

Occupational Asthma following Inhalation of Cimetidine and Amoxicillin Powder

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There have been very few reported cases of worker in the pharmaceutical industry with allergies caused by handling amoxicillin and cimetidine. In this paper, we report a case of occupational asthma and rhinitis caused by both cimetidine and amoxicillin in a worker who handled powders to make tablets. His bronchial sensitivity was confirmed by separate specific bronchoprovocation tests with cimetidine and amoxicillin powders. Skin prick test and patch test revealed negative responses both to cimetidine and amoxicillin powders.

This is the first case of occupational asthma caused by dual sensitization to cimetidine and amoxicillin in a single exposed worker. Further studies are needed to investigate the pathogenic mechanism of bronchoconstriction triggered by cimetidine and amoxicillin.

Key Words: Occupational asthma, Cimetidine, Amoxicillin

INTRODUCTION

Inhalation of commonly used drug powders can cause occupational asthma in atopic and non-atopic subjects. Inducing agents in the pharmaceutical industry include penicillin¹, cephalosporin², penicillamine³ and psyllium⁴, isonicotinic acid⁵ and hydralazine⁶. Cimetidine is commonly used to treat peptic ulcers, while amoxicillin is a common antibiotic. Coutts II et al⁷ reported one case of occupational asthma caused by cimetidine in an employee who made cimetidine tablets. They did not do skin prick test or patch test with this powder. To our best knowledge, there have been very few reports of occupational asthma caused by the inhalation of both amoxicillin and cimetidine powders.

In this paper, we report a case of occupational rhinitis and asthma caused by both cimetidine and amoxicillin powder inhalation, as confirmed by individual specific bronchoprovocation tests.

SUBJECTS AND METHODS

Case summary

The patient, a 23-year-old male, non-smoker, was admitted to the Allergy Clinic of Ajou University Hospital, Suwon, Korea. Three years earlier, he began to work at a pharmaceutical manufacturer, and his job responsibilities included mixing drug powders to make tablets. He began to experience coughing and shortness of breath 1 year before this study, and suffered from rhinorrhea and sneezing for the last 2 months. He complained that the above symptoms were further aggravated after handling cimetidine and amoxicillin, and improved when he was on vacation. On admission, physical examination showed clear breathing sound.

Total IgE level by paper radioimmunosorbent assay (PRIST) was 615 IU/ml. The total eosinophil count was 500/mm³.

A chest x-ray and PNS showed no abnormal finding. A skin prick test provoked immediate positive responses to *Dermatophagoides(D). farinae* and *D. pteronyssinus*. Radioallergen sorbent test showed class 2 response to *D.farinae*. A patch test including amoxicillin and cimetidine powder was negative.

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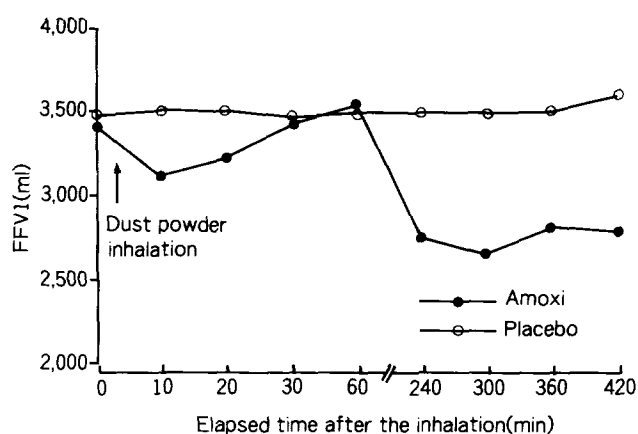


Fig. 1a. Result of bronchoprovocation test with amoxicillin powder. No significant bronchoconstriction was noted after inhalation of placebo. An isolated late asthmatic response was observed after inhalation of amoxicillin powder.

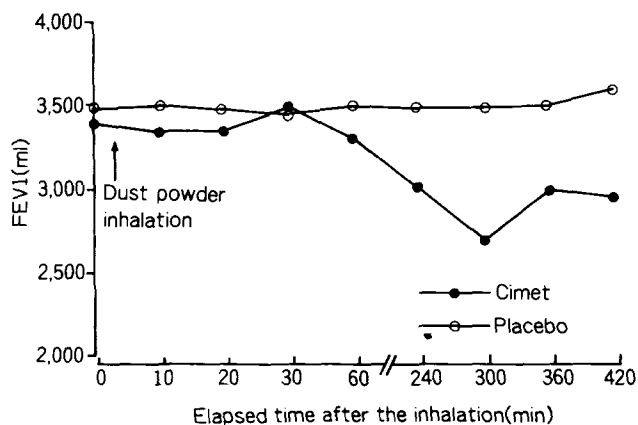


Fig. 1b. Result of bronchoprovocation test with cimetidine powder. An isolated late asthmatic response was noted after inhalation of cimetidine powder.

Inhalation challenge test with methacholine

Airway responsiveness to methacholine was tested according to a previously described method⁸, which revealed a positive response with 2.5 mg/ml. A subsequent methacholine challenge test, done 24 hours after the each specific bronchoprovocation test, yielded the same result at 2.5 mg/ml.

Bronchoprovocation tests with cimetidine and amoxicillin

Bronchoprovocation test was performed in a similar manner as the previous occupational asthma study⁹. One gram lactose capsule as placebo was inhaled through a spinhaler capsule.

The forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEFR) were measured with a spirometer (Chest, Japan). Then, FEV1 was measured every 10 min during the first hour, and pulmonary function tests were performed every hour for 7 hrs after the challenge. On a different day, amoxicillin and cimetidine powders (50 mg) from the patient's own workplace were each put into a capsule, which he inhaled using a spinhaler. As shown in Fig 1, isolated late asthmatic reactions were noted after inhalation of amoxicillin powder, and also after inhalation of cimetidine powder; rhinitis and asthmatic symptoms were observed after inhalation. To exclude bronchial sensitization to house dust mite, *D. farinae*-bronchoprovocation test was performed. No significant bronchoconstriction was found. The subject gave his written informed consent as required by the Ajou University Hospital, Suwon, Korea.

DISCUSSION

This study reveals that two commonly used drug powders, cimetidine and amoxicillin, can induce occupational asthma in a worker handling them. This was confirmed by individual specific bronchoprovocation tests. Although we did not try to detect serum specific antibodies to these chemicals, it would be unlikely that his bronchoconstriction was induced by immunologic mechanism, since the skin-prick tests with amoxicillin and cimetidine extracts were negative. Patch tests with these chemicals also showed negative responses.

There have been a few reports of occupational asthma triggered by the exposure to drug powders. An immunologic mechanism was suggested for occupational asthma in workers exposed to penicillin¹⁰. In contrast, a non-immunologic mechanism was suggested in occupational asthma cases caused by ampicillin, benzyl-penicillin and 6-amino penicillanic acid¹¹, which have similar chemical structures to amoxicillin. In this patient, there had been no history of adverse reactions from exposure to cimetidine and amoxicillin. Further investigations are needed to clarify their pathogenic mechanisms.

There have been several reports that atopy plays an important role in the development of occupational asthma, especially when induced by high molecular weight allergens^{12,13}. Although he showed a negative response on *D. farinae*-bronchoprovocation test, this subject showed a strong positive response to house dust mite on skin prick test and

radioallergosorbent test (RAST).

In conclusion, this study demonstrates that amoxicillin and cimetidine powders can induce occupational asthma in an exposed pharmaceutical industry worker. The possibility of non-immunologic mechanisms is suggested.

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