

Positive patch-test reactions to para-phenylenediamine, their clinical relevance and the concept of clinical tolerance

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406 patients were patch tested over an 18-month period (January 1998 to June 1999) at a dermatology referral centre. 33 patients (8.1%) had a positive reaction to para-phenylenediamine (PPD). 20 patients were experiencing PPD hair dye dermatitis (present relevance, 61%), 2 were using PPD hair dyes without developing dermatitis (clinical tolerance, 6%), 4 had previously used PPD hair dyes with dermatitis in the past (past relevance, 12%), 3 had previously used PPD hair dyes without dermatitis (past exposure, 9%) and 4 had no known exposure to PPD (unknown relevance, 12%). Of the 20 patients whose test results were of present relevance, 17 avoided PPD hair dyes, resulting in total clearance of the dermatitis in all except 3, who had concurrent endogenous eczema. 3 continued using PPD hair dyes: 2 had recurrent contact dermatitis and 1 avoided dermatitis with meticulous technique. The 2 patients with clinical tolerance continued using PPD hair dyes with no dermatitis.

Key words: para-phenylenediamine; hair dye; allergic contact dermatitis; behaviour; outcome; relevance; clinical tolerance; past exposure; unknown relevance. © Munksgaard, 2001.

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Para-phenylenediamine (PPD) hair dye dermatitis is not uncommon in Singapore. PPD-containing hair dyes are the preferred hair dyes for restoring dark hair colour, as they impart a long-lasting jet-black colouration.

This study was done to find the frequency of positive patch test reactions to PPD. We also wanted to know the clinical relevance of these positive patch test reactions in relation to PPD hair dye usage. We propose categorizing clinical relevance into: (1) present relevance (experiencing hair dye dermatitis); (2) clinical tolerance (no dermatitis in spite of using PPD hair dyes); (3) past relevance (had hair dye dermatitis in the past and had since avoided PPD hair dyes); (4) past exposure (used PPD hair dyes in the past with no problems); (5) unknown relevance (never used PPD hair dyes).

In our centre, patients with positive patch test reactions to PPD are always told to avoid using PPD-containing hair dyes. We wanted to know whether they followed instructions to avoid PPD hair dyes and the subsequent outcome of their action.

Patients and Methods

A total of 406 patients presenting to the National Skin Centre (NSC), a dermatology referral centre in Singapore, over an 18-month period (January 1998 to June 1999) with suspected contact dermatitis were patch tested to the NSC standard series, which included PPD 1% in petrolatum (pet.).

The testing agents were applied to Finn Chambers (Epitest Ltd., Helsinki, Finland) which were fixed to the upper back with 3M tape. The patches were removed after 2 days (D) and the test sites were examined for evidence of reaction at D3. Positive reactions were graded from + to +++, as recommended by the International Contact Dermatitis Research Group. We recorded all weakly positive reactions as negative reactions. We did not, as a routine, do a patch test reading on D7 to look for late reactions.

33 patients (8.1%) had a positive test reaction to PPD. They were advised to avoid the use of PPD-containing hair dyes. They were told to use non-PPD-containing hair dyes as alternatives if they needed to dye their hair.

We went through the case-records of these 33 patients to evaluate their progress. In addition, all the patients were interviewed by telephone by a dermatologist to confirm the findings in the case-records, to obtain missing details as well as to ascertain their current clinical progress.

Results

Frequency

Of the 33 patients, 15 were males and 18 were females. The median age was 53 years, with a range of 25 to 80 years. There were 25 Chinese, 3 Malay, 3 Indian, 1 Sikh and 1 Eurasian; this was close to the racial distribution in the general population.

Clinical relevance

The test result was of present relevance in 20 patients, as they were using PPD-containing hair dyes and experiencing hair dye dermatitis at the time of the patch test.

2 patients were using PPD-containing hair dyes at the time of the patch test but did not experience hair dye dermatitis. They appeared to have "clinical tolerance" to PPD-containing hair dyes.

The test result was of past relevance in 4 patients: they had previously used PPD-containing hair dyes and this had resulted in hair dye dermatitis. They were no longer using these hair dyes at the time of the patch test and did not currently have hair dye dermatitis.

3 patients had previously used PPD hair dyes without experiencing hair dye dermatitis. They were no longer using PPD hair dyes at the time of the patch test. They had "past exposure" to PPD.

Despite extensive investigations, the last 4 patients had neither used PPD-containing hair dyes nor had any occupational exposure or exposure to cross-reacting substances like azo or aniline dyes, procaine, benzocaine, sulfonamides, etc. Their source of exposure was "unknown".

Behaviour and outcome

All the patients were advised to avoid PPD-containing hair dyes. Synthetic semi-permanent dyes, natural dyes like henna, metallic hair dyes and temporary colourings were offered as alternatives if they needed to dye their hair. A telephone interview was conducted at a mean duration of 25 months from the date of their patch test to evaluate their clinical progress (Table 1).

Of the 20 patients whose test result was of present relevance, 3 continued using these hair dyes. 2 had recurrent contact dermatitis and put up with it; 1 avoided dermatitis with meticulous technique (case no. 1). 17 stopped dyeing their hair or used alternative hair dyes. This resulted in total clearance of the dermatitis in all except 3. These 3 patients had partial clearance: 2 had concurrent seborrhoeic dermatitis and 1 had unspecified endogenous eczema.

Case Reports

Case no. 1

A 51-year-old female teacher would coat her hair-line, neck and ears with Pond's cold cream and wear a pair of gloves before applying a small amount of the PPD-containing hair dye onto the distal shafts of her hair. She took great care to minimize contact with her scalp. With these precautions, she was able to continue dyeing her hair without problems. However, on those occasions when she happened to miss any one of the precautionary steps, she would develop a pruritic eczematous rash within a day.

