

p-Phenylenediamine sensitization and occupation

Andrea Malvestio¹, Massimo Bovenzi¹, Mohamad Hoteit¹, Anna Belloni Fortina², Andrea Peserico², Maria Teresa Corradin³ and Francesca Larese Filon¹

¹Clinical Unit of Occupational Medicine, University of Trieste, 34129 Trieste, Italy, ²Institute of Dermatology, University of Padua, 3510 Padova, Italy, and

³Dermatology Unit, Santa Maria degli Angeli Hospital, 33170 Pordenone, Italy

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Summary

Background. p-Phenylenediamine (PPD) is an extreme delayed-type skin sensitizer, and is relevant in both occupational and non-occupational exposures.

Objectives. To estimate the prevalence of PPD sensitization in a population of consecutive patients with suspected allergic contact dermatitis who attended units of dermatology or occupational medicine in north-eastern Italy and to investigate the association between their PPD sensitization and occupation.

Patients/Materials/Methods. A total of 14 464 patients (67.6% women and 32.4% men) with suspected allergic dermatitis underwent patch testing. The associations between patch test results and occupations were studied by multivariate logistic regression analysis.

Results. In both sexes, PPD sensitization was significantly associated with hairdressing and beauty occupation [women, odds ratio (OR) 6.58, 95% confidence interval (CI) 3.76–11.50; men, OR 22.3, 95% CI 4.18–119]. In the female group, PPD sensitization was also significantly higher in professional drivers (OR 5.31, 95% CI 1.76–16.1), barmaids (OR 1.89, 95% CI 1.04–3.44), and cleaners (OR 1.82, 95% CI 1.24–2.68). In the male group, PPD sensitization was significantly higher in bakers and waiters (OR 13.0, 95% CI 1.38–123), household workers (OR 8.46, 95% CI 1.68–42.8), and printers (OR 5.68, 95% CI 1.50–21.5).

Conclusions. Our study showed that workers in several occupations may be at higher risk of developing sensitization to PPD. It is of importance to reduce possible exposure to PPD-crossreacting substances in these occupations.

Key words: dermatitis; occupation; patch test; p-phenylenediamine (PPD).

The importance of p-phenylenediamine (PPD) as an extreme delayed-type skin sensitizer has increased considerably in recent years (1). This colouring agent has been used in hair dyes for decades as a precursor in oxidative permanent hair dye products. PPD is currently

considered to be the main allergen causing adverse reactions to hair dyes in women (2, 3).

The issue of severe allergic reactions to hair dye products has also become relevant in men and children (1, 4–6), and cases of contact urticaria, lymphomatoid reactions and anaphylaxis have been reported (7–9). Although PPD is used in hair dyes, crossreacting substances may be present in textile dyes (10), leather dyes (11), fur dyes, and 'black' rubbers (12). Furthermore, PPD is used in so-called 'black henna tattoos', where it intensifies the colour, speeds up the staining process, and makes the 'tattoo' last longer (13, 14); such use is illegal in Europe.

Correspondence: Francesca Larese Filon, UCO Medicina del Lavoro, via della Pietà 19, 34129 Trieste Italy. Tel: +390403992215; Fax: +39368199. E-mail: larese@units.it

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Contact dermatitis caused by PPD in hair dyes often extends beyond the scalp to include the forehead, neck, eyelids, and face (13). These allergic reactions may continue for several weeks or even months, because the allergen persists in the skin. In professional hairdressers, skin lesions are almost always limited to the hands, and less frequently include the face, forearms, or knees, but spread of lesions has been reported, although rarely (15). Skin lesions usually include pruritic, oedematous, erythematous scaly patches and plaques; sometimes, vesicular lesions may occur. These lesions can take weeks to fully resolve, and may require treatment with oral corticosteroids (13). In rare cases, the reaction to PPD can be so severe that hospitalization is required (4, 16).

The role of occupation in PPD sensitization has not been fully explored: although it is known that there is an association between PPD allergy and hairdressing, there is insufficient information about other occupations that could be associated with PPD sensitization.

The aim of the present study was to estimate the prevalence of PPD sensitization in a population of consecutive patients with suspected allergic contact dermatitis who attended units of dermatology or occupational medicine in north-eastern Italy. A further aim was to investigate the association between PPD sensitization and various individual and occupational risk factors.

Patients and Methods

Patients

From 1997 to 2004, a total of 15 217 consecutive patients with symptoms and/or signs of suspected allergic dermatitis were patch tested in eight units of dermatology or occupational medicine in north-eastern Italy (Belluno, Bolzano, Padova, Pordenone, Rovereto, Rovigo, Trento, and Trieste). A standardized questionnaire was used to collect information including occupational history, personal and familiar history of atopy (asthma and/or allergic rhino-conjunctivitis with at least one positive prick test reaction to relevant aeroallergens), and dermatitis localization (17). We excluded 753 patients with missing responses for personal and occupational history or with incomplete patch testing. Finally, 14 464 consecutive patients were included in the study.

