Occupational asthma due to sodium iso-nonanoyl oxybenzene sulphonate, a newly developed detergent ingredient

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ABSTRACT Research with sodium iso-nonanoyl oxybenzene sulphonate (SINOS) for use in a detergent product was complicated by the development of asthma in an atopic 38 year old laboratory technician. Inhalation challenge tests with nebulised SINOS solutions over a dose range of 0-01–32 µg gave reproducible late asthmatic reactions after the higher doses and an increase in bronchial reactivity to methacholine. The magnitude of the late reaction was related to the challenge dose.

Rashes, rhinitis, and conjunctivitis were noted in three of 60 detergent workers engaged for 12–18 months in research with a newly developed ingredient (sodium iso-nonanoyl oxybenzene sulphonate, SINOS) and investigations suggested that delayed contact hypersensitivity to SINOS was probably responsible for some at least of the rashes. A fourth worker then developed asthma. This paper describes investigations suggesting that this was causally related to SINOS.

Case report

A 38 year old laboratory technician, who had worked in the research and development plant of a detergent manufacturer since the age of 19 years, had had moderately severe asthma as a child from the age of 2 to 14 years but recalled neither rhinitis nor eczema. He had been well until January 1985, when, 18 months after starting work with SINOS, he began to have rhinitis, a rash, a dry cough, and undue breathlessness on exertion. Four weeks later he woke on two successive nights during the working week with wheezing, chest tightness, and breathlessness, the last being severe on the second occasion. He stayed away from work and his symptoms resolved completely within two weeks.

He had never smoked, he had no pets or other relevant domestic exposures, and he took no regular medications. While he was symptom free away from work he had no abnormal physical signs and ventilatory indices were within normal limits, but a chest radiograph showed some evidence of overinflation. Skinprick tests gave positive immediate reactions to various common allergens, and total serum IgE was substantially raised at 1000 (normal range 10–150) IU.

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Accepted 17 March 1988

There was no excess binding in antigen specific IgE assays with SINOS directly attached to ELISA plastic plates (Dynatech, Billingshurst) but, in the absence of a positive control serum, the ability of the test to exclude a specific IgE response was not validated. Tests to detect anti-SINOS precipitating IgG antibodies also gave negative results. Results of a routine biochemical screen and a full blood count were normal apart from an eosinophil count of $1.188 \times 10^9$/L.

The patient returned to work after three weeks. There was a minimal recurrence of his symptoms, and a mild increase in circadian change in peak expiratory flow (PEF), the mean daily difference between maximum and minimum daily PEF readings increasing from 54 to 97 l/min. The cumulative dose of methacholine required to provoke a 20% decrement in FEV$_1$ (PD$_{20}$), measured by a dosimeter method, fell from 400 and 500 µg when he was absent from work to 280, 240, and 200 µg after his return to work. He ceased work once more after two weeks and SINOS inhalation tests were carried out within a few days, when his symptoms had resolved.

SINOS INHALATION TESTS

It was estimated from workplace exposure measurements that he had tolerated hourly inhalations of 0-02–100 µg SINOS without undue discomfort, so an initial challenge dose of 0-01 µg was chosen. For the maximum dose 100 µg was chosen (equivalent to a full working day’s dose at

Fig 1 FEV$_1$-time plots after an initial control challenge with 0-4% phenol in normal saline and the first challenge with 32 µg sodium iso-nonanoyl oxybenzene sulphonate (SINOS).
Fig 2  Dose-response relationship between SINOS and FEV₁, area decrement (numbers indicate the chronological order of the control tests and 32 µg tests).

exposure levels close to the hourly maximum over the preceding six months.

A locally designed dosimeter was used to deliver both methacholine and SINOS. The onset of inspiration from functional residual capacity triggered the nebulisation of 10 µl (±5%) of test solution during the initial 2 seconds of a 5 second inspiration. There was no subsequent breath holding. SINOS was administered in 50 µl doses (five inhalations) from solutions of increasing concentration (0-2-640 µg/ml in phenol saline). Daily increments of about 3.2 fold (√10) were given to provide a dose range of 0.01-32 µg over the course of two weeks, during which three blinded control tests with phenol saline alone were interspersed at random.

Late asthmatic reactions of increasing severity were observed with the higher doses of SINOS, and these were accompanied by a further decrease in PD₁₀ (which was 110 µg on the day after the last SINOS challenge) despite full recovery of the baseline FEV₁. The reaction to the 32 µg dose was considered unequivocal by both patient and physician (fig 1), and no further dose increments were administered. It proved to be reproducible (fig 2). No asthmatic symptoms were noted after the control tests but circadian changes in FEV₁ increased slightly as the level of bronchial responsiveness increased.

The FEV₁ response 2-12 hours after control and SINOS challenge was expressed as the area above the FEV₁-time plot, baseline FEV₁ (mean of five sets of three technically satisfactory measurements at 10 minute intervals before challenge) being used to define the upper boundary of the area measured. Regression analysis, which excluded the results from the control challenges, showed a significant linear relationship (fig 2) between this area decrement (A) and the log challenge dose:

\[ A = 4.53 \times \log_{10} \text{dose} \]

[standard error, 0.10; 2.14]

The patient was transferred to another of the company’s plants and had no further exposure to SINOS. He had no more symptoms and PD₁₀ methacholine increased steadily over three months to 800 µg.

**References**

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*Thorax* 1988 43: 501-502
doi: 10.1136/thx.43.6.501