

Dust Exposure Challenge Test as a Measure of Potential Allergenicity and Occupational Disease Risk in Handling of Ispaghula Products

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It is known that workers in the pharmaceutical industry, and nurses, can become sensitized and develop allergic respiratory symptoms by handling bulk laxatives containing Ispaghula powder. Fifteen individuals allergic to Ispaghula were challenged with a commercially available Ispaghula product and three other products manufactured in a way to make them less dusty. The results show that the use of products with smaller amounts of airborne particles results in a lower incidence of symptoms and thus probably reduces the potential occupational risk of sensitization to the Ispaghula allergen.

Key words: allergens; dust; Ispaghula; occupational disease.

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Ispaghula powder is obtained from the crushed seeds of *Plantago ovata*. It is used as the active substance in bulk laxatives because of its water retaining capacity. Workers in the pharmaceutical industry, and nurses, may become sensitized and develop allergic symptoms when handling products containing Ispaghula (1, 5). Obviously, the symptoms and probably also the sensitization are caused by the part of the product which contains particles small enough to be airborne. Thus measures taken to reduce the amounts of dust should also reduce the risk of sensitizing exposed subjects. The effect of Ispaghula products containing less dust were studied by using various pharmaceutical preparations in an exposure challenge test.

MATERIAL AND METHOD

Patient material

Six nurses working on geriatric wards and nine workers from a pharmaceutical industry (Astra

Pharmaceutical Production), which manufactures an Ispaghula product, were tested. All of the subjects developed allergic symptoms after handling these products during their daily work. The most common complaints were rhinitis and itching of the eyes, throat and hands, but dyspnoea and wheezing were also reported in four cases. All the tested subjects had RAST and prick tests that were positive to Ispaghula.

Tested products

- A commercial Ispaghula powder preparation (Lunelax[®] powder, batch EL 868 in the first study and batch GD 1054 in the second study).
- A special granulated Ispaghula powder preparation.
- A special dust-reduced Ispaghula powder preparation.
- Placebo (lactose coloured by charcoal and ferric fumarate).

E. A commercial preparation based on the same principles as products B and C (Lunelax[®] powder, batch GM 1500).

The dust test was performed in the following way. One dose, corresponding to 3.3 g of Ispaghula, was allowed to fall freely from a height of 23 cm into a bowl. The nozzle of a light scattering particle counting and sizing instrument (Royco, model 225/518) was placed 18 cm above the edge of the bowl. The instrument counted the number of particles in an air volume of 0.1 cf, passing the sensor during 1 min. Eight tests were performed. The number of particles were divided into three classes based on the sizes 2–4 μm , 4–8 μm and 8–20 μm . Using this method, it was not possible to count particles smaller than 2 μm .

Challenge tests

Sitting in a provocation cabin, the subjects poured the product to be tested from one disposable bowl into another for 5 min. The amount corresponded to 25 g of Ispaghula powder. The physical status and peak expira-

tory flow (PEF) or flow expiratory volume in 1 sec (FEV₁) were assessed before, immediately after and 15 min after exposure. Signs and symptoms developing during and/or after the challenge were noted and arbitrarily graded as – none, + slight, ++ moderate and +++ pronounced. Any complaints developing during the evening of, or the night after the tests, were recorded. The final judgement was made about 24 h after the challenge. Two studies were done. In the first study, we tested 15 individuals with products A, B, C and D leaving at least a 24-h interval between the tests. In the second study, six subjects from the previous study were challenged with products A, E and D.

Sign test was used for the statistical analysis.

RESULTS

The particle size distribution for products A and E used in the second study are shown in Fig. 1.

All tested individuals developed symptoms when tested with product A in both studies

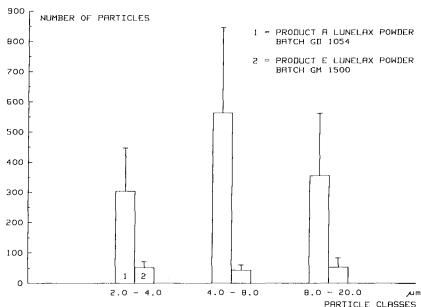


Fig. 1. Size distribution of airborne dust from two different batches of Lunelax powder. Bars indicate SD.

Table 1

Symptom scores in persons challenged with different Ispaghula products. (Study I)

Patients	A	B	C	D (Placebo)
1	+++	+	-	-
2	++++*(50)	+	-	+
3	+++	+++	++	-
4	++++*(20)	-	-	+
5	+++	+	+	-
6	+	+	+	+
7	+	-	-	+
8	+++	++	+	-
9	++++*(46)	-	++*(15)	+
10	++++*(12)	-	-	-
11	+++	-	-	-
12	+	+	-	-
13	++	-	-	+
14	+++	-	+	-
15	++++*(12)	+	-	+

* Patients who developed obstructive symptoms.

Numbers in brackets show decrease in FEV₁ in % 15 min after challenge.

Statistical analysis:

Placebo - product A: $P < 0.0002$.Product B - product A: $P < 0.0004$.Product C - product A: $P < 0.0001$.

Placebo - product B: n.s.

Placebo - product C: n.s.

Table 2

Symptom scores in persons challenged with different Ispaghula products. (Study II)

Patients	A	E	D (Placebo)
9	++++*(38.7)	++	+
7	++	-	-
15	+++	++*(8)	-
8	+++	-	+
14	+++	+	-
13	+++	+	-

* Patients who developed obstructive symptoms.

Numbers in parenthesis show decrease in PEF % 15 min after challenge.

Statistical analysis:

Product A - placebo: $P < 0.05$.

Product E - placebo: n.s.

Product E - product A: $P < 0.05$.

(Tables 1 and 2). The most common symptom was rhinoconjunctivitis, but even itching and rash involving the exposed skin, i.e. hands and face, were reported. In five cases the patients developed a reaction with airway obstruction as the main symptom. When exposed to products B, C and E, containing less dust, the subjects developed significantly fewer symptoms than when exposed to product A.

DISCUSSION

The symptoms provoked by the challenge were identical with those noted by subjects when handling products containing Ispaghula during their daily work. Moreover, the six subjects challenged in both studies usually reacted with the same main symptom at both occasions. These facts show that the method used for challenge is useful and simulates the exposure in daily work.

From a theoretical point of view it could be argued that an interval of 24 h between the episodes of challenge could be short enough to give a decrease in sensitivity at the time of the next challenge. The order in which the products were administered was, however, randomly varied and the source of error could thus be neglected.

Reduction of the amount of airborne allergen may be a very effective measure for preventing sensitization. This has been shown in the enzyme detergent industry, where granulation and encapsulation of the "dusty enzyme" have markedly diminished the occurrence of occupational allergy (3, 6).

As regards Ispaghula products, it seems that the dustiness of the product also influences the type of symptoms. Respiratory obstructive symptoms were far more common and the degree of obstruction was more pronounced when the subjects were exposed to the commercial Ispaghula powder (product A). It is known that particles of different sizes are deposited in different sites in the airways (2, 4), but it is not clear in what way the deposition sites or the amount of respired allergen influence the type of symptoms.

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