

What Is the Relevance of Contact Allergy to Sodium Metabisulfite and Which Concentration of the Allergen Should We Use?

Nicola Ralph, MB, BCh, BAO, MRCPI, Saroj Verma, MB, BCh, BAO, MRCPI, Subha Merry, RGN, Aoife Lally, MD, Brian Kirby, MD, and Paul Collins, MD

Background: The prevalence of contact allergy to sodium metabisulfite (SMB) has increased from the range of 1.4% to 1.7% to the range of 3.4% to 6.8% in published series over the past 20 years.

Aims: The aims of this study were to review contact allergy to SMB in our cohort and to investigate different concentrations to define the most appropriate concentration for patch testing.

Methods: Patient records were reviewed between February 2009 and December 2011 to obtain information on patient demographics, clinical presentation, and prevalence of contact allergy to SMB. Patients attending for patch testing, between January 2012 and June 2013, were tested with 3 strengths of SMB as part of the British standard series (1%, 0.1%, and 0.01%).

Results: Nine hundred ninety-six patients were patch tested to the British standard series including SMB 1% in petrolatum between February 2009 and June 2013, and 70 (7%) were positive. In the prospective group, 380 were tested to 3 concentrations of SMB (1.0%, 0.1%, and 0.01%). Fourteen patients (3.68%) had a positive patch test with 1% SMB, 7 to 0.1% SMB, and 3 to 0.01% SMB. There was exposure to SMB in 10 patients who cleared with avoidance at review 3 months later. The most frequent location of rash included face, hands, vulval, and perianal region.

Conclusions: Our study confirms reports of increasing prevalence of SMB allergy. A detailed review of exposure in the prospective study showed that SMB is relevant in most patients, and 1% in petrolatum is the best concentration for patch testing.

The prevalence of contact allergy to sodium metabisulfite (SMB) has increased from the range of 1.4% to 1.7% to the range of 3.4% to 6.8% in published series over the past 20 years as described in a recent comprehensive review.¹ However, the relevance of SMB-positive patch test reactions is still debated.¹⁻³ Well-defined erythema occurs at test sites in some of our patients, but the relevance and whether this is true contact allergy are uncertain.¹⁻³ The aims of this study were to determine the incidence and relevance of contact allergy to SMB in our cohort and to investigate patch testing with different concentrations of the allergen to define the most appropriate concentration for patch testing.

MATERIALS AND METHODS

We added SMB to the British standard series (1% in petrolatum; Chemotechnique, Vellinge, Sweden) in February 2009. We performed

From the Charles Centre, Department of Dermatology, St Vincent's University Hospital, Dublin, Ireland.

Address reprint requests to Nicola Ralph, MB, BCh, BAO, MRCPI, Department of Dermatology, Mater Misericordiae University Hospital, Eccles Street, Dublin 7, Ireland. E-mail: nicolaralph@hotmail.com.

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a retrospective review of the patient medical records with positive patch test reactions between February 2009 and December 2011. Patients attending for patch testing between January 2012 and June 2013 were tested to 3 strengths of SMB (1%, 0.1%, and 0.01% in petrolatum). Hospital ethics committee approval was obtained for the study. IQ Ultra chambers were used, and if not tolerated, Finn chambers with Scanpore tape were substituted, and results were read on day 2 (after 48 hours) and day 4 (after 96 hours) according to the International Contact Dermatitis Research Group criteria. Patient demographics, clinical presentation, and occupation were recorded. Current or past relevance was defined as the relationship between the dermatitis and exposure to sulfite based on the patient's history. Repeat open application test was not performed for patients with a past history of exposure to SMB.

