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Allergic contact dermatitis to phenol-formaldehyde resin at a single tertiary dermatology centre

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Key words: phenol-formaldehyde resin, allergic contact dermatitis, occupational skin disease

Abstract:

Background:

Phenol-formaldehyde resin 2 (PFR2) has been shown to be a useful marker of contact allergy (CA) to various phenol-formaldehyde resins. These compounds are used in various industries as solids, powders or semisolid resins and are known to be sensitising agents.

Objectives:

The aims were to investigate the contact allergy to PFR2 in a single tertiary dermatology centre, to investigate associated simultaneous allergic reactions, and to identify cases of allergic contact dermatitis (ACD) to PFR2.

Methods:

A retrospective study was performed of patients patch tested to PFR2 between 1 January 2003 and 17 June 2020.

Results:

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Some 337 of 7922 patients were tested to PFR2 and 16 (4.7%) reacted. Of those 16 individuals, 6 (37.5%) had a relevant reaction (1.8% of total). Simultaneous allergic reactions were noted to colophonium in 8 (50.0%), *Myroxylon pereirae* in 5 (31.3%), and fragrance mix 1 in 4 cases (25.0%).

Conclusion:

Contact allergy to PFR2, even in a selected population of patients, is uncommon. However, patients exposed to plastic and glues, or who work with wood products should be routinely patch tested to a plastics and glues series containing PFR2. We recommend that all centres include PFR2 in their plastics and glues series.

Main text:

Introduction

Phenol-formaldehyde resins (PFR) are polymers manufactured from the combination of phenol (e.g. phenol, bisphenol A, cresol, *p*-tert-butylphenol formaldehyde (PTBP-FR), resorcinol) and aldehydes (usually formaldehyde, acetaldehyde, glyoxal).^{1,2} The first commercial product made from PFR was 'Bakelite', a wholly synthetic polymer manufactured in 1909.³ Since the first resins, many other varieties have been developed and now PFR can be considered a group of related polymers. Consequently, resins are composed of different phenols containing different allergens.

PFR are used in electrical insulation, wood varnishes, wood glues, in rubber modification and in components of footwear, flooring, paints, coatings, waterproof canvases and paper.⁴ The material's versatility enables it to be used as a solid resin (bakelite type), a powder resin (which can be melted and poured into various forms), a semi solid resin (such as adhesives), and as a liquid resin (in paints, varnishes and polishes).⁴

The allergen *p*-tert-butylphenol-formaldehyde resin is included in many baseline series as it is a common sensitizer, however patch testing alone with *p*-tert-butylphenol-formaldehyde resin will not identify patients with contact allergy (CA) to PFR.^{5,6} PFR2, which contains low

molecular weight methylol phenols, has been shown to be a useful marker of CA to various phenol-formaldehyde resins.^{7,8}

Methods

A retrospective study of cases of allergic contact dermatitis (ACD) to PFR2 at our tertiary dermatology centre was performed. A total of 337 patients with suspected contact dermatitis and a possible history of exposure to PFR were patch tested with PFR2 1.0% pet between 1 January 2003 to 30 June 2020 in our Occupational Dermatology and Contact Dermatitis clinics, from a total of 7922 patients patch tested. Allergens were obtained from Chemotechnique Diagnostics (Vellinge, Sweden) and previously Trolab (now SmartPractice, Phoenix, Arizona, U.S.A) and were fixed to the skin with Finn Chambers or Allergeaze test chambers (SmartPractice, Phoenix, Arizona, U.S.A) for 48 hours. Testing with PFR (novolac) was performed in the early part of this study when it was available from Trolab. Patch test readings were performed according to the International Contact Dermatitis Research Group (ICDRG) guidelines at day 2 (D2) and day 4 (D4).

The MOAHLFA (male, occupational dermatitis, atopic dermatitis, hand dermatitis, leg dermatitis, face dermatitis, age >40) characteristics of the study population are shown in Table 1.

Results

Of 337 patients tested, 16 patients had a positive reaction to PFR2, with 6 relevant reactions and 10 of unknown relevance. The characteristics of patients with relevant reactions are detailed in Table 2. Five out of 6 patients were male, and all cases of ACD to PFR2 were occupationally related. Two patients were wood workers, and the other four patients worked with PFR in processing plants. Occupational contact dermatitis and atopic dermatitis were significantly associated with sensitisation to PFR2.

