

CASE SERIES

Allergic contact dermatitis to para-phenylenediamine

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ABSTRACT

Exposure to hair dye is the most frequent route of sensitisation to para-phenylenediamine (PPD), a common contact allergen. International studies have examined the profile of PPD, but Australian-sourced information is lacking. Patients are often dissatisfied with advice to stop dyeing their hair. This study examines patients' characteristics, patch test results and outcomes of PPD allergy from a single Australian centre, through a retrospective analysis of patch test data from 2006 to 2013 at the Liverpool Hospital Dermatology Department. It reviews the science of hair dye allergy, examines alternative hair dyes and investigates strategies for hair dyeing. Of 584 patients, 11 were allergic to PPD. Our PPD allergy prevalence rate of 2% is at the lower end of international reported rates. About half these patients also react to para-toluenediamine (PTD). Affected patients experience a significant lifestyle disturbance. In all, 78% tried alternative hair dyes after the patch test diagnosis and more than half continued to dye their hair. Alternative non-PPD hair dyes are available but the marketplace can be confusing. Although some patients are able to tolerate alternative hair dyes, caution is needed as the risk of developing an allergy to other hair dye ingredients, especially PTD, is high.

Key words: allergic contact dermatitis, dermatitis, eczema, para-phenylenediamine, para-toluenediamine, patch tests, hair dye, phenylenediamine.

INTRODUCTION

Para-phenylenediamine (PPD) is used as a dye and antioxidant in consumer and industry products, including hair dye,

black henna tattoos, textiles, leather, fur, printer ink, and black rubber products.¹ Its small size, high penetrance of cutaneous structures, effective binding of proteins and rapid polymerisation when oxidised, make PPD an elegant dye that is present in most hair colouring products. Unfortunately, these traits also make it a class 1 allergen on local lymph node assay.² It is as potent as diphenylcyclopropenone.⁵ As one of the most common causes of allergic contact dermatitis in the world, it is included in the standard series.

The profile of PPD allergy has been well described in the international literature; however, there is yet to be a significant analysis of this allergen in the Australian population. Furthermore, traditional medical advice given to these patients has been one-dimensional ('stop the hair dye'), and is often not followed. This study examines the profile of PPD allergy and the outcome of patch testing in an Australian clinic, reviews the science of hair dye allergy and investigates strategies for hair dyeing.

METHODS

A review of patch test data at the Liverpool Hospital Dermatology Department from January 2006 to January 2013 was performed to identify patients who are allergic to PPD, and analyse their characteristics and patch testing profile. Allergens were sourced from Chemotechnique Diagnostics (Malmö, Sweden), applied with IQ chambers (Chemotechnique Diagnostics) to the upper back and evaluated at days 2 and 4, according to the International Contact Dermatitis Research Group scoring system. Ethics approval was obtained from the South-Western Sydney local health district ethics and research governance office. All PPD-allergic patients were tested to the hairdressing series, but only some were tested to the sunscreen and textile series.

A 15-part questionnaire on aspects of the dermatitis, patient behaviour, sensitisation and quality of life, was administered to the identified cohort. A literature review on the current science of PPD was performed using Medline and EMBASE. Medline, Google searches, responses to the questionnaire, discussion with industry representatives and

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Conflict of interest: none.

Submitted 22 December 2013; accepted 17 March 2014.

Abbreviations:

PPD	para-phenylenediamine
PTD	para-toluenediamine

Table 1 Patients' characteristics, patch test characteristics and concomitant reactions

Age	Gender	PPD reaction	Allergens including PPD (<i>n</i>)	Chemical classes (<i>n</i>)
39	F	+	4	3
42	M	+++	5	1
53	M	++	1	1
55	F	++	1	1
45	F	+++	3	1
33	F	++	3	3
56	F	++	4	4
19	M	+++	4	2
51	F	++	3	2
64	F	+	5	4
45	M	++	6	3

+, ++, +++ denote the strength of the patch test reaction according to the international contact dermatitis research group scoring system. PPD, para-phenylenediamine; PTD, para-toluenediamine. Reactions to PTD, O-nitro PPD, p-aminophenol, disperse orange, benzocaine and n-isopropyl PPD are classified as reactions to single chemical class.