RESULTS

Nine hundred ninety-six patients were patch tested to the British standard series including SMB 1% in petrolatum between February 2009 and June 2013, and 70 (7%) were positive. Thirty-nine were female, and 31 were male (56% female, 44% male). No patients reported systemic symptoms. The face was the most frequently

TABLE 1. Prospective Study: Results of 14 Patients With Positive Patch Tests to SMB

Number, Sex, Age	Occupation	Site	SMB 48 h			SMB 96 h			Other Allergens	Using a Product With SMB
			1%	0.1%	0.01%	1%	0.1%	0.01%		
1, F, 36	Housewife	Perivulval	+	—	—	++	+	—	Nivea soft cream, Palmolive shaving cream	+ Moisturizing cream
2, F, 48	Florist	Face (eyebrow)	—	—	—	+	+	—	Negative	+ Eyebrow tint
3, F, 62	Nun	Face	++	+	+	++	++	++	Amerchol L101 50%, propolis 10%, fragrance mix I 8%	+ Facial cream
4, M, 57	Electrician	Hands, feet	—	—	—	++	—	—	MI 0.2%, methylidibromoglutaronitrile 0.3%	+ Medicated cream
5, F, 36	Nurse (atopic)	Hands, face, eyelid	+	+	—	++	+	—	<i>Myroxylon pereirae</i> 25%, isoeugenol 2%	
6, M, 55	Photographer (atopic)	Hands	—	—	—	+	—	—	Negative	+ Photographic developer
7, F, 74	Retired	Upper and lower limbs	—	—	—	+	—	—	Negative	
8, M, 67	Farmer	Perianal	—	—	—	++	+	—	Negative	+ Baby powder, perianal cream
9, M, 23	Retail	Face (lip)	+	—	—	+	—	—	Nickel sulfate 5%	
10, F, 58	Lecturer	Face (periorbital)	+	—	—	+	—	—	Nickel sulfate 5%, epoxy resin 1%, tea tree oil 5%	+ Bleaching shampoo, tea tree oil cream
11, F, 31	Waitress	Hands	++	±	±	+	—	—	Formaldehyde 2%, MCI/MI 0.02%, MI 0.2%	+ Cleaning product
12, M, 60	Priest (atopic)	Upper and lower limbs, hands	—	—	—	+	+	+	Nickel sulfate 5%, cobalt chloride 1.0%	— Own products
13, M, 74	Retired	Perianal	+	+	—	+	+	±	Potassium dichromate 0.5%, neomycin 20%, cobalt chloride 1.0%, Anugesic HC cream	+ Topical medication
14, F, 63	Retired	Face (eyebrow)	—	—	—	++	+	—	Nickel sulfate 5%, fragrance mix II 14%,	+ Eyebrow tint

Patient 4 tested with Finn chambers.

M, male; F, female; MCI, methylchloroisothiazolinone; MI methylisothiazolinone.

affected (20/70, 28.5%), and other sites included the hands (16/70, 23%), pruritus ani/vulval dermatitis (16/70, 23%), and legs (7/70, 10%). Occupations included office work (18), housewife (13), and manual work (11). The reactions were considered to be of current relevance in 24 cases (34%), of possible past relevance in 14 (20%), and of unknown relevance in 32 cases (46%). Sodium metabisulfite was the only positive reaction in the standard and added series in 37 cases (53%), and 9 of these had been referred from the dental hospital with oral lichenoid reactions. Fourteen patients (20%) presented with 1 other positive patch test and 19 (27%) with 3 or more positive reactions (Table 1). There were incomplete data about potential exposure to SMB in 10 of 56 patients in the retrospective arm of the study.

In the prospective group, 380 were tested to the British standard series, which contained the 3 concentrations of SMB. They were tested to extended series including cosmetic and facial series (12), fragrances and essential oils (9), medicaments (3), and own

products (6 patients asked to bring their own products before patch testing but only 4 complied), and other series included hair-dressing (2), steroid (2), plant (1), footwear (1), rubber additives (1), textile color (1), and finish and bakery batteries (1). Additional series were applied from the outset based on the history.

