

Primin sensitization in north-eastern Italy: a temporal trend from 1996 to 2012

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Summary

Background. Primin is the main contact allergen found in the ornamental plant *Primula obconica* Hance.

Objective. To analyse the temporal trend of sensitivity to primin in north-eastern Italy and to evaluate the associations with occupations in our geographical area.

Methodology. From 1996 to 2012, 24 052 consecutive patients with suspected allergic contact dermatitis were patch tested in north-eastern Italy. Individual characteristics were collected through a standardized questionnaire in eight departments of dermatology or occupational medicine.

Results. The overall prevalence of primin sensitization was 1.9%; the prevalence was significantly higher in women (2.6%) than in men (0.5%). The Pordenone area had the higher prevalence of sensitization, which reached 6% in 1999–2001. We found a significant association between primin sensitization and household workers [odds ratio (OR) 2.3; 95% confidence interval (CI): 1.61–3.35], retired people (OR 1.8; 95%CI: 1.22–2.81), woodworkers (OR 2.1; 95%CI: 1.10–6.18), and chemical industry workers (OR 2.9; 95%CI: 1.05–8.29).

Conclusion. Our study showed that contact allergy to primin is still relevant in north-eastern Italy. The frequency of sensitization is decreasing, but for retired and household workers it is still >4%. Our results suggest the need to promote the use of primin-free *P. obconica* in Italy.

Key words: allergic contact dermatitis; epidemiology; occupational; patch test; primin.

Primin (2-methoxy-6-pentyl-1,4-benzoquinone) is the main allergen in *Primula obconica* Hance, family Primulaceae, an ornamental plant introduced to the United Kingdom from China in 1880 that soon became popular as a pot plant in other countries of Europe and in the United States (1).

The first case of allergic contact dermatitis caused by this species was described in the horticultural literature by White in 1888 (2). Sensitization to *P. obconica* can occur by direct contact with plants, while an individual is removing dead flowers and leaves, or by indirect contact, for example via handshakes or door handles. Primin can be directly emitted from the plant, causing airborne allergic reaction in some sensitized patients. Airborne allergic contact dermatitis may also be induced by small dust particles derived from the plant surface or pollen (3, 4).

Allergic contact dermatitis caused by *P. obconica* is more common in females over the age of 35 years (3); it typically

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affects older woman who take an interest in tending the plant, but occupational cases have also been seen (5).

Although primin has been detected in several other species of primula, allergic contact dermatitis caused by other species has been reported only rarely (3).

Primin-free cultivars of *P. obconica* have been available in Europe since 2000. In Italy, primin-free plants have been sold since 2007 with the 'Touch me' label (6, 7).

In testing with the European baseline series from 1985 to 2005, there was a prevalence of 1.1% of sensitization to primin (0.3% in men and 1.6% in women) (8). It is not tested in the US baseline series, owing to the low incidence of primin-induced dermatitis (9).

In the present study, we investigated the prevalence of primin sensitization in a patch test population from north-eastern Italy, evaluated between 1996 and 2012, in order to:

- analyse the temporal trend of this sensitization during this period;
- find associations between primin sensitization and occupations in our geographical area.

Patients and Methods

Patients

From 1996 to 2012, 24 052 consecutive patients (aged >15 years) with symptoms and/or signs of suspected allergic dermatitis were patch tested in eight departments of dermatology or occupational medicine in north-eastern Italy: Bolzano, Trento, Rovigo, Padua (three clinics), Pordenone, and Trieste (Bolzano, Trento and Rovigo participated only from 1998 to 2004). Individual characteristics, occupational history and a personal and family history of atopy (asthma and/or allergic rhino-conjunctivitis with at least one positive prick test reaction to relevant aeroallergens) were collected through a standardized questionnaire (10).

After exclusion of 278 patients because of a lack of the data that were necessary for the study design (related to personal history – e.g. sex or age – or incomplete patch testing), 23 774 patients were finally included in the study.