Patch tests

The patients were patch tested with the European baseline series, using Finn Chambers® on Scanpor® tape. The tested allergens included PPD 1% in petrolatum (FIRMA,

Firenze, Italy; Chemotechnique Diagnostics, Vellinge, Sweden). All allergens were applied on the upper back and removed after 48 hr. The sites were examined on removal and 24 hr after removal, according to the International Contact Dermatitis Research Group guidelines. Reactions of grades +, ++ and +++ were considered to be positive.

Statistical analysis

Data analysis was performed with the software STATA v. 10.1 (Stata Corporation, College Station, TX, USA). Continuous variables were summarized with the median as a measure of central tendency and the range as a measure of dispersion.

The difference between independent groups was tested with the Mann–Whitney test. The differences between categorical data cross-tabulated into contingency tables were tested with the χ^2 -statistic.

The associations between patch test results and occupation were investigated by means of multivariate logistic regression analysis, while controlling for age (five categories: 14–25 years; 26–35 years; 36–45 years; 46–55 years; ≥ 56 years), patch testing unit, personal and familiar history of atopy, and site of skin lesions. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from the coefficients and the standard errors of logistic regression output, taking office workers as the reference category. Logistic analysis was conducted by sex separately. A p -value < 0.05 was considered to be significant.

Results

The study population included 9771 women (67.6%) and 4693 men (32.4%) (Table 1). Men were slightly older than women (mean difference: 0.8 year), but the difference was significant because of the large samples involved

Table 1. Characteristics of the study population. Age is given as median (range). The other variables are given as numbers (%)

	Women (<i>n</i> = 9771)	Men (<i>n</i> = 4693)	Total (<i>n</i> = 14 464)
Age (years)	39 (14–94)	39 (19–85)*	39 (14–94)
Personal atopy	1627 (16.6)	702 (15.0)**	2329 (16.1)
Familiar atopy	895 (9.2)	310 (6.6)***	1205 (8.3)
Hand/forearm dermatitis	2625 (26.9)	1486 (31.7)***	4111 (28.4)
Face eczema	2165 (22.1)***	588 (12.5)	2753 (19.0)
p-Phenylenediamine sensitization	399 (4.1)	110 (2.3)***	509 (3.5)

Mann–Whitney test: * $p < 0.01$. χ^2 -statistic: ** $p < 0.05$; *** $p < 0.001$.

Table 2. Prevalence of p-phenylenediamine sensitization among females in various occupational groups. The odds ratios (ORs) and 95% confidence intervals (CIs) for the associations with occupation are adjusted by age, patch testing unit, personal and family history of atopy, and site of skin lesions; office workers are the reference category

Occupation	Sample, n (%)	Prevalence of p-phenylenediamine sensitization, n (%)	OR	95% CI
Office workers	2206 (22.6)	66 (3.0)	1.0	—
Printing trades workers	44 (0.4)	0 (0)	—	—
Glass plant workers	11 (0.1)	0 (0)	—	—
Bakers and food serving workers	11 (0.1)	0 (0)	—	—
Pensioners	1084 (11.1)	34 (3.1)	0.84	0.51–1.40
Metal and mechanical workers	216 (2.2)	6 (2.8)	0.93	0.40–2.21
Wood processing workers	57 (0.6)	2 (3.9)	0.94	0.22–3.99
Food processing workers	96 (1.0)	3 (3.1)	1.00	0.31–3.28
Electrical and electronic workers	34 (0.3)	1 (2.9)	1.01	0.14–7.60
Other professions*	1637 (16.8)	60 (3.7)	1.07	0.73–1.57
Personal healthcare workers	719 (7.4)	25 (3.5)	1.12	0.69–1.81
Domestic workers	1641 (16.8)	79 (4.8)	1.30	0.89–1.89
Textile and leather workers	291 (3.0)	12 (4.1)	1.31	0.70–2.48
Building and related trades workers	214 (2.2)	10 (4.7)	1.42	0.71–2.83
Chemical processing workers	97 (1.0)	5 (5.2)	1.57	0.61–4.04
Agricultural workers	62 (0.6)	4 (6.5)	1.80	0.63–5.17
Cleaners	932 (9.5)	54 (5.9)	1.82	1.24–2.68
Bar workers	252 (2.6)	14 (5.6)	1.89	1.04–3.44
Car, bus and truck drivers	31 (0.3)	4 (12.9)	5.31	1.76–16.10
Hairdressers and beauticians	136 (1.4)	20 (14.7)	6.58	3.76–11.5

*Students, teachers, etc.

