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Case report

Occupational Asthma due to psyllium (*Plantago ovata*) dust

Psyllium (*Plantago ovata*) powder is a component of bulk laxatives and cause allergic reactions when inhaled by occupationally exposed person. The cases are presented of two presented of two nurses working in a geriatric nursing home who evidenced occupational asthma secondary to psyllium powder inhalation administering to patients laxatives containing this product. The skin prick test with a 1:10 (w / v) psyllium extract were detected (CAP system). The challenge test with psyllium powder elicited an immediated bronchial response in one patient and a dual one in the other. One of the patients evidenced nonspecific bronchial hyperreactivity in the methacholine challenge test; this test was negative in the other one (who had not been exposed to psyllium powder for over one year and had remained asymptomatic throughout this period). These two new cases of occupational asthma caused by psyllium-containing laxatives confirms the need to change the presentation of such laxatives from the powder form to another one not containing inhalable particles (e.g., granulates). Psyllium hypersensitivity should be ruled out in asthmatic patients who are occupationally or otherwise exposed to this product.

Key words: Allergy to psyllium. Occupational asthma. Ispaghula. Laxatives. *Plantago ovata*.

Asma ocupacional por polvo de psyllium (*Plantago ovata*)

El polvo de psyllium (*Plantago ovata*) se utiliza como laxante de volumen y puede producir reacciones alérgicas cuando es inhalado por personas expuestas ocupacionalmente. Se presentan dos casos de enfermeras de una residencia geriátrica que presentaban asma ocupacional al inhalar el polvo de psyllium que administraban como laxante a sus pacientes. Se realizaron pruebas cutáneas en *prick* con un extracto de psyllium (1:10 p/v) que fueron positivos en ambos casos. En uno de ellos se detectaron cifras elevadas de IgE específica frente a psyllium (CAP System). En las pruebas de exposición a polvo de psyllium que se realizaron se obtuvieron una respuesta bronquial inmediata y otra dual. Una paciente tenía un test de hiperreactividad bronquial inespecífica con metacolina positivo; en el otro caso este test fue negativo (esta paciente llevaba un año asintomática y sin exponerse a polvo de psyllium). Estos dos nuevos casos de asma ocupacional por laxantes que contienen psyllium confirman la necesidad de cambiar la presentación en polvo por otra que no contenga partículas inhalables (p.e. gránulos). En el caso de pacientes asmáticos expuestos a polvo de psyllium (de forma ocupacional o tomadores del fármaco) se debe descartar una hipersensibilidad a psyllium.

Palabras clave: Alergia a psyllium. Asma ocupacional. Ispaghula. Laxantes. *Plantago ovata*.

Psyllium, or ispaghula, is a product derived from the skin of the seeds of *Plantago ovata*, a plant of the genus *Plantago* (family *Plantaginaceae*) that is frequently used as a bulk laxative. Another well-known member of this family is *Plantago lanceolata*, the pollen of which is a cause of rhinoconjunctivitis and asthma. Immediate IgE-mediated hypersensitivity reactions to psyllium (asthma, rhinitis and anaphylaxis) have been reported in nurses who administered to their patients laxatives containing this product¹⁻⁵, in pharmaceutical industry workers manipulating psyllium^{6,7}, and also in association to ingestion in patients taking psyllium-containing laxatives^{1,5,8}. We report the cases of two nurses working at the same geriatric nursing home who developed occupational asthma related to the inhalation of psyllium-containing laxatives.

METHODS

Preparation of the psyllium extract and skin tests. Psyllium powder (3.5 g; Plantaben®, Madaus Cerafarm, Barcelona, Spain) was added to 35 ml normal saline (10% concentration, w/v) and the mixture was vigorously stirred for 30 seconds. Stirring could not be continued for a longer period as a mucilaginous mass resulted.

Skin tests were performed with the usual prick technique with a panel of 17 common pneumoallergens (including *Plantago lanceolata*) and with the above 10% psyllium extract. Normal saline and 10 mg/ml histamine were used as controls. Skin tests with the same psyllium extract were performed on five atopic and five non-atopic control subjects, with negative results.

Total and specific IgE determination. The quantitation of the total and allergen-specific serum IgE to pneumoallergens and psyllium was carried out using the CAP-FEIA technique (Pharmacia Diagnostics, Uppsala, Sweden), according to the manufacturer's instructions.

Nonspecific bronchial hyperreactivity test. Bronchial challenge tests with methacholine were performed on both patients according to the method described by Chatham *et al.*⁹. The results were expressed as PD₂₀ (the dose required for inducing a 20% decrease in the forced expiratory volume in the first second, or FEV₁), in cumulative units (CU). In case 2 the nonspecific bronchial hyperreactivity test was repeated six months after the patient had abandoned all contact with psyllium.

Psyllium exposure test. This was performed on the two patients after a period without working with psyllium

(one year in case 1 and two months in case 2). None of the two patients had symptoms at the time of the test, nor were they receiving any medication that might have interfered with the results. No end-point titration of the skin tests was performed. Prior to the exposure test a forced spirometry was carried out for determination of the forced Vital Capacity (FVC), FEV₁, peak expiratory flow rate (PEFR) and MMEF 25-75%. The patients then transferred (dusted) the psyllium powder from one tray to another for one minute; the spirometry was repeated and, if no significant changes occurred, they continued to transfer the psyllium powder for successive 5-minute periods, up to a maximum of 15 minutes. The spirometry was repeated after each five-minute period, 15, 30 and 60 minutes after the test, and again at hourly intervals up to eight hours after the end of the exposure. In order to detect late bronchial responses, the PEFR was monitored with a portable peak flow meter (Mini-Wright type) over the following 24 hours. The test was defined as positive when a drop occurred in the FEV₁ $\geq 20\%$ of the baseline value, or one in the PEFR $\geq 35\%$ of the baseline value. One of the two patients (case 1) transferred 17.5 g of psyllium powder (five Plantaben® sachets); as she experienced severe bronchospasm, the other patient (case 2) only transferred 7 g of the powder (two sachets). On the day preceding the actual exposure test the two patients transferred lactose powder for 15 minutes in the same way, and their spirometric values and PEFR were monitored as above. Two patients with bronchial asthma and grass and olive pollen sensitization were used as control subjects; the exposure tests were carried out when the patients were asymptomatic and not during their specific pollen seasons, but they both had at the time of the exposure positive nonspecific bronchial hyperreactivity tests, with PD₂₀ values of 100 and 120 CU, respectively. The exposure tests were negative in these two control subjects. The exposure tests were carried out at the Allergy Section premises, in a room with approximately 20 m³ volume. The environmental levels of psyllium dust/powder were not measured.

CLINICAL OBSERVATIONS

Case 1. A 27-year-old female nurse had been working for three months in a geriatric nursing home prior to consultation. Two months after starting work at this nursing home she began developing bronchospasm episodes occurring when she administered to the patients a powdered laxative containing psyllium (Plantaben®). In the

course of her work she usually administered 10 to 12 sachets once or twice daily. The patient did not smoke, and she had no personal or family history of atopy. The symptoms disappeared after quitting work at the nursing home.

Among the results of the studies performed, this patient had eosinophilia (600 cells/ μ l) and a total IgE level of 580 kU/l. The results of the specific IgE assessments were negative for *Plantago lanceolata*, *Lolium perenne*, *Olea europaea*, *Salsola kali*, *Alternaria alternata*, *Dermaphagoides pteronyssinus* and cat and dog danders. No increased specific IgE to psyllium was detected. The nonspecific bronchial hyperreactivity test was negative up to 800 CU methacholine. The skin tests with psyllium extract were positive (6 x 5 mm wheal) with the tested 10% w/v concentration; the wheal elicited by histamine was 5 x 4 mm. The skin tests were negative for all the common airborne allergens tested.

The exposure test with psyllium elicited an immediate bronchial response. After five minutes' exposure, the FEV₁ evidenced a 28% drop; this drop increased to 35% after 10 minutes and to 43% after 15 minutes, and the patients developed cough, dyspnoea and wheezing. Treatment was instituted with inhaled salbutamol and 6-methylprednisolone, 80 mg intravenously; the patients' situation gradually improved, and she regained her baseline spirometric values after one hour. There was no late bronchial reaction.

Case 2. A 33-year-old woman, smoker of 20 cigarettes/day, who worked as a nurse at the same geriatric nursing home as patient No. 1. She had no personal history of atopy, but one brother had extrinsic bronchial asthma. Since one year before her first consultation she had been administering her patients one or two sachets of Plantaben® daily. She had been absent from her work for four months; after returning to it, she had been administering 10 to 12 sachets of the laxative once or twice daily. One month after this she began experiencing pharyngeal pruritus, rhinorrhoea, nasal congestion, cough, wheezing and dyspnoea appearing some 8 to 10 hours after being exposed to psyllium powder. By the time of her first consultation her symptoms appeared within 15 minutes of the exposure and persisted for the whole day, with slight improvement on the days she did not work. She had started using a face mask during work, with little positive results. The physical examination of the patient during her working periods revealed wheezing in both lung fields.

The patient's PEF_R was monitored three times a day for two weeks while she was handling and administering

psyllium, for a further two weeks while she was on leave from her work, and for a final two weeks during which she was working at the nursing home but without exposure to psyllium (it had been substituted by a different laxative). The PEF_R record evidenced a clear deterioration when she manipulated the psyllium powder: during her periods of absence from work her PEF_R was about 400 l/min, and similar values were recorded while she was at work without psyllium exposure; the PEF_R fell to 250 l/min (a 37% drop) when she was working with the psyllium powder.

The complete blood cell count yielded normal results, as did the total IgE quantitation (83 kU/l). Increased specific IgE levels were detected against *D. pteronyssinus* (2.29 kU/l) and psyllium (1.42 kU/l), with negative values for *Lolium perenne*, *Olea europaea* and *Plantago lanceolata*. The nonspecific bronchial hyperreactivity test disclosed mild bronchial hyperreactivity (PD₂₀ = 70 CU methacholine). The same test was repeated after six months of avoiding contact with psyllium, and at this time revealed less bronchial hyperreactivity (PD₂₀ = 155 CU). The skin test with psyllium extract was positive (12 x 6 mm wheal) at the 10% w/v concentration tested; the histamine wheal was 5 x 6 mm, and the tests with the remainder of the airborne allergens yielded negative results. A conjunctival challenge test with *D. pteronyssinus* was negative.

The exposure test with psyllium elicited an immediate bronchial response followed by a late one (dual response). Ten minutes after starting manipulating the powder the FEV₁ fell by 32% and the patient developed cough, wheezing, conjunctival reddening with ocular pruritus and sneezing. These symptoms improved 15 minutes after the administration of inhaled salbutamol, and the spirometric values returned to normality within one hour. Eight hours later the FEV₁ again fell by 28%, and the patient once more developed cough, dyspnoea and wheezing, which remitted under inhaled salbutamol. The patient remained asymptomatic after the psyllium-containing laxative was removed from her place of work.

DISCUSSION

The seeds of *Plantago ovata* (psyllium or ispaghula) are ground to a fine powder for the preparation of bulk laxatives; such laxatives are used by millions of persons world-wide. The powder of the psyllium seeds is a potent allergen that can induce IgE-mediated hypersensitivity when it is inhaled by nurses who dispense psyllium-con-

taining laxatives to their patients^{1,5}, and also in pharmaceutical industry workers who manipulate it in the course of the preparation of psyllium-containing bulk laxatives^{6,7}. The frequency of sensitization among exposed individuals is high: 32% of the industry workers tested had positive skin tests and/or increased specific IgE to psyllium⁷, and 25% of the exposed nurses examined were sensitized¹⁰.

The present paper reports two new cases of nurses with occupational IgE-mediated bronchial asthma caused by psyllium. In both cases, the symptoms disappeared when they avoided contact with the psyllium powder. In case 2, the PEFr monitoring while at home and at work revealed a clear deterioration in the occupational setting; in case 2 no PEFr study was performed, as the patient was asymptomatic at the time of consultation and she had abstained from exposure to psyllium for one year. The methacholine test was positive in case 2 and negative in case 1; negativisation of the nonspecific bronchial hyperreactivity test in patients with occupational asthma who have not been exposed to the causative agent for a long time has been reported previously^{6,11}. The patient of case 1 had not exposed herself to psyllium for one year at the time of testing, and the one of case 2 evidenced a decrease in bronchial hyperreactivity after six months without exposure. We cannot ascertain if this change in the degree of bronchial hyperreactivity was significant, as the reproducibility of the test in our laboratory is not yet established.

The pharmaceutical preparation used for the skin tests and also for the exposure test (Plantaben®, Madaus Cerafarm, Barcelona, Spain) contained the following excipients: saccharine, sodium bicarbonate, tartaric acid, essence of oranges and the orange colour Pal Super. For an unequivocal confirmation that the asthma in our patients had been due to psyllium, and not to any of the excipients, exposure tests either with pure psyllium powder or with the excipients would have been required. Such tests could not be carried out, as both patients refused submitting to further exposure testing. Nevertheless, it is our opinion that the excipients were not the cause of their asthma, because those excipients have not been implicated as aetiological agents in asthma and also because in case 2 the presence of specific IgE antibodies to psyllium was demonstrated.

One patient (case 1) had a positive skin test with psyllium, but her specific IgE levels were not increased. This could have been due to the time she had not been exposed to the agent. This phenomenon has been previously described in some patients with pollen allergy, in whom there are no detectable levels of specific IgE prior to the pollen sea-

son¹². The skin tests with psyllium and the quantitation of the specific IgE have been demonstrated to be highly useful in the diagnosis of psyllium allergy^{1,6,8}. In the two patients here reported, the exposure test with psyllium demonstrated that this was the responsible allergen. The bronchial challenge test with the suspected causative agent is very important in the diagnosis of occupational asthma¹¹. Some authors⁶ have used the technique of having psyllium extract inhaled as an aerosol with the help of a nebuliser, while others^{2,5,7} have tried to reproduce the actual workplace conditions in the allergy laboratory, by having the patient transfer (dust) psyllium powder from one tray to another. Both procedures have been shown to be useful. In our two patients the second procedure was used, eliciting a dual immediate and late response in case 2. The patient of case 1 had only an isolated immediate bronchial response, although the use of corticosteroids after this immediate response might have prevented the late one. Hinojosa *et al.*⁶ observed only immediate responses after the specific bronchial challenge in four patients with occupational asthma induced by psyllium. Cartier *et al.*² found one immediate and three dual responses after exposure tests with psyllium; one further patient required orotracheal intubation because of severe bronchospasm. High-molecular-weight antigens (such as psyllium) induce an immediate response, which in 50% of the cases is followed by a late one (dual response)¹³.

The exposure test with psyllium powder is useful for diagnosing occupational asthma induced by this seed. It is a simple, easy to carry out test, although it must be performed with all due precautions because of the possibility of inducing severe bronchospasm, as in our own case 1 and in the patient reported by Cartier *et al.*². At the beginning of the test the exposure time should be short and the amount of psyllium powder used should be small; they can later be gradually increased as suggested by the patient's tolerance to the exposure.

Some authors have found cross reactivity between psyllium and *Plantago* pollen¹⁴, although this observation has not been confirmed by others^{15,16}. We have not detected *Plantago* pollen hypersensitivity in either of our patients.

Although occupational asthma triggered by ispaghula powder has been previously reported in nurses who poured the contents of the sachets of the laxative into glasses for its administration to the patients, as well as in workers occupied in the manufacture of the laxative and in patients who use it therapeutically, we have considered it interesting to report these two new cases for the following reasons: firstly, in order to call attention onto the

fact that a possible sensitization to psyllium should be investigated in patients with respiratory allergy who are exposed to or have contact with laxatives containing this product; and secondly, in order to strongly suggest that the pharmaceutical industry should change the presentation of those laxatives and substitute the powder with another less inhalable galenic form, such as granules, although this would possibly not prevent those cases of allergy triggered by the ingestion of the preparation.

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