All patients were assigned to occupational categories, with related job groups being aggregated into larger categories (for example, nurses, physicians and other hospital workers were collapsed into a 'healthcare workers' category). In a similar way, all body site categories were aggregated into larger categories (for example, fingers, palms and dorsa of hands were collapsed into 'hands').

We performed occupational category-related analysis on 20 711 patients from our population, discarding the

rest of the sample because of incomplete or inaccurate collection of information on patients' occupations.

We estimated exposure by considering the patient's occupation. As sensitization is often acquired within a short period of exposure, we did not take into account the complete occupational history, but instead only the patient's job at the time of evaluation. Because the study population included patients who attended health services for suspected allergic dermatitis, there may have been a potential source of selection and observational bias. However, this was minimized by the large study population analysed, and by the fact that all patients were enrolled in the same way.

Because we considered patients in occupational categories, we performed statistical analysis taking into account sex and age differences in order to minimize confounding factors, as described in 'Statistical analysis'. Moreover, we compared our findings with literature data, confirming and, in turn, strengthening several of the associations that we found.

Patch tests

Finn Chambers® on Scanpor® tape (Epitest Ltd, Tuusula, Finland) and allergens from FIRMA (Firenze, Italy) were used to perform patch tests on patients with the European baseline series (11).

The tested allergens included primin 0.01% pet. Patches were applied on the upper back, and removed after 48 hr. The sites were examined on removal and 24 or 48 hr after removal, according to ICDRG guidelines (12).

Reactions of grades +, ++ and +++ in the second examination were considered to be positive. Doubtful reactions ($\pm$ and '?') were considered to be negative.

Statistical analysis

Data analysis was performed with the software STATA™ v. 12.0 (Stata Corp., LP, College Station, TX, USA). Categorical data were cross-tabulated into $k \times k$ contingency tables, and compared by use of the chi-square test. The associations between patch test results, year of patch testing (according to 3-year calendar periods: 1996–1998, 1999–2001, 2002–2004, 2005–2007, 2008–2010, after 2010) and occupations were investigated by means of multivariate logistic regression analysis. We performed stratification by cities of provenance of the data, and studied the different incidence rates of primin sensitization during the study in the different cities in north-eastern Italy. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from the coefficients and the standard

errors of logistic regression output. Logistic analysis was conducted with adjustment of results by age, and with white collar workers as the reference group. A trend test across ordered groups was performed with Cuzick's test for trend.

Patients with missing data for relevant variables were excluded from analysis.

A *p*-value of <0.05 was established as the limit of statistical significance.

Results

The study population included 16 056 women (67.5%) and 7718 men (32.5%), and the results are shown in Table 1.

The mean age of the population was similar for male and female patients. There was a higher frequency of occupational dermatitis in males (9.3%) than in females (6.9%), and dermatitis most frequently involved the hand/forearm in both sexes (30–33.2%) and the face in women (17.3%). The overall prevalence of primin sensitization was 1.9%; the prevalence was significantly higher in women (2.6%) than in men (0.5%) (*p* < 0.01).

The relevance of sensitization was 55% for present contact with the plant and 31% for past contact with the plant.

Primin sensitization in different occupational group is shown in Table 2, where bold type indicates occupations that were significantly associated with primin sensitization as compared with white collar workers.

We found significant associations between primin sensitization and household workers (OR 2.3; 95%CI: 1.61–3.35), retired people (OR 1.8; 95%CI: 1.22–2.81), woodworkers (OR 2.1; 95%CI: 1.10–6.18), and chemical industry workers (OR 2.9; 95%CI: 1.05–8.29).

Primin sensitization was associated with female sex (2.72%; OR 5.02; 95%CI: 3.64–6.93), residence in the Pordenone area (4.4%; OR 3.44; 95%CI: 2.85–4.16), hand dermatitis (3.34%; OR 2.18; 95%CI: 1.80–2.65), and fragrance mix sensitization (3.88%; OR 4.95; 95%CI: 1.8–8.1) (Table 3).

The temporal trends for primin sensitization in different geographical areas are shown in Fig. 1.

