

Occupational asthma induced by thiamine in a vitamin supplement for breakfast cereals

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Key words: cereal manufacture; occupational asthma; thiamine.

We describe occupational asthma related to breakfast cereal manufacture. Anaphylaxis to thiamine has been previously reported (1–5).

Occupational asthma due to thiamine.

A 46-year-old man worked manufacturing breakfast cereal enriched with vitamins. The vitamins in solution were atomized and sprayed across conveyor belts of the cereal. For 6 years prior to his symptoms he worked on a rotating programme where for 1 week in seven he was responsible for the spraying of breakfast cereal with vitamins.

His first attack of asthma occurred during a night shift when he was performing this process. He commenced bronchodilator treatment. He improved rapidly away from work. Over the next 5 months he developed progressive breathlessness. He improved on days off and on holiday.

Skin prick testing to common environmental allergens including wheat were negative. Lung function testing showed airways obstruction (FEV1 2.95–85% predicted; FVC 4.12–97% predicted). He kept 2 hourly serial peak flow recordings for a period of 6 weeks, which were analysed by OASYS-2 (6). This shows a severe deterioration in his asthma during the week he was working with the vitamins. Recovery took 8 days, the first six of which he was off work. There was no clinical respiratory

infection at this time. He was admitted for occupational broncho-provocation testing. After a control day with no exposure he had an exposure to 10 min of powdered thiamine preparation supplied by his employer. The powder was transferred between two bags for 10 min with no obvious reaction. A second challenge day, involving a 30 min exposure resulted in a late asthmatic reaction, maximal at 8 h (Fig. 1). His IgE RAST to thiamine was negative.

He has now changed job within the factory, and drives forklift trucks in the warehouse department. He experiences no work related symptoms, but his asthma remains difficult to control.

A 43-year-old production worker at the same cereal production plant had mild background asthma for 8 years. Over a 6-month period he developed symptoms of increased cough and wheeze. Symptoms coincided with his work shifts where he atomized the vitamin mixture supplement on to breakfast cereal products. He had performed this work for 4 years before onset of symptoms.

Symptoms resolved on holidays and improved on days off.

Initial investigations showed an obstructive defect (FEV1 59% predicted,

FVC 88% predicted) and severe bronchial hyper-reactivity with a PC20 to histamine of less than 0.25 mg/ml.

Occupational Peak flow recordings were performed and were suggestive of occupational asthma, but he failed to keep sufficient readings on days off work.

An occupational challenge was performed in blinded fashion. Histamine reactivity was performed on the day preceding the occupational challenge (0.78 mg/ml). Control challenge was with aerosolized saline. Aerosolized vitamin mix was generated in the challenge laboratory on active days. On the first day of active challenge, exposure was for three periods of 30-s exposure to the aerosolized vitamin. On the second challenge day, the exposure was increased to two periods of 2 min exposure.

On the higher exposure challenge a 24% fall in FEV1 occurred at 5 h post-exposure (Fig. 2). Blood gases demonstrated a significant hypoxia (pO₂ 45 mmHg, pH 7.46, pCO₂ 38.4 mmHg). Histamine reactivity on the day after the challenge had deteriorated to 0.28 mg/ml.

The individual has not returned to work since and symptoms have progressively improved.

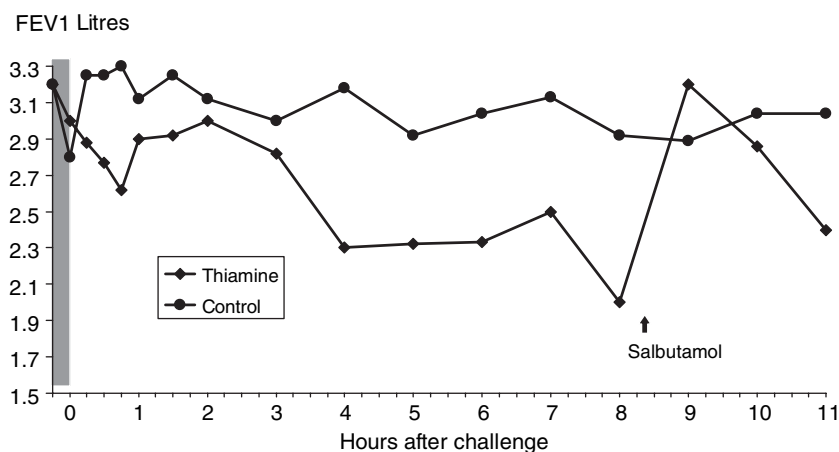


Figure 1. Case A challenge to powdered thiamine supplied by employer. Control challenge and exposure to 30 min of powder pouring.