The average age of patients with relevant reactions was 41 years. All 6 patients had dermatitis in an airborne distribution affecting the exposed areas of the skin including the face, neck, and upper limbs. One patient also had dermatitis affecting the chest as well as the arms and neck. All patients reacted at D2 and D4, with one patient (case 4) having a doubtful reaction at D2 followed by a positive reaction at D4. Three out of 6 patients with relevant reactions had an extreme or strong (+++ or ++) reaction at D4.

Simultaneous reactions to PTBP-FR, formaldehyde, PFR (novolac), *Myroxylon pereirae*, colophonium, fragrance mix 1 (FM1) and 2-monomethylol phenol are shown in Table 3. The most frequent simultaneous reactor was colophonium, with 8 patients (50.0%) having positive reactions, followed by *M.pereirae* (5 patients, 31.3%), FM1 (4 patients, 25.0%), p-tert-butylphenol-formaldehyde resin and 2-monomethylol phenol (2 patients each, 12.5% each). There was only one simultaneous reaction to formaldehyde (6.3%).

Discussion

This case series describes occupational ACD to PFR2 in 6 workers over a period of 17 years.

Our study found a CA rate of 4.7% of those tested with PFR2 or 0.2% of the total tested, with 37.5% of these reactions being of clinical relevance. There was an overall relevant reaction rate of 1.8% in a targeted population tested to PFR2 based on their possible exposure history, or 0.08% of the total tested. It is likely that our centre sees a disproportionately higher number of cases of PFR allergy because of the selected population attending the tertiary referral occupational dermatology clinic. However, worldwide few centres have reported rates of PFR2 allergy.

To our knowledge, PFR2 is included only in the Swedish and Mayo Clinic baseline series. This may explain why rates of CA to PFR2 in populations of patients patch tested are scarcely reported. In 3824 patients patch tested for suspected ACD by the Mayo Clinic between 2001 and 2005, a CA rate of 1.5% to PFR2 was found. Almost half of reactions were considered relevant.⁹

A recent review of cases of occupational skin disease at a Finnish centre found 35 cases (1.95%) of ACD caused by PFRs including “plywood glues” of 1863 patients with occupational ACD over a time period of twelve years (2005-2016).¹⁰ Other older studies have reported positive reaction rates to PFR of between 0.1% and 2.3% in patients tested to plastics and glues series.^{11,12}

A study from Sweden in which 5 centres included PFR2 in their baseline series between 2006 and 2007 found a rate of 1.1% of CA in the patch tested population, however clinical relevance was not assessed.¹³ Similarly, the ICDRG reported a comparable frequency of positive reactions of 1.2% (28 patients) out of 2259 patients assessed to PFR2 as part of a baseline series in 13 centres between September 2012 and February 2013.¹⁴ This study concluded that the relatively high frequency of CA to PFR2 merited inclusion of this allergen into the International baseline series. Clinical relevance was noted in 25% of cases (7 patients). It was noted that one fifth of allergic reactions would have been missed if a day 7 reading had not been performed. Similarly, a study from the Netherlands found that 20% of positive reactions to PFR were only seen on the D6/D7 reading.¹⁵ In our study, readings were only performed on D2 and D4, therefore it is probable that some reactions were missed.

We found a higher number of simultaneous reactions to colophonium (50.0%) than in the Swedish multicentre study (22.2%) and the ICDRG study (10.7%). Simultaneous reactions in our study were also higher than the ICDRG study for *M.pereirae* (31.3% vs 17.9%) but lower than the Swedish multicentre study (31.3% vs 51.9%). Reactions for FM1 were lower in our study (25.0%) compared to the ICDRG (28.5%) and the Swedish multicentre study (55.6%). Several patients reacted to PFR (novolac) and to their own samples of resins. At the time of this study, we were additionally testing with PFR (novolac) obtained from Trolab (now Smart Practice). However, novolac resins (produced with a deficit of formaldehyde) are now thought to be inferior for testing.³

Only one patient also reacted to formaldehyde, however, this is expected as PFR and formaldehyde do not usually sensitize concomitantly nor cross-react.¹⁶ Simultaneous

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reactions to these allergens are caused by low molecular weight phenols in these compounds and this phenomenon has been shown before.¹⁷

