

compared with radioallergosorbent test (RAST) inhibition technique (6). It appeared that *F. elastica* only weakly inhibited IgE binding to *F. benjamina*, whereas *F. benjamina* completely inhibited IgE-binding to *F. elastica*. This taken together with our findings suggest that *F. elastica* has only one cross-reacting 12 kDa IgE-binding band.

This study demonstrated that the best source of *F. benjamina* allergens is the sap extract and that the allergens in the sap are species-specific except for the 12 kDa band.

*Department of Dermatology

University of Turku

Turku

Finland

E-mail: outi.kortekangas-savolainen@tyks.fi

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Three cases of occupational asthma induced by thiamphenicol: detection of serum-specific IgE

Y.-M. Ye, H.-M. Kim, C.-H. Suh, D.-H. Nahm, H.-S. Park*

Key words: occupational asthma; specific IgE; thiamphenicol.

Thiamphenicol, a derivative of chloramphenicol, has been widely prescribed in Korea. A few cases of contact dermatitis caused by thiamphenicol have been reported and cross-reactivity with chloramphenicol was suggested (1, 2). To date, there has been no report of rhinitis or asthma caused by thiamphenicol.

Although exposure to antibiotics including β -lactams are known to cause asthma in workers in the pharmaceutical industry (3), the pathogenesis of occupational asthma induced by antibiotics still remains unclear. This is the first case of occupational asthma and rhinitis caused by thiamphenicol inhalation in which both immunoglobulin-E (IgE)-mediated and non-IgE-mediated responses were at work.

In this report we describe the clinical findings of three patients with thiamphenicol-induced occupational asthma who had worked in the same pharmaceutical plant. All three patients were non-atopic and in their late twenties. They had no history of medical illness, in particular, no other drug allergy, and no

Inhalation of thiamphenicol powder could induce asthma and rhinitis.

family history of allergic disease. The durations of asthmatic symptoms were 2 years, 6 and 9 months, respectively. Though all three cases had concurrent rhinitis symptoms, none had contact dermatitis.

To evaluate the IgE response, a skin prick test (SPT) was performed in the three exposed workers and 20 unexposed healthy controls. To confirm bronchial sensitization, methacholine bronchial challenge and specific bronchial provocation test (BPT) with thiamphenicol solution were performed. Thiamphenicol-human serum albumin (HSA) conjugates were used to detect serum-specific IgE and IgG4 antibodies to thiamphenicol by means of enzyme-linked immunosorbent assay (ELISA) (4). Twenty nonatopic, healthy subjects with no history of exposure, and who had negative SPT to thiamphenicol were enrolled as control subjects. The positive cut-off value for specific IgE was determined by the mean $\pm$ 3 SD of the absorbance values. Table 1 summarizes the clinical features of the three workers. All three had work-related, upper and lower respiratory symptoms and airway hyperresponsiveness to methacholine. Two (cases 1 and 2) showed early asthmatic responses and one (case 3) showed late only asthmatic response. ELISA results demonstrated that the former two had high serum-specific IgE to thiamphenicol-HSA conjugate (Fig. 1A). Also, case 3 developed significant bronchoconstriction on thiamphenicol BPT, but she had a negative response to thiamphenicol on SPT and undetectable serum-specific IgE to thiamphenicol. To exclude nonspecific bronchial response, we performed thiamphenicol BPT in two asthmatic patients sensitive to house dust mites, and who had no history of thiamphenicol exposure. But both of them showed

Table 1. Clinical features of three patients

Case	Age	Sex	Atopy	SPT (A/H)	Specific IgE	Specific IgG4	PC ₂₀ methacholine (mg/ml)	BPT result
1	28	F	Absence	3+	Positive	Negative	5.0	Early
2	26	F	Absence	2+	Positive	Negative	2.5	Early
3	26	F	Absence	0	Negative	Negative	5.0	Late

SPT, skin prick test to thiamphenicol; A/H, the ratio of the size of the wheal caused by thiamphenicol and histamine (1 mg/ml); BPT, bronchial provocation test.

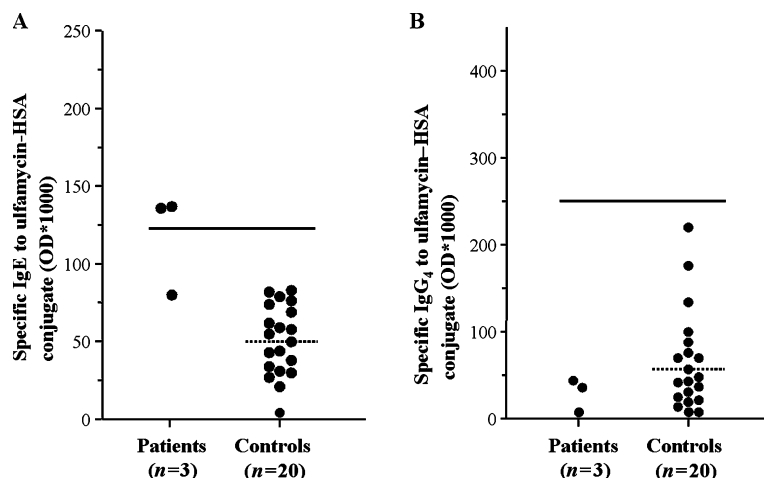


Figure 1. Specific IgE (A) and IgG4 (B) bindings to thiamphenicol-human serum albumin (HSA) conjugate by enzyme-linked immunosorbent assay in three asthmatic patients and unexposed healthy controls. The horizontal bar indicates a positive cut-off value derived from mean $\pm$ 2 SD of absorbance value of controls.

negative response on thiamphenicol BPT. We also detected serum-specific IgG₄ to thiamphenicol-HSA conjugate by ELISA in the three study subjects (Fig. 1B). No significant differences were noted between the three cases and the 20 unexposed healthy workers, suggesting that the possibility of specific IgG₄-mediated response in these cases was very low.

The pathogenesis of occupational asthma induced by low-molecular-weight drugs requires further study. These drugs may act as haptens and combine with a protein to elicit an immunologic response (5). In this study, we can suggest two different pathogenic mechanisms leading to occupational asthma caused by thiamphenicol. In cases 1 and 2, an IgE-mediated mechanism played an important role in the pathogenesis, as they showed positive responses on SPT and

BPT to thiamphenicol and had high serum-specific IgE to thiamphenicol-HSA conjugate. By contrast, although case 3 had work-related asthma symptoms and a positive response to thiamphenicol on BPT, there was no detectable serum-specific IgE with negative response on thiamphenicol SPT, therefore suggesting a non-IgE-mediated mechanism in the pathogenesis. Further investigation will be needed to understand other immunologic or nonimmunologic mechanisms in thiamphenicol-induced asthmatic workers.

In conclusion, we report three patients with occupational asthma caused by thiamphenicol. Both IgE-mediated and non-IgE-mediated mechanisms were at work.

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*Department of Allergy & Rheumatology
Ajou University School of Medicine
Yongtonggu Wonchondong San-5
Suwon 443-721
South Korea
Tel: +82 31 219 5196/5150
Fax: +82 31 219 5154
E-mail: hspark@ajou.ac.kr

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