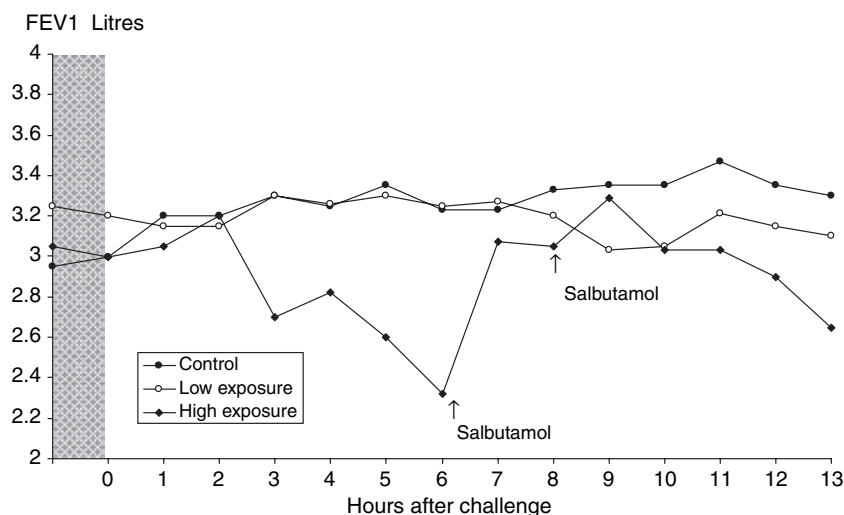


Figure 2. Case B challenge with aerosolized vitamin mixture. Control challenge aerosolized saline. Two active challenge days represent low and high exposure to the aerosolized solution containing raw vitamin as provided by the cereal company.

We believe these two cases are the first reports of occupational asthma related to the use of thiamine in an industrial setting. The production of a fine aerosol of vitamin mixture facilitates the pulmonary deposition. Both cases are confirmed by occupational challenge, which demonstrated predominantly late asthmatic reactions.

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C1-INH and C3/C4 levels do not correlate with long-term danazole dosage and HAE-1 attack-free interval

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Key words: C1-INH; C3; C4; danazole; hereditary angioedema.

Patients with hereditary angioedema are rare in clinical practice and thus therapeutic experience is rather based on individual cases. A

Long-term follow-up showed no correlation between C3/C4/C1-INH, danazole dosage and absence of HAE-attacks.

46-year old man was first diagnosed to have hereditary angioedema type-1 (HAE-1) on the basis of clinical history and serological findings in March 2002. He presented in casualty with a recent onset of spontaneously evolving, angioedema at various sites, triggered sometimes by manual labor such as gardening work. Complement C4 and C1-esterase inhibitor (C1-INH) levels were found to be far below the normal baseline. A functional assay of C1-INH came back as normal and thus the diagnosis HAE-1 was confirmed.

As attack frequency was high, continuous therapy was needed. In absence of any contraindications, and facing a male patient, we decided to start danazole 200 mg/day according to the Budapest protocol, as the second drug of choice Tranexamic acid is regarded as less effective and the patient was worried about the particular side effects (1). As expected, the attacks ceased within a few days. The dosage was reduced step-by-step over time as shown in Fig. 1A, based on absence of clinical symptoms. The patient's compliance was high, follow-up was every 3–4 months until today. Monitoring included routine biochemistry, yearly abdominal ultrasound, full blood count and control of serum levels for C3, C4 and C1-INH. Up to today no side effects of danazole became evident. In April 2004, the patient ran out of medication for 2 weeks and suddenly HAE attacks relapsed, but stopped again within 2 weeks of restarting danazole 50 mg/day. In January 2005 the minimum maintenance dose of 50 mg/d 5 days a week was reached (1). As evident from our time course analysis of serum C3, C4 and C1-INH levels shown in Fig. 1B there was no evident correlation between the values of these three parameters and the clinical success of therapy in our patient. The serum C4 gradually went back to normal, C3 was always normal and C1-INH stayed below the normal range for the whole monitored time of 3 years. This observation is in accordance with the small study ($n = 8$) by Zimmermann (2), who found similar long-term patterns for C4 and C1-INH. Gelfand described in the first danazole study in 1976 an initial increase of C1-INH and C4 within the first days of