One third of our cases were wood workers. A Finnish study found a CA rate to PFR2 of 1.6% in patients exposed to glues and plastics and patch tested to a screening series for suspected occupational ACD. There was clinical relevance in 70% of cases and the majority of these patients were working in wood-product industries.¹⁸ Two cases of PFR allergy in plywood workers in New Zealand have also been reported.¹⁹ Similarly, Ezughah et al reported a case in a carpenter in the United Kingdom who presented with dermatitis in an airborne distribution with patch testing revealing allergy to PFR2 and the medium-density-fibreboard dust with which he worked.²⁰

Occupational ACD to PFR has been reported in workers from other industries including foundry workers exposed to phenol-formaldehyde-impregnated casting sand,^{18,21} workers involved in the production of laminates,¹⁸ and workers handling resin-impregnated filter papers.^{3,18} Recently, a case of CA to PFR in a worker involved with spray-coating metal beverage cans was described.²² However, cases of ACD to PFR is not only seen in occupational cases. A case of a well demarcated erythematous scaly rash in the periorbital area of a 12-year-old girl which was associated with wearing swimming goggles was described by Azurdia & King.²³ Patch testing revealed positive reactions to PFR and benzoyl peroxide, which were thought to be components of the rubber or glue in the swimming goggles.

All of our patients presented with dermatitis in an airborne distribution affecting exposed areas including the face, neck and upper arms. Airborne dermatitis caused by formaldehyde resins in MDF has been reported previously, often in occupational cases.^{20,24,25} There have been few reports of PFR causing dermatitis elsewhere, however Downs et al reported 4 cases of palmoplantar dermatitis with positive patch test responses to PFR2 and resolution of the dermatitis on changing footwear.²⁶

We have no explanation for the association of ACD to PFR2 and atopic dermatitis.

When PFR2 is not present in baseline series, it would be expected to be present in an additional plastics and glues series. A study from the United States found nearly 40% of patients with ACD had allergens detected on the plastics and glues series which would not have been picked up if the baseline series had been used alone.²⁷ It is therefore imperative that patients, particularly with a history of occupational exposures to plastics and glues or those who work with wood products, are tested with additional plastics and glues series.

Limitations to this study include the retrospective nature of data collection with reliance on the clinician's interpretation of patch test reactions and determination of relevance. Furthermore, our centre sees a high proportion of occupational ACD which may have influenced our rates. Our centre also does not routinely perform a patch test reading on day 7.

In conclusion, CA to PFR in a selected population is not uncommon, but in the general population of patients patch tested to exclude ACD, relevant reactions to PFR are infrequent. More than one third of patients with positive reactions have relevant reactions. Patients with occupational exposure to PFR or those who work with plastics, glues or wood products should be patch tested to PFR2. Simultaneous reactions should also be identified. It would be beneficial for more centres to report their recent CA rates for various allergens, such as PFR2, and others in the plastics and glues series.

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Tables:

Table 1: MOAHLFA (male, occupational dermatitis, atopic dermatitis, hand, face, leg, and age >40) characteristics in 337 subjects patch tested to PFR2 at our institution from 1 January 2003 to 17 June 2020, with p values for Chi squared test using SSPS (Version 26, IBM Corp. Armonk, N.Y, USA).

Index	Reactions of all relevance and strength (% of total sensitised) n=16	Non sensitised patients (% of total non-sensitised) n= 321	P value using Chi squared test
Male	11 (68.8)	157 (48.9)	0.12
Occupational dermatitis	10 (62.5)	99 (30.8)	0.01
Atopic dermatitis	7 (43.8)	60 (18.7)	0.01
Hand dermatitis	2 (12.5)	103 (31.2)	0.10
Leg dermatitis	0 (0.0)	31 (9.7)	0.19
Face dermatitis	3 (18.8)	46 (14.3)	0.63
Age above 40	8 (50.0)	199 (62.0)	0.34

Table 2: Patients with relevant reactions to PFR2 at our tertiary dermatology centre between 1 January 2003 and 17 June 2020

