodies.⁵

Skin tests were not performed in our patient since no standardized extracts were available and oral challenge with paracetamol was the first diagnostic step with a positive response.

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FENOTEROL FAILS TO INCREASE RISK OF LIFE-THREATENING ASTHMA

To investigate further the association of fenoterol with life threatening asthma the authors analyzed data from a retrospective cohort of 655 asthmatic patients 15 to 55 years of age treated at an Auckland hospital in 1986 and 1987. They were followed for occurrence of death or admission to the intensive care unit for asthma through May, 1989. There were 90 subsequent admissions to the intensive care unit and 15 deaths from asthma. Patients using inhaled fenoterol had a greater incidence of severe life threatening asthma than patients using albuterol before adjustment for asthma severity (rate ratio 2.1, 95% CI 1.4 to 3.1). After controlling for a hospital admission in the previous year and prescribed oral corticosteroids the relative risk decreased to 1.5 (95% CI 1.0 to 2.3). After controlling for number of hospital admissions during the study period, continuous oral corticosteroid use, severity of previous acute asthma requiring hospital visit, and race, fenoterol was not associated with life threatening asthma (rate ratio 1.0, 95% CI 0.6 to 1.7).

After adjustment for severity of asthma fenoterol did not increase risk of severe, life threatening asthma. Previous studies may have implicated fenoterol as a risk factor because it was prescribed more often for patients with severe asthma. It is noteworthy that sales of fenoterol in New Zealand did not decrease until four years after rates of death from asthma began to decrease.

—RMS

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