The 2 patients who were using PPD-containing hair dyes but did not experience hair dye dermatitis at the time of the patch test continued using these hair dyes without developing any dermatitis. They seemed to be able to tolerate PPD-containing hair dyes (case nos. 2 and 3).

Table 1. Behaviour and subsequent outcome of patients with positive patch test reactions to para-phenylenediamine

Relevance	Behaviour	Outcome
present relevance (20)	11 continued dyeing hair	8 used alternative hair dyes with total clearance of rash 2 used PPD hair dyes with recurrent contact dermatitis 1 used PPD hair dye but avoided contact dermatitis (case no. 1)
	9 stopped dyeing hair	6 had complete clearance of rash 3 had partial clearance due to concomitant endogenous eczema
clinical tolerance (2)	2 continued dyeing hair	used PPD hair dyes without problems (cases nos. 2 and 3)
past relevance (4)	2 continued dyeing hair	used alternative hair dyes with no recurrence of rash
	2 stopped dyeing hair	no recurrence of rash
past exposure (3)	1 continued dyeing hair	used alternative hair dye without problems
	2 stopped dyeing hair	never had contact dermatitis due to hair dye
unknown (4)	had never used PPD hair dyes	

Case no. 2

A 44-year-old female office assistant presented with a generalized urticarial and eczematous rash 2 weeks after pruning some trees in her garden and 1 week after taking a health food supplement containing *Chlorella*. She had been dyeing her hair with PPD-containing hair dyes for more than a decade. The clinical impression was that of an allergic contact reaction to plants or an adverse reaction to the food supplement. Patch testing was positive to PPD (++), nickel (++) and gold (+). She stopped taking the food supplement, avoided exposure to the latter 2 allergens and was treated with topical corticosteroids with complete resolution of her rash. She then continued using her PPD-containing hair dye without any problems.

Case no. 3

A 25-year-old female hairdresser presented with an eczematous rash on her hands since she started working as a hairdresser 10 years ago. She used gloves whenever she did hair-dyeing for her customers but not during shampooing. She had also dyed her own hair using PPD-containing hair dyes for 4 years with no scalp or facial dermatitis. Patch testing was positive to PPD (+) only and negative to a "hairdresser" panel. She was diagnosed as having cumulative insult irritant contact dermatitis from wetwork. Her dermatitis improved after she minimized her contact with shampoo and water. She continued to dye her own hair with PPD-containing hair dyes without developing any rash on her scalp or face.

Discussion

Currently, a true positive patch test reaction is interpreted by many as being of present relevance, past relevance or not relevant (1). We would like to propose the use of the following 5 categories:

(i) present relevance: the patch test has unmasked an allergen that is causing the current dermatitis;

(ii) past relevance: the patch test has unmasked an allergen that has caused a dermatitis in the past, but is of no present relevance;

(iii) clinical tolerance: the patch test has unmasked an allergen that the patient is currently encountering, but no clinical dermatitis is experienced despite continual encounter with the allergen;

(iv) past exposure: the patch test has unmasked an allergen that the patient has encountered in the past, but at that time of exposure, did not produce a dermatitis;

(v) unknown relevance: no known exposure in the past.

Our proposed classification refines the current "not relevant" grouping. This new classification has significant clinical implications. Labelling a patient as having "clinical tolerance" states the facts clearer than using the term "not relevant". The phenomenon of "clinical tolerance" is not unique to PPD. Many patients who show a positive patch test reaction to gold are able to continue wearing gold jewellery without developing clinical dermatitis (2, 3). These patients may be said to have "clinical tolerance" to gold jewellery.

A patient who has "past exposure" to a contact allergen may or may not develop clinical dermatitis if he is now re-exposed to a product containing the allergen. If he develops dermatitis on re-exposure, the allergen becomes relevant. If he does not develop dermatitis despite continual exposure, he has clinical tolerance to the product containing the allergen.

The "unknown relevance" category is one of exclusion and is assigned after extensive history taking has failed to reveal a possible source of exposure to the allergen or a cross-reacting substance.

The explanations for our 2 patients who exhibit clinical tolerance to PPD may be a low contact sensitivity to PPD, short contact time (4), meticulous technique and low concentration of PPD in their hair dyes. Patch testing, on the other hand, is a higher level of "elicitation stress" as they are exposed to the allergenic unoxidised PPD for 2 D.

We would like to extend the analogy to gold contact allergy. The most widely used agent in patch testing for gold allergy is gold sodium thiosulfate 0.5% pet. Gold ions are readily available in this compound. In contrast, metallic gold, being a noble metal, is not easily corroded and is a poor source of gold ions. This may explain the clinical tolerance of the majority of patients with gold sodium thiosulfate contact allergy to gold jewellery.

Given the alluring qualities of PPD-containing hair dyes, some patients disregarded their dermatologist's advice and continued using them, even when this might result in a recurrent contact dermatitis. 3 out of 20 patients (15%) whose patch test result was of present relevance continued to use PPD-containing hair dyes. 2 had recurrent contact dermatitis. 1 patient was more ingenious and discovered that if she took great care to avoid contact with the allergen, she would be able to get her hair dyed, albeit partially (case no. 1). It appears that, with great care, it may be possible to avoid contact with PPD and hence avoid dermatitis.

The outcome of patients with PPD hair dye dermatitis who either totally stopped dyeing their hair or changed to non-PPD-containing hair dyes was excellent. All except 3 had complete clearance of their rash. The incomplete clearance of the rash in these 3 patients could be adequately explained by the concurrent occurrence of an endogenous eczema like seborrheic dermatitis.

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