Patient	Age (years)	Sex	Occupation	Exposure to phenol formaldehyde resins	Medical history	Presentation	D2 reaction to PFR2	D4 reaction to PFR2	Other reactions
1	29	M	Quality control engineer	Involved in blending Cellobond® resin with raw materials including urea, as part of a process which produces insulation foam which then hardens and is used to make insulation panels	None	Facial rash, periorbital swelling and vesicular hand rash	+	+	Colophonium D2: ?/+ D4: + Benzalkonium D4: ?/+ Iodopropynylbutyl carbamate D4: ?/+
2	48	F	Process worker in timber mill	Operated machinery that handled thin sheets of plywood which are glued together with an adhesive glue. Also exposed to sheets of overlay paper which are impregnated with formaldehyde resin and are layered onto the plywood	None	Pruritic, erythematous rash affecting arms, chest and neck	++	++	<i>M. Pereirae</i> D2: + D4: + PTBP-FR D2: + D4: + Phenol formaldehyde (Novolac) D2: + D4: + Own resin D2: + D4: +
3	18	M	Apprentice cabinet maker	Involved in sawing medium density fibreboard and making cupboards	Atopy	5-month history of pruritic erythematous eyelid rash and oedema	++	++	Phenol formaldehyde resin (Novolac) D2: + D4: + Own particle board D2: ?/+ D4: ?/+

4	37	M	Laminating processing plant worker	Involved in laminating process. Subsequently moved to treating area where craft paper and overlay paper were treated	None	Rash affecting hands, flexural areas and face	?/+	+	Phenol formaldehyde resin (Novolac) D2: ?/+ D4: ?/+ Own sample of resin D4: ?/+ Own sample of resin MSP6114 D2: + D4: + Own sample of paper 463 D2: + D4: +
5	62	M	Plant operator	Previously involved in fillers and hardening process. Subsequently moved to loading and unloading trucks with exposure to resins through the occasional leak from pipes carrying resins	Diabetes mellitus, hypertension	14-year history of rash affecting face, neck, forehead, upper limbs	+++	+++	2-monomethylol phenol D2: ++ D4: +++ Phenol formaldehyde resin (Novolac) D2: + D4: +
6	49	M	Chemical process operator	Involved in taking samples of formaldehyde resins from a large tank to a laboratory for testing	None	2-3-year history of rash affecting forehead and ventral aspects of the arms	+	+	Colophony D2: ++ D4: ++ 2-monomethylol phenol D2: ++ D4: ++ Phenol formaldehyde resin (Novolac) D4: ?/+ Thiuram mix D2: + D4: ?/+

Strength of reactions: +++ *extreme strong positive*, ++ *strong positive*, + *weak positive*, ?/+ *doubtful*

PTBP-FR: p-tert-butylphenol-formaldehyde resin

Table 3: Strength of reactions to PFR2, PTBP-FR, formaldehyde, *M.pereirae*, colophony, FM1 and 2-monomethylol phenol in 16 patients who had positive reactions at D4 to PFR2 between 2003 and 2020 at our tertiary dermatology centre

No.														
	PFR2		PTBP-FR		Formaldehyde		<i>M.pereirae</i>		Colophonium		FM1		2-Monomethylol phenol	
	D2	D4	D2	D4	D2	D4	D2	D4	D2	D4	D2	D4	D2	D4
1	-	+	-	-	-	-	+	+	+	+	+	+	NT	NT
2	++	++	-	-	-	-	?/+	+	++	++	-	+	NT	NT
3	-	+	-	-	NT	NT	NT	NT	-	+	NT	NT	NT	NT
4	-	?/+	-	-	-	-	-	-	-	+	-	-	NT	NT
5	-	+	-	-	-	-	-	+	-	+	-	?/+	NT	NT
6	+	+	-	-	-	-	-	-	+++	+++	+	+	NT	NT
7	+	+	-	-	-	-	-	-	++	++	-	-	++	++
8	?/+	+	-	-	-	-	-	-	-	-	-	-	NT	NT
9	+++	++	-	-	-	-	-	+	-	-	-	-	+++	++
10	++	++	-	-	-	-	-	-	-	-	-	-	NT	NT
11	+	?/+	-	-	-	?/+	-	-	-	-	-	-	NT	NT
12	-	+	-	-	-	-	-	-	-	-	-	-	NT	NT
13	+	?/+	-	?/+	-	-	-	-	-	-	-	-	NT	NT
14	++	++	+	+	-	-	+	+	-	-	-	-	NT	NT
15	-	?/+	-	-	-	-	-	-	-	-	-	-	NT	NT
16	+	+	-	-	-	-	-	-	?/+	+	-	-	NT	NT

Key: +++ very strong positive, ++ strong positive, + positive, ?/+ doubtful, - negative, NT not tested.

PTBP-FR: p-tert-butylphenol-formaldehyde resin