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Title Page

Title: Patch test reactivity to iodopropynyl butylcarbamate between 2011 - 2018 in Melbourne, Australia

Running title: Patch test reactivity to iodopropynyl butylcarbamate

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Conflicts of interest: There are no conflict of interests.

Keywords: allergic contact dermatitis, iodopropynyl butylcarbamate, patch test, preservatives, biocides, case reports

Main Text

Iodopropynyl butylcarbamate (IPBC) is a broad spectrum preservative initially used in wood and paint products and now increasingly used in consumer products including cosmetics, moisturisers, shampoos, baby products, powders, paper, alcohol rubs and wet wipes.[1, 2] In 1996 the U.S. Food and Drug Administration reported that IPBC was used in 122 cosmetic products which increased to 942 by 2013.[3, 4] Increasing rates of contact allergy have been reported over the last 20 years from Europe and the United States[2], but there have been no studies from Australia.

Methods

All patients who underwent routine patch testing with the Australian Baseline Series (ABS) which included IPBC, between 1 January 2011 and 31 December 2018 at the Skin Health Institute (formerly Skin and Cancer Foundation), Carlton, Victoria were included in the study. IPBC was obtained from Chemotechnique Diagnostics® (Vellinge, Sweden) and tested at 0.2% in pet. Reactions were read on day 2 and 4 according to ICDRG guidelines. The clinical relevance of the positive patch test reaction was based on the patient's exposure history by reviewing patient's products.

Results

A total of 3113 patients (71.9% women, 28.1% men) were patch tested with IPBC. Overall, 71 (2.3%) patients had positive reactions to IPBC, with 22 (31%) of these positive reactions are considered to be relevant. Figure 1 demonstrates a steady increasing rate of positive reactions to IPBC from 0.5% in 2011 to a peak of 3.7% in 2018. The rate of relevant reactions to IPBC remained relatively stable between 0.2% to 1.8%, although declined in 2018.

Relevant allergic reactions to IPBC are summarised in Table 1. Among 22 patients who had relevant reaction to IPBC, all except one occurred in females. The mean age of these patients was 52.4 (range: 24-80). The affected sites included the face (45.5%), hands (22.7%), face and hands (22.7%) or generalised (9.1%). Most of the relevant allergic reactions occurred in a non-occupational setting (87.0%). Products causing reactions included moisturiser (48.0%), sunscreen (16%), cleanser (12.0%), antiseptic hand rub (12.0%), cosmetic wipe (8%) and hair gel (4%). Concomitant allergic reactions were seen in 91.3% of patients.

Discussion

Contact allergy to IPBC has increased gradually over time in the US and Europe and we present the first Australian data for contact allergy and allergic contact dermatitis.

In the 1990s, contact allergy in Europe was reported to be 0.2% to 0.3%, increasing to 0.5% to 1.2% in various studies conducted between 1996 and 2017.[5-8] In 2005, most European countries changed the IPBC testing concentration from 0.1% to 0.2% pet which could have contributed to the higher rates of IPBC contact allergy.[9]

Between 1998 to 2006, the rate of contact allergy in the US when tested at 0.1% pet was similar to Europe at 0.3% to 0.5%.[2] After the introduction of IPBC 0.5% pet for patch testing, the rate increased from 2.4% in 2005 to 2006 to a peak of 4.7% in 2013 to 2014, with the latest data from 2015 to 2016 at 3.9%.[10] The higher sensitivity rate to IPBC observed in US could be as a result of the higher concentration of IPBC used in patch testing, as well as the higher concentration of IPBC allowed in products of up to 0.1% in cosmetics, compared to the European regulation of 0.02% for rinse off, 0.01% on leave on products and 0.0075% for deodorants and antiperspirants.[4, 11, 12]

Australia's situation is unique in that regulations allow the same level of 0.1% IPBC in products as the US, however the test concentration is the same as in Europe, 0.2% in pet.[13] Despite use of a lower IPBC concentration in testing, positive rates were similar to the US, particularly from 2015. This suggests that there could be higher usage of IPBC in products in Australia, though this is yet to be documented. The highest rate of contact allergy occurred in 2018, and yet there were no relevant reactions. We suspect this could be caused by patients not bringing all the items they were exposed to or the non-listing of IPBC in ingredients. There may also be some degree of irritancy contributing to the interpretation of the result, as irritation have previously been reported in IPBC tested at 0.2% pet concentration although this risk is much high at concentrations above 0.2%.[9]

Interestingly, in our population, IPBC contact allergy was found mostly in females and facial dermatitis followed by hand dermatitis to be most frequently reported. These cases were attributed mainly by cosmetics in a non-occupational setting. Our findings suggest IPBC to chiefly be a cosmetic allergen contrasting with a previous study whereby males, affecting the hands, in an occupational setting predominated.[7] In another study, IPBC contact allergy was also reported in household detergents which was not evident in our study.[8] These differences are likely to be due to the variation of exposure in the patients.

Further studies would help to ascertain whether IPBC is in fact commonly found in products in Australia and confirm its status as a cosmetic allergen.

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Table

Table 1: Patient characteristic with relevant reactions to iodopropynyl butylcarbamate

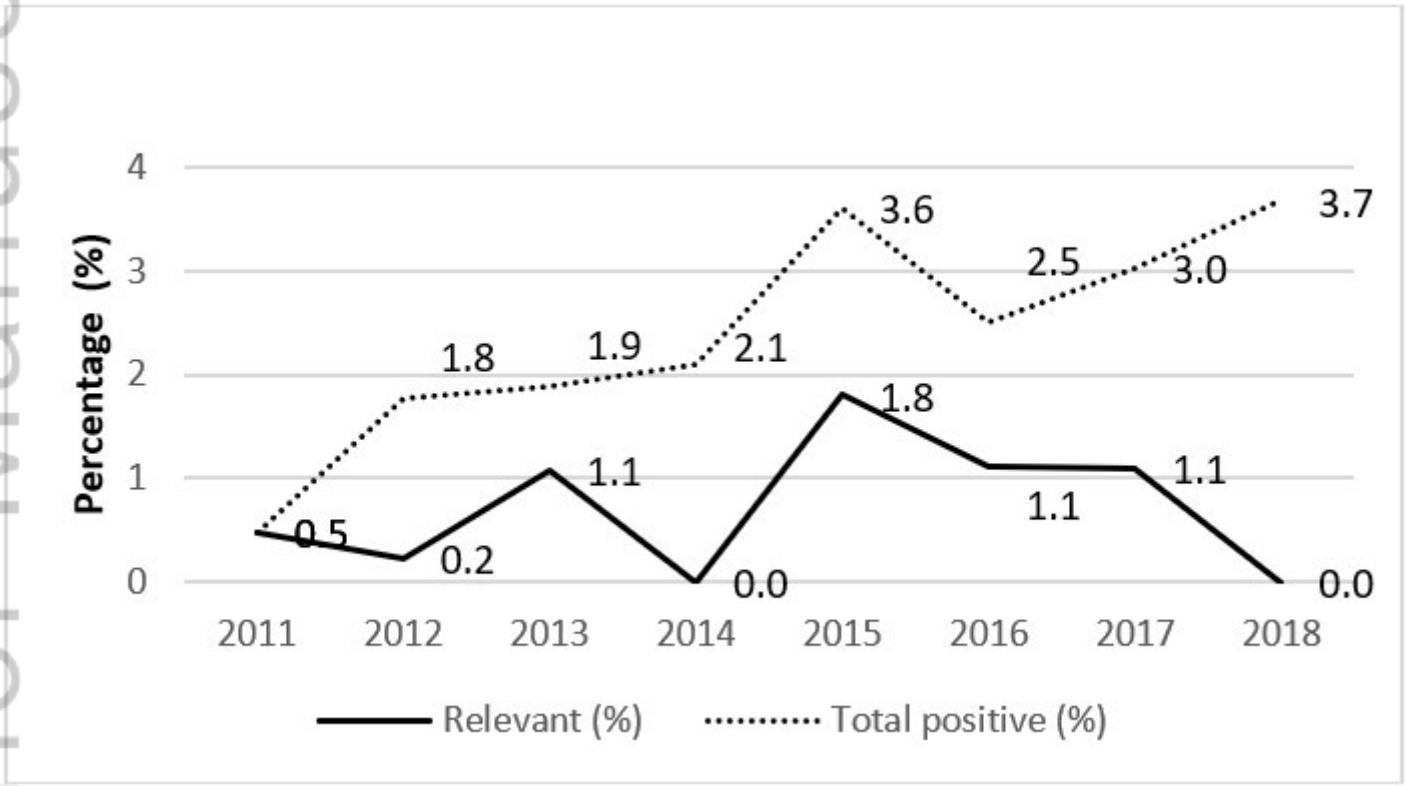
n	Age(y)/ sex	Occupational related	Site	Duration (month)	Patch test reaction[#]		Likely source of exposure	Other reactions[$]
					Day 2	Day 4		
1	50/F	No	Face	24	+	+	Face moisturising cream	Cetyl stearyl alcohol, propylene glycol
2	34/F	Yes	Hands	12	+	+	Antiseptic hand rub	Amerchol L 101
3	58/F	No	Generalised	24	+	+	Hand moisturising cream	-
4	80/M	No	Face	1	+	+	Face moisturising cream	FM, FM2, tea tree oil, MP , bronopol
5	62/F	No	Face	4	+	+	Face moisturising cream	MI, MCI
6	58/F	No	Hands	36	+	+	Face cleanser	MI, MCI
7	52/F	No	Hands	60	++	++	Face cleanser	FM, FM2, MP, MI, MCI, formaldehyde, nickel
8	34/F	No	Face	24	+	+	Face moisturising cream	Nickel
9	67/F	No	Face	14	+	+	Sunscreen	FM2, MI
10	35/F	No	Face	9	±	+	Face moisturising cream, cosmetic wipe	Nickel, cobalt, compositae mix
11	70/F	No	Face, hands	12	-	+	Sunscreen	FM, MP, cobalt
12	78/F	No	Face	60	+	+	Sunscreen	-
13	60/F	No	Hands	6	+	+	Face moisturising cream	Methylene-bis-benzotriazolyl tetramethylbutylphenol (tinosorb M)
14	42/F	No	Face, hands	4	+	+	Face moisturising cream	FM, formaldehyde, DMDM hydantoin, bronopol, MI, MCI, MDBGN, nickel
15	74/F	No	Face	-	-	+	Face moisturising cream	Carvone, MDBGN, Indium chloride, goldsodium thiosulfate
16	45/F	No	Face	12	-	+	Face moisturising cream	FM2, MP, compositae mix, MI
17	48/F	No	Generalised	1.5	-	+	Face moisturising cream and sunscreen	FM, FM2, spearmint, citral, lavandin oil, lavender spike oil
18	24/F	No	Face, hands	72	±	+	Antiseptic hand rub	MI, MCI, chlorhexidine digluconate
19	42/F	No	Face, hands	36	-	+	Cosmetic wipe	DMDM hydantoin, nickel, mercaptobenzothiazole,
20	41/F	No	Face, hands	60	-	+	Face moisturising cream, face cleanser	FM, FM2, linalool, colophonium, formaldehyde, MI, MCI, nickel, lanolin alcohol
21	46/F	No	Face	1	-	+	Hair gel	FM, FM2, linalool, limonene, HICC, MI,MCI, thiuram

22	33/F	Yes	Face, hands	24	++	++	Antiseptic hand rub	Formaldehyde, quaternium 15

[$]**FM**; fragrance mix, **MP** Myroxylon pereirae, **HICC**; hydroxyisohexyl 3-Cyclohexene Carboxaldehyde, **MI**; methyisothiazolinone, **MCI**; methylchloroisothiazolinone, **MDBGN**; methyldibromoglutaronitrile
[#]Equivocal (±), weak positive (+), strong positive (++) or extremely positive (+++)

Figure legend

Figure 1: Positive and relevant reactions to iodopropynyl butylcarbamate.



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