The Pordenone centre had the higher prevalence of sensitization, which reached 6% in 1999–2001, decreased to 2.8% in 2008–2010, and increased in the last 2 years analysed (4.7%). In the Trieste and Padua centres, the prevalence of sensitization was very low, decreasing constantly in the years considered (*p* < 0.001).

Table 1. Characteristics of the studied population (n° = 23 774)

	Women 67.5%	Men 32.5%	Total 100%
Age (years ± SD)	42.9 ± 17	43.2 ± 17	43.0 ± 17
Occupational dermatitis (%)	6.9	9.3**	7.7
Hand/forearm dermatitis (%)	30	33.2**	31.0
Atopic eczema (%)	7.2	7.0	7.2
Leg (%)	5	7.4**	5.7
Face (%)	17.3**	9.4	14.8
Other sites (%)	29.4	31.5**	30.0
Positive primin patch test, no. (%)	422 (2.6)**	41 (0.5)	463 (1.9)

SD, standard deviation.

***p* < 0.05.

Table 2. Prevalence of primin sensitization in occupational groups

Occupation	Total, n	Primin-positive, n (%)	OR	95% CI
White collar workers	5355	48 (0.95)	1	–
Chemical processing	198	4 (2.08)	2.9	1.05–8.39
Household workers	2917	146 (5.16)	2.3	1.61–3.35
Wood processing workers	345	6 (1.76)	2.1	1.10–6.18
Professional drivers	236	2 (0.89)	2.0	0.47–8.47
Retired	3416	142 (4.37)	1.8	1.22–2.81
Farmers	208	3 (1.49)	1.6	0.50–5.35
Waitress and restaurant workers	997	12 (1.24)	1.3	0.70–2.5
Healthcare workers	2534	33 (1.33)	1.2	0.79–1.95
Construction workers	1118	9 (0.84)	1.2	0.59–2.52
Mechanics	1110	7 (0.67)	1.0	0.48–2.38
Textile and leather workers	530	5 (0.96)	0.9	0.38–2.47
Unemployed	410	4 (0.98)	0.9	0.35–2.79
Other occupations	851	6 (0.74)	0.8	0.37–2.08
Hairdressers and beauticians	282	2 (0.78)	0.7	0.18–3.19
Domestic workers	288	1 (0.38)	0.2	0.03–1.98
Paper production workers	54	0	–	–

CI, confidence interval; OR, odds ratio

The ORs and 95% CIs were evaluated with multinomial logistic analysis adjusted for age, with office workers as the reference category. Statistically significant results are in bold.

Discussion

P. obconica is a very common plant in Italy, being used in gardens and in flower boxes, grown in Italy, and imported. Often, during the spring, *P. obconica* can be found in many houses with a garden.

Table 3. Factors associated with primin sensitization

	%	OR	95% CI
Female	2.72	5.02	3.64–6.93
Body site*			
Hand	3.34	2.18	1.80–2.65
Face	2.48	1.13	0.90–1.45
Geographical area†			
Pordenone	4.44	3.44	2.85–4.16
Padua	1.82	0.86	0.70–1.05
Trieste	0.88	0.35	0.26–0.47
Associated haptens			
Fragrance mix	3.88	4.95	1.8–8.1

CI, confidence interval; OR, odds ratio

*Reference category: subjects not sensitized to primin.

†Analysis was performed only for centres that participated for the entire duration of the study.

This study investigated the prevalence of primin sensitization in a database of 23 774 subjects with suspected allergic contact dermatitis, patch tested during 1996–2012 in north-eastern Italy. The overall average prevalence rates of primin sensitization from 1996 to 2012 were 2.6% in female subjects and 0.5% in male subjects (overall prevalence 1.9%); this prevalence decreased from 2.2% to 1.35% in 1996–1998 and 2008–2010, respectively, and increased after 2010 only in the Pordenone area. These figures are slightly higher than those in other European studies, which have reported an overall prevalence from 0.2% to 1.7% (3, 6, 8, 13–18). This prevalence may still be high because of the relatively late