($p < 0.01$). The crude prevalences of personal and familiar atopy and sensitization to PPD were significantly greater in women than in men ($p < 0.001$). In the male population, symptoms and/or signs of dermatitis were more frequently localized in the hands and/or forearms, whereas in women dermatitis was more often confined to the face ($p < 0.001$) and other sites.

Tables 2 and 3 show the occupations in the study population, the prevalence of PPD sensitization, and the association with occupations, with adjustment for potential confounders.

Descriptive analysis of employment sectors showed that women were more prevalent in domestic, cleaning, healthcare and hairdressing occupations (Table 2), whereas men predominated in industrial, agricultural and driving professions (Table 3).

In both sexes, PPD sensitization was significantly associated with hairdressing and beauty occupation (women, OR 6.58, 95% CI 3.76–11.50; men, OR 22.3, 95% CI 4.18–119).

When compared with the office workers, in the female group PPD sensitization was significantly higher in professional drivers (OR 5.31, 95% CI 1.76–16.1), barmaids (OR 1.89, 95% CI 1.04–3.44), and cleaners (OR 1.82, 95% CI 1.24–2.68) (Table 2). The association with domestic work was positive in women, but not statistically significant (OR 1.30, 95% CI 0.89–1.89).

In the male group, PPD sensitization was significantly higher in bakers and waiters (OR 13.0, 95% CI 1.38–123), domestic workers (OR 8.46, 95% CI 1.68–42.8), printers (OR 5.68, 95% CI 1.50–21.5), and pensioners (OR 3.0, 95% CI 1.29–6.99) (Table 3).

Age was a significant predictor of PPD sensitization in both sexes, although limited to age group 46–55 years (women, OR 2.10, 95% CI 1.46–3.02; men, OR 2.29, 95% CI 1.10–4.80) (Table 4). Personal and familiar atopy were not associated with PPD sensitization.

Discussion

In this study, PPD sensitization was found to be more prevalent in women (4.1%) than in men (2.3%). This finding may be attributable to the higher use of hair dye products containing PPD in the female group. Søstved (2) found that 74.9% of women and 18.4% of men had, at one time, dyed their hair, and 5.3% of them had experienced an allergic-like reaction to the hair dye. Kiec-Swierczynska et al. (18) found the prevalence of PPD sensitization to be twice as high in men (7.5%) as in women (3.4%), with an overall positive response in 4.8% of the tested patients. In 2008, Thyssen et al. (19) reviewed the available literature on patch testing data from dermatitis patients. They found that the median prevalence of PPD sensitization among dermatitis patients was 4.3% in Asia, 4.0% in

Table 3. Prevalence of p-phenylenediamine sensitization among males in various occupational groups. The odds ratios (ORs) and 95% confidence intervals (CIs) for the association with occupation are adjusted by age, patch testing unit, personal and family history of atopy, and site of skin lesions; office workers are the reference category

Occupation	Sample, <i>n</i> (%)	Prevalence of p-phenylenediamine sensitization, <i>n</i> (%)	OR	95% CI
Office workers	1024 (21.8)	15 (1.5)	1.0	—
Electrical and electronic workers	113 (2.4)	0 (0)	—	—
Bar workers	108 (2.3)	1 (0.9)	0.59	0.08–4.58
Car, bus and truck drivers	146 (3.1)	2 (1.4)	0.93	0.21–4.16
Healthcare workers	187 (4.0)	3 (1.6)	1.06	0.30–3.76
Textile and leather workers	108 (2.3)	2 (1.9)	1.15	0.26–5.15
Metal and mechanical workers	436 (9.3)	8 (1.8)	1.24	0.51–2.99
Others	689 (14.7)	15 (2.2)	1.38	0.65–2.95
Agricultural workers	78 (1.7)	2 (2.6)	1.45	0.32–6.60
Cleaners	239 (5.1)	6 (2.5)	1.52	0.56–4.11
Building and related trades workers	331 (7.0)	9 (2.7)	1.68	0.71–3.95
Chemical processing plant workers	114 (2.4)	4 (3.5)	2.35	0.75–7.34
Wood processing workers	75 (1.6)	3 (4.0)	2.37	0.65–8.62
Glass plant workers	25 (0.5)	1 (4.0)	2.53	0.31–20.8
Pensioners	888 (18.9)	29 (3.3)	3.0	1.29–6.99
Food processing workers	52 (1.1)	2 (3.8)	3.58	0.77–16.6
Printing trades workers	39 (0.8)	3 (7.7)	5.68	1.50–21.5
Household workers	18 (0.4)	2 (11.1)	8.46	1.68–42.8
Bakers and food serving workers	9 (0.2)	1 (11.1)	13.0	1.38–123
Hairdressers and beauticians	13 (0.3)	2 (15.4)	22.3	4.18–119

Table 4. Association between p-phenylenediamine sensitization and age and personal and familiar atopy by sex. The odds ratios (ORs) and 95% confidence intervals (CIs) are adjusted by occupation, patch testing unit, and site of skin lesions

	Women		Men	
	OR	95% CI	OR	95% CI
Age groups (years)				
14–25	1.0	—	1.0	—
26–35	0.90	0.63–1.28	0.88	0.40–1.97
36–45	1.30	0.91–1.85	1.88	0.90–3.93
46–55	2.10	1.46–3.02	2.29	1.10–4.80
>55	1.47	0.96–2.26	0.90	0.36–2.27
Personal atopy	0.98	0.73–1.32	0.56	0.27–1.15
Family atopy	1.09	0.77–1.54	0.55	0.20–1.57

Europe, and 6.2% in North America. In 2009, the same authors (20) compared PPD patch testing results from dermatitis patients investigated between 2003 and 2007 in 10 European centres: the median prevalence of PPD sensitization was 5.1%, with the highest prevalence being found in Leuven (7.1%) and the lowest in Malmö (2.1%). Other authors reported that the frequency of PPD sensitization in a series of consecutive patients ranged from 4% to 7% (21–29). Overall, these findings seem to be consistent with those of our study, in which the overall prevalence of PPD sensitization was 3.5%.

In 2008, Schnuch et al. (21) analysed PPD sensitization in 83 030 patients in Europe; they found a prevalence rate of 4% and associations with some occupations, such as hairdressing, construction work and farming. They did not analyse the data by sex.

In our study, the highest prevalence of PPD sensitization was found among hairdressers and beauticians, in both men (15.4%) and women (14.7%). It is well known that hair dye is one of the most frequent causes of sensitization and occupation-related allergic eczema in hairdressers (15, 18, 21, 30–32). Guerra et al. investigated a group of 302 hairdressers with dermatitis, and found that 24.2% of them were sensitized to PPD. Valks et al. (33) found that the cumulative incidence of sensitization to PPD among hairdressers increased from 45.9% in the calendar period 1980–1993 to 54.0% in 1994–2003.

In our study, PPD sensitization was significantly higher in female drivers (12.9%) than in the internal control group of office workers (3.0%). This finding might be explained by exposure to leather and synthetic leather dyed with crossreacting dyes (34) and used to cover the steering wheel, or the handling of rubber materials in grips of tools, tyres, hoses, or tubes (21). Similarly, the presence of crossreacting antioxidants in some rubber products (19) may explain the increased risk for PPD sensitization in barmaids and cleaners, and in male bakers, waiters, and domestic workers.

The excess risk for male printing trades workers may be related to the presence of crossreacting dyes in inks, as suggested by Morris (35). Despite these associations, it must be considered that people in certain occupations may simply dye their hair more frequently (fashion), for example, barmaids more than barmen, and this should be considered as a critical confounding factor.

On studying the association between age and PPD sensitization, we found that the latter was significantly higher in the 46–55-year-old age group in both sexes. A possible explanation of this finding is that people in this age group tend to use hair dye more often when their hair starts to turn grey.

Retired men had a higher risk of sensitization to PPD, but we did not find an elevated risk among males older than 55 years and still working; this could be explained by retired men using hair dyes more than men in the same age who still work. It is known that the reactivity to patch tests is lower in old people (36).

The large sample of individuals investigated in this study ($n = 14\,464$) enabled exploration of occupations that may be at risk for sensitization to PPD. In addition to the well-known increased risk in hairdressers and beauticians, we found significant associations between

PPD sensitization and other occupational groups, such as printers, professional drivers, bar workers, cleaners, bakers, waiters, and domestic workers. These findings may be attributable to the presence of crossreacting substances in products handled by these groups.

Our study showed stronger associations with occupations than the study performed by Schnuch et al. (21); this may be explained by the fact that, in our study, 20% of the patch tests were performed in a centre for occupational dermatitis.

PPD is an extreme skin sensitizer, and may cause severe allergic contact dermatitis. The maximum concentration allowed in hair dye products in the EU is 4% (2% on hair when mixed 1:1 with oxidizer) (37). There is clinical and epidemiological evidence to support the reduction (or elimination) of PPD in hair dye products. In Europe, in cosmetic products, PPD may be used only for dyeing hair; its presence in 'temporary henna tattoos' is illegal, but enforcement may be poor. The latter may cause active sensitization, especially in the young people who have them. As well as minimizing the use of PPD in hair dyes, there may be a need to reduce exposure to crossreacting colouring agents used in other product types and crossreacting rubber antioxidants.

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