Fourteen patients (3.68%) had positive patch tests with 1% SMB; 7 of these had a positive reaction to 0.1% and 3 to 0.01% SMB. One patient was tested with Finn chambers because he had an angry back reaction to IQ Ultra chambers (patient 4, Table 1). No patients reacted to 0.1% or 0.01% who were not positive to 1.0%. The age range was 19 to 81 years (mean age, 54 years). Six patients had facial eczema often involving the periorbital area; 5 had hand eczema, and 3 had perianal or perivulval involvement. Seven patients had a positive reading to 1% on day 2; 3 of these were positive to 0.1% and one to 0.01%. Five of these were using a product containing SMB. Two patients had a ++ reaction on day 2 to 1%; one had a + reaction to both 0.1 and 0.01%; and the other

TABLE 2. Occupational and Nonoccupational Sources and Use of SMB²**Nonoccupational sources of SMB**

- Cosmetics (hair colors and bleaches, skin fading/lighteners, false tan lotions, antiaging creams and moisturizers, facial cleansers, around-eye creams, body washes/cleansers, hair sprays, perfumes, blush, bronzers/highlighters)
- Swimming pool water
- Medications (trimovate, timodine, etc)
- Food preservative (E223)

Occupational sources and uses of SMB

- Food and drink (preservation and sterilization, refining sugar)
- Brewing, wine making (sterilization in fermentation processes)
- Photographic chemicals (formulation of developers and fixers)
- Dye houses/laundries (color stripper and antichlor)
- Leather (tanning [acidifying agent], solubilizing agent for tannins, reducing chrome liquors)
- Mineral extraction (ore flotation aid)
- Effluent treatment (to reduce chromium salts)
- Chemical manufacture (in the manufacture of sulfosuccinates and sodium formaldehyde bisulfite)
- Rubber manufacture (latex anticoagulant)
- Parenteral solutions (prevent oxidation of adrenaline)

Sulfite-containing foods (E221-E227)

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| <ul style="list-style-type: none"> • Apricots • Avocados • Baked products • Beer • Beet sugar • Canned seafood • Canned soups • Cider • Corn sweeteners • Dried fruits • Food starches • Fresh fruits • Gelatin • Grapes (grape juice) | <ul style="list-style-type: none"> • Lemon juice • Maraschino cherries • Mushrooms • Potatoes (french fries and potato chips) • Raisins • Salads (especially in restaurants) • Sausage meats • Shrimp (uncooked) • Some fruit drinks • Vegetables wrapped in cellophane • Vinegar • Vitamin K3 metabisulfite • Wine |
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had a $\pm$ to both. Fourteen patients had a positive reaction on day 4; 6 patients of these had ++ reactions on day 4; 5 had a clear history of exposure; and one (patient 14) did not have a history of current or past exposure.

Two patients presented with hand dermatitis because of their occupation. One was a photographer, who was atopic and had a + reaction on day 4 only, and was using a developer. The second patient was a waitress using a cleaning product containing SMB who had a ++ reaction on day 2 and + on day 4, but this was an allergic rather than irritant reaction. A thorough review of all products used by patients in the prospective study revealed 10 patients with a history of SMB exposure (Table 1), and all cleared on review at 3 months having eliminated exposure. There was no apparent exposure in 4 patients. Ten patients had contact allergy to other allergens in the standard and added series, and metals, fragrances, and preservative allergies were prevalent. Moisturizing creams, topical medication, and eye-brow tint were the most common sources of exposure to SMB, but many of these contained other relevant allergens (Table 1). One patient was allergic to tea tree oil and SMB in a tea tree

oil cream product. There were no irritant reactions in the prospective series.

DISCUSSION

Patch test reactions to SMB occurred in 70 patients (7%), and so in keeping with recent studies, they are frequent, increasing in prevalence, and often relevant, although a significant proportion of positive results remains unexplained.¹ Sodium metabisulfite 1% in petrolatum was the optimum concentration compared with lower concentrations and was recommended recently as the concentration of choice.¹ The relevance of SMB-positive patch test reactions has been debated in the literature and is not easy to resolve.¹⁻⁸ Sulfites are naturally occurring antioxidants and are used as preservatives in cosmetics, pharmaceutical products, and by the food industry (Table 2).² In our study, 24 patients (34%) had current exposure to SMB based on history, site, and use of cosmetic and topical pharmaceutical products.

However, a more extensive patch testing and detailed review of potential exposure to SMB in the prospective study uncovered

SMB exposure in 10 of 14 patients who improved once the product was avoided. Not all of these were apparent until a detