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Ispagula powder - an allergen in the work environment
by Göransson K, Michaelson G

Affiliation: Industrial Health and Medical Service, Volvo Lastvagnar AB, Umeverken, S-90005 Umeå, Sweden.

Key terms: allergen; asthma; bulk laxative; conjunctivitis; dust; ispagula; ispagula powder; psyllium seed; rhinitis; type 1 allergy; work environment

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Ispagula powder

An allergen in the work environment

by KERSTIN GÖRANSSON and N. GUNNAR MICHAELSON 1

Ispagula powder: An allergen in the work environment. Scand. j. work environ. & health 5 (1979) 257—261. Bulk laxatives based on ispagula powder have given no known allergic side effects when administered perorally. Twenty-seven out of 64 workers in a pharmaceutical factory developed rhinitis, conjunctivitis or asthma when engaged in the packing of ispagula husks, an operation which gives rise to dust. The symptoms are accounted for by a type 1 allergy acquired from ispagula husks. This allergy can be demonstrated by intracutaneous and provocation tests. Occupational health measures were taken which reduced the dust content to a minimum; thereafter only one new case of sensitization was recorded during the next 24 months of observation. Five similar cases were reported among nursing staff exposed to the dust of ispagula while administering doses of bulk laxative.

Key words: asthma, bulk laxative, conjunctivitis, dust, ispagula, psyllium seed, rhinitis, type 1 allergy.

Bulk laxatives are taken daily by millions of people, and their use appears to be increasing, particularly in long-term nursing. In many bulk laxatives the effective component comes from the psyllium seed (Testa ispagula) of Plantago ovata. The manufacturing process consists of grinding the seeds to a fine-grained powder. The seeds are then used in the laxative, either in a pulverized form or as a granulate, because of their powerful hygroscopic properties. No side effects have hitherto been reported among patients or nursing staff (Socialstyrelsens biverkningsämnd, personal communication).

In 1969 Bernton (1) reported a case in which a man developed attacks of asthma triggered by the inhalation of psyllium powder while preparing a dose of bulk laxative for his wife. An intracutaneous test with psyllium extract proved positive, and peroral provocation with the laxative led to asthma. In 1975 Busse and Schönenwetter (2) described three workmen who developed asthma after working with pulverized psyllium seed at a pharmaceutical factory. All of them showed a positive reaction to the psyllium extract when given an intracutaneous test, and two developed asthma after inhaling the extract.

In December 1974 bulk laxatives made from ispagula husks began to be packed in dosing sizes at a pharmaceutical fac-
The powder was poured from a large vessel into a packaging machine, an operation which led to dust formation. As production increased, the dust formation grew, and at the same time more employees became involved in the process. In March 1975 employees began to complain of irritation of the eyes and nose, accompanied by running or obstructed noses. The symptoms can be difficult to distinguish from complaints of the type which may be expected to arise during work with a powerful hygroscopic powder in a dry environment with a relative humidity of less than 20%.

When a growing number of employees developed symptoms, the company started an investigation to determine and eliminate the causes of the trouble, and the health service of the company began to cooperate with the Department of Dermatology of the University Hospital, Umeå, to examine whether the syndrome could have an allergenic origin.

MATERIAL

Subjects

A total of 64 employees had had varying degrees of exposure to ispagula dust. The group consisted of 9 men and 55 women, and their average age was 36.5 years. The controls consisted of 77 persons, 31 men and 46 women, with an average age of 37 years. Of these, 43% had atopic rhinoconjunctivitis or asthma, while 57% had no atopic history. The employees and the control group were interviewed regarding their previous medical history and current state of health, and the employee group was also asked about exposure to dust.

Test methods

A water extract of ispagula husk in a concentration of 1:200 was used as the test substance. The extract was prepared by the shaking of ispagula powder for 24 h in a physiological saline solution to which 0.4% phenol had been added. The water phase was then centrifuged and sterile filtered. A more concentrated extract could not be prepared because of the strong hygroscopic properties of ispagula. The same extract was used for the skin test and for the provocation test. A physiological saline solution to which 0.4% phenol had been added was used as a control solution in the skin test and the provocation test.

For the skin test 0.04 ml of the ispagula extract, the histamine solution (0.1 mg/ml), and the control solution was administered intracutaneously. The test reaction was read after 15 min, and the size of the weal was evaluated in relation to the histamine reaction, which was graded to 2+. (With the prick method the skin reaction was too weak and difficult to evaluate because the concentration of the extract was weak. Therefore we used the intracutaneous skin test, which is more sensitive than the prick method even if the risk for false positive results is greater.)

Provocation was given either by the application of 1–2 drops of ispagula extract to the conjunctiva or the mucous membrane of the nose or by the inhalation of 2 ml of the extract in a nebulizer. All the provocation results were compared with the corresponding reaction to the control solution. In two cases provocation was achieved when dust from ispagula powder was raised in front of the subject.

All 64 of the employees were given intracutaneous tests, and provocation tests were carried out in 35 cases. A total of 60 intracutaneous and 17 provocation tests, both nasal and conjunctival, was made on the controls.

RESULTS

Preliminary investigation

Of the 64 employees, 27 complained of discomfort when handling ispagula, while 37
experienced no discomfort. Thirteen had rhinoconjunctivitis, seven rhinitis only, and one conjunctivitis only. Six were affected by both rhinitis and irritation of the air passages. Three employees who experienced discomfort in the respiratory passages had more pronounced asthma, and the other three displayed moderate symptoms, with an urge to cough and a certain tightness of the chest.

The majority of them had developed their symptoms within two months after starting work which involved exposure to ispagula dust. Some stated that the symptoms had appeared immediately, whereas a few had worked for up to six months with the ispagula preparation before the symptoms had developed. Most of them were troubled within the first hour of starting a shift, but three employees did not develop the symptoms until some hours after finishing work. In the case of most of those examined the symptoms abated after a few hours, and all were free of discomfort after 1—2 days' absence from the workplace.

Of the 64 persons exposed to ispagula, 28 had positive intracutaneous tests, with skin reactions between 0.5 + and 4 +. In the control group there were six positive reactions, their strength ranging from 0.5 + to 2 +. The number of positive intracutaneous reactions in the group exposed to ispagula was higher than that in the control group; the difference was statistically significant ($\chi^2 = 16.07; p < 0.01$) (table 1).

Twenty-seven of the 64 persons exposed to ispagula had symptoms, while 37 did not. Eighteen of the 27 with symptoms had positive reactions to the intracutaneous test. Of the 37 who were free of symptoms, 10 had positive intracutaneous tests. If the groups experiencing and not experiencing discomfort are compared, the frequency of positive intracutaneous tests in the group reporting discomfort is greater to a statistically significant degree ($\chi^2 = 9.97; p < 0.01$) (table 2).

Provocation tests were given to all employees who had experienced discomfort. Of the 27 thus involved, 12 had a positive reaction to both the provocation and the intracutaneous test, and six had a positive reaction only to the provocation test. Six displayed a positive reaction only to intracutaneous testing. Three had negative intracutaneous and provocation tests (table 3).

Nasal and conjunctival provocation tests were carried out on eight of the ten exposed individuals who had no symptoms but who had had positive intracutaneous tests. For all of them the result was negative.

Seventeen persons from the control group were given nasal and conjunctival provocation tests, all with negative results.

The 64 employees included 11 who reported previous or current atopic illness (atopic eczema and/or atopic rhinoconjunctivitis). Of these 11, 5 had trouble when handling ispagula and positive intracutaneous and/or provocation tests.

Table 1. A comparison of the immediate reactions of exposed employees and controls to intracutaneous tests with ispagula extract.

| Skin test | Exposed | Controls | Total |
|-----------|---------|----------|-------|
| Positive  | 28      | 6        | 34    |
| Negative  | 38      | 54       | 90    |
| Total     | 64      | 60       | 124   |

Table 2. A comparison of the skin test reactions of ispagula-exposed employees with and without symptoms.

| Skin test | Number with symptoms | Number without symptoms | Total |
|-----------|-----------------------|-------------------------|-------|
| Positive  | 18                    | 10                      | 28    |
| Negative  | 9                     | 27                      | 36    |
| Total     | 27                    | 37                      | 64    |

Table 3. Results of the provocation and skin tests of the 27 ispagula-exposed employees with symptoms.

| Provocation test | Skin tests |
|------------------|------------|
| Positive         | 12         | 6          |
| Negative         | 6          | 3          |
Follow-up investigation

In 1974, when the packaging of ispagula powder in dosing sizes started, the work generated a lot of dust. In August 1975 the production facilities were rebuilt, and the work environment was radically improved. No specific method of measuring the ispagula dust content of the air breathed was available, so the overall dust level was measured. At the place where the machine operators were working, it was 1.1—1.5 mg/m³ before the rebuilding and less than 0.05 mg/m³ after the rebuilding.

The preceding results describe the symptoms and reactions developing among the employees during the eight months up to August 1975. Twenty-four months after the work environment was redesigned, a new examination was made of the 37 persons not reporting discomfort when working with ispagula. In the new work environment one additional employee showed a positive reaction to an intracutaneous test, while two who had previously had positive reactions to intracutaneous tests had developed symptoms.

DISCUSSION

Ispagula powder dissolved in water has not given rise to any known side effects. (Socialstyrelsens biverkningsnämnd, personal communication). We have, however, found that irritation of the mucous membranes of the eye and of the air passages can occur after exposure to ispagula in the form of dust, even though the period of exposure may have been relatively short.

Our study shows, by comparison with a control group, that the group exposed to ispagula had a distinctly higher frequency of positive reactions to intracutaneous testing, especially when discomfort had been experienced. But 6 of the 60 controls also had a positive intracutaneous test. Most of them could have been false positive reactions. In one case however the reaction was as high as 2+. It is improbable that this reaction can be accounted for by a nonspecific local and irritant effect of the ispagula extract. A more likely explanation might be cross-sensitization with a closely related allergen of which we are not aware.

The frequency of positive reactions was very high in the group exposed to ispagula, and particularly in the subgroup reporting discomfort. This fact, together with the negative reaction of the control group, suggests that the ispagula extract does not cause nonspecific irritation of the mucous membrane. Six persons in the group complaining of discomfort and showing positive reactions to intracutaneous tests reacted positively to provocation attempts. Unfortunately we did not have a more concentrated extract available, so the study could not be completed.

The study suggests that ispagula husks can induce type I allergy, as defined by Gell and Coombs (3). This conclusion is also supported by a preliminary supplementary open study of peroral provocation with ispagula powder of employees reporting discomfort and showing a positive reaction to intracutaneous and provocation tests. Peroral provocation of these persons with a therapeutic single dose caused the same symptoms in the respiratory passages and the eyes as had been observed both in the dusty environment and after provocation with ispagula extract.

As the ispagula extract is obtained from a plant, Plantago ovata, it was of interest to investigate whether exposed individuals with atopic diathesis showed a greater tendency to develop ispagula allergy than "nonatopics." There was no overrepresentation of atopics with ispagula allergy among the employees.

As the plant from which ispagula powder is obtained is a Plantago species, there was also interest in discovering whether ispagula sensitization could involve a risk of cross-allergy with meadow plants such as grass pollen. Eight individuals experiencing symptoms but without any known atopic disease were therefore given intracutaneous tests for ten common pollens (commercially produced allergen). One of these meadow plants was Plantago lanceolata, a member of the same family as Plantago ovata. All of these tests were negative. The study gives no evidence of cross-reaction.
If positive intracutaneous or provocation tests are regarded as evidence of allergy, 34 of the 64 persons exposed to ispagula dust in concentrations of more than 1 mg/m³ were demonstrated to have ispagula allergy. The risk of sensitization can be reduced very substantially by effective occupational health measures.

In conclusion it may be mentioned that the manufacture of bulk laxatives containing ispagula is not the only situation in which high levels of ispagula dust can arise. When dispensing medicines in hospitals, through the open doors of the medicine cabinets, for example, nursing personnel may be exposed to such high dust levels that a risk of sensitization ensues. We have confirmed five cases of allergy to ispagula dust in the air passages of the nursing staff of a long-term clinic. The sensitization appears to apply to all products giving rise to ispagula dust and not just to a particular preparation.

Dust from ispagula husks is clearly a potent allergen with the ability to cause manifestations of allergic disease in the form of conjunctivitis, rhinitis and asthma. Anyone handling the substance in such a way that dust forms, either producer or consumer, may run the risk of being sensitized.

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