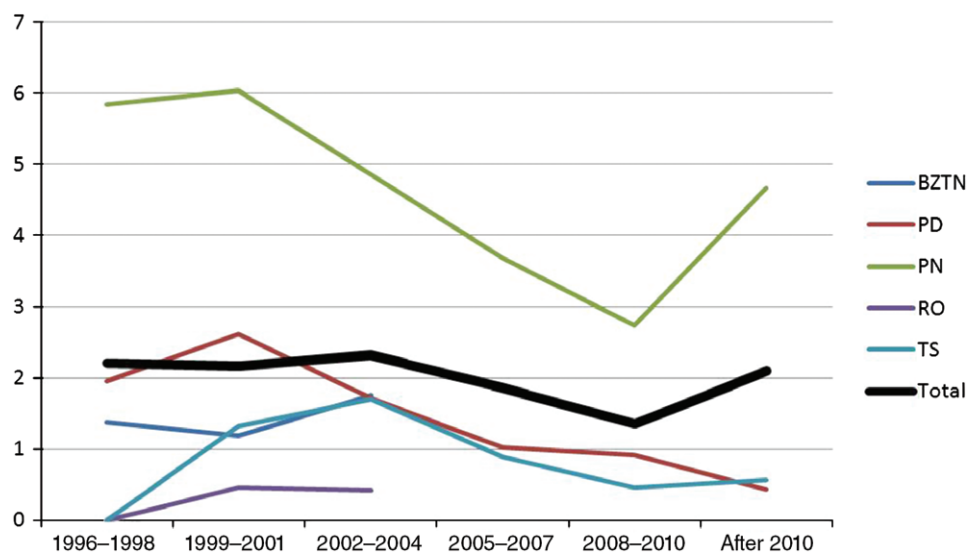
introduction of primin-free *P. obconica* into the Italian market. Because of the very low sensitization recorded, primin is not tested in some other countries, such as the United States and some African states (9, 18, 19).

We found large differences in the prevalence of primin sensitization between different areas, including a very high prevalence for patients living in the Pordenone area. This finding could be explained by the geographical characteristics of this region, with small towns and very large rural areas where every house has flowers outside and people love gardening.

As in other studies (3, 5), the hands were the most frequently involved, because of contact with flowers and other parts of the plant. Dermatitis of the face was also seen following either direct or indirect (i.e. airborne) contact (3, 5, 6), and females were more frequently sensitized than males (3). As reported by other authors, we found a significant association between primin sensitization and retirement and household work, owing to the more frequent non-occupational exposure to this plant in these subjects (16, 20, 21).

The significantly higher sensitization rates in woodworkers and in chemical industry workers could be explained by possible cross-reactions with woods containing quinones (22) and hydroquinone-related chemicals, respectively. However, few of the workers were sensitized, and the majority of them were employed in the Pordenone area, where we found the highest prevalence of primin sensitization.

This is the first study of primin sensitization in north-eastern Italy, and the results are interesting.

**Fig. 1.** Prevalence (%) of primin sensitization in different centres over time. BZTN, Bolzano and Trento; PD, Padua; PN, Pordenone; RO, Rovigo; TS, Trieste.

Nevertheless, some limitations of this study deserve attention. Although the study was based on a large sample of individuals, the study population included patients who attended health services for suspected allergic dermatitis, and, for this reason, our results may be affected by selection bias.

The merging of smaller groups into larger ones – because of the statistical limitations of small group analysis – may also have led to some loss of data, although we paid more attention to categories previously reported in the literature and/or having a higher prevalence than the average. Another possible limitation of this study is related to its multicentre design, which may have affected the data recording in different centres, although all participants accepted a standardized protocol.

Conclusion

Our study showed that contact allergy to primin is still relevant in north-eastern Italy, and we therefore suggest

that this hapten should be retained in the baseline patch test series. Although the prevalence of primin-positive reactions decreased in the years from 1996 to 2012, the prevalence is still very high (> 4%) in retired persons and household workers. Data from other countries show a similar decreasing trend (5, 17), but the prevalence of sensitization is <1%. Our results suggest the need to promote the use of primin-free *P. obconica* also in Italy, particularly in the Pordenone area, where we found the highest sensitization rate.

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