Table 2 Male, occupation, atopic, hand, leg, face (MOAHLF) index of 584 patients (%)

Male	36
Occupation	5
Atopy	28
Hand	23
Leg	9
Face	18

manufacturers were used to examine alternative hair-colouring products currently available in the market.

RESULTS

The prevalence rate of PPD allergy in our population was 2% (11/584), with a female : male ratio of 1.8:1 and an age range of 19–64 years. Most (10/11) were non-occupational cases, with only one hairdresser sensitised through occupational exposure. The sites affected were the face, scalp or neck (91%) followed by hands (36%) and trunk (18%). Underlying atopy affected 73% of the cohort. The patients' characteristics, patch test reactions and concomitant reaction profile are presented in Table 1 and the male, occupation, atopic, hand, leg, face (MOAHLF) index of our patch test population in Table 2.

In 10 of the 11 patients (91%) the reaction to PPD was relevant to their presenting dermatitis: all had reacted to dark-coloured hair dyes and none had a black henna tattoo. Two patients reacted to PPD in isolation, 82% (9/11) reacted to multiple allergens and 55% (6/11) reacted to multiple hair dye components. Polysensitised patients who react to three or more chemically unrelated allergens, constituted 45% (5/11) of our series. The co-existing hair dye allergens were para-toluenediamine (PTD) (45%), O-nitro PPD (27%), p-aminophenol (18%), disperse orange (18%), ammonium

Table 3 Questionnaire result: behaviour after patch testing

Patch test reaction (1% PPD in pet)	Patients	Patients continuing to dye their hair	Hair-dye product used after diagnosis
+	2	2	1 PPD, 1 non-PPD
++	5	3	All non-PPD
+++	2	0	Nil
Total	9	5/9 (56%)	

+, ++, +++ denote the strength of the patch test reaction according to the international contact dermatitis research group scoring system. PPD, para-phenylenediamine.

persulfate (18%) and resorcinol (9%). Reactions to other para-amino compounds were uncommon: benzocaine (9%) and n-isopropyl-n-phenyl-4-phenylenediamine (9%).

Eight of the nine patients who responded to the questionnaire had a clear history of reaction to hair dye. Table 3 correlates the intensity of the patch test reaction with patient behaviour. Despite being advised to stop, 78% (7/9) tried other hair dyes after their diagnosis and 56% (5/9) continued to dye their hair 4–60 months after patch testing. All patients with a strong (3+) patch test result reacted to multiple components of hair dye and stopped dyeing their hair. Many respondents required time off work and reported a significant disturbance to their quality of life. All reported improvement or clearance of their dermatitis after diagnosis.

Table 4 lists the available PPD-free hair dyes.

DISCUSSION

Millions of people worldwide are allergic to PPD. The prevalence of PPD allergy in patch testing clinics ranges from 2–7% in the international literature, with a median prevalence rate of 4% in Asia, 4% in Europe and 6% in North America.² Our prevalence rate of 2% is at the lower end of this range, and may be due to referral bias.

PPD allergies predominantly affect users of hair dye. As in most studies, we found that occupational cases constitute a minority of PPD-allergic individuals.³ The intensity of patch test reaction is significant: the stronger responders are more likely to manifest an allergic reaction on re-exposure to hair dye and react to more than one component of hair dye ingredients. Our findings concur with other published data.⁴

Oxidative metabolites of PPD are the haptens that cause PPD sensitisation.⁵ During the process of hair dyeing, most of the applied PPD forms non-reactive, polymerised, hair-colouring molecules. A small amount (<1%) of unconsumed PPD is acetylated in the epidermis and does not activate the dendritic and T-cells of sensitised individuals. However, the acetylation pathway can become saturated with exposure to a large dose⁵ and this increases the amount of oxidative metabolites in the skin. This may be the situation when hair dye is carelessly applied and subsequently contaminates adjacent areas, or when it is left on for longer than the intended 30 minutes. It also occurs with black henna tattoos, which contain up to 16% PPD compared to the allowable limit of 3% in hair dyes.⁶

Table 4 Leading para-phenylenediamine-free hair dyes

Para-toluenediamine-based	Temporary dyes (Azo)	Totally plant-based dyes
Aveda 'Full Spectrum protective creme'	Hennaplus 'Colour cream'	Henna Boy UK
Hairwonder 'Colour and care'	Sanotint 'Reflex natural temporary hair dye'	Light Mountain 'Hair Color Range'
Hennaplus 'Colour creations'	Surya 'Henna cream'	Logona
'Long-lasting color'		
Keune 'So pure color'		Palette by nature
L'Oréal 'Casting crème'		Sante
Napro 'Palette'		Surya 'Henna Powder'
NaturVital 'Colorsafe range'		
Original mineral		
Sanotint 'Sanotint Light'		
Schwartzkopf 'Brilliance luminance'		
'Live permanent foam'		
'Live salon permanent'		

Aveda (Minneapolis, USA), Hairwonder (Frenchtop natural products, Hoogwoud, The Netherlands), Henna Boy (Cornwall, England), Hennaplus colour cream (Frenchtop Natural Products, Hoogwoud, The Netherlands), Keune (Soest, The Netherlands), L'Oréal (Clichy, France), Light Mountain hair colour range (Lotus Brands, Twin Lakes, USA), Napro Palette (Schwarzkopf – Dusseldorf, Germany), NaturVital (Barcelona, Spain), Original mineral (Botany, Australia), Palette by nature (Minneapolis, USA), Sanotint Light and Sanotint reflex natural temporary hair dye (Cosval, Milan Italy), Sante Herbal Hair Colours (Logocos, Salzheimendorf, Germany), Schwarzkopf brilliance (Dusseldorf, Germany), Surya Henna Cream and Surya Henna Powder (Sao Paulo, Brazil).

The elicitation of an immune response to PPD in allergic patients is time and dose dependent. Five minutes is the minimum application time required to elicit a reaction in patch testing. Repeat applications will elicit a positive reaction with a significantly lower concentration per application.² In addition, there is a genetic component to the risk of PPD sensitisation. The high-secreting tumour necrosis factor- α GA and AA genotypes are more prevalent in PPD-allergic individuals, and are associated with polysensitisation.⁷ This may explain the high frequency of multiple allergies in our PPD allergic-patients, particularly those with strong (2+, 3+) responses.

Extrapolating from this information, it is suggested that users should minimise skin contact by applying the dye meticulously, immediately removing the dye from contaminated skin, applying petrolatum to the hair line and using hair foils or a highlight cap to reduce the risk of sensitisation. In addition, using lighter shades of dye, keeping within the time limit of applying the dye, and dyeing hair less frequently, will reduce the cumulative dose of dye on the skin.

Our data reflect how motivated hair dyers typically are, with three of four PPD-allergic patients attempting to dye their hair again after diagnosis. Although some are able to tolerate alternative dyes, caution is needed as the risk of developing a further allergy to their components is high. This is especially true in regard to PTD, which has a similar structure to PPD, and is an equipotent sensitiser as PPD in guinea pig maximisation tests.⁸ Our rates of cross-sensitisation are consistent with previous findings.⁹

In the authors' experience, many PPD allergic patients seek information from family, friends, hairdressers and internet chat forums, and find the commercial hair dye market confusing. This is not surprising as many products are designed to sound natural, pure or organic, yet often contain aromatic amines – some examples are Hennaplus (Frenchtop Natural Care Products, Hoogwoud, The Netherlands), Herbatint (Rome, Italy) and NaturVital (Barcelona, Spain). It is important to examine the lists of ingredients rather than relying on the name of the product.

The biggest limitation of this study is its small sample size. Implications drawn from a small cohort are necessarily limited. However, much of our data concur with larger published studies^{3,4,9} and so the trends seen here are likely to be reflective of a wider cohort.

CONCLUSION

Our PPD allergy prevalence rate of 2% is at the lower end of the international reported rate. PPD-allergic patients are predominantly users of hair dyes, often react to multiple allergens, most commonly to other ingredients of hair dye, especially PTD. Cross-reactions to other para-amino compounds occur less frequently than is assumed. The intensity of the patch test reaction has significance, as strong responders are more likely to manifest clinically relevant allergic contact dermatitis with hair dye usage. Although more than half the PPD-allergic patients continue to dye their hair, caution is needed, as their risk of developing an allergy to other ingredients of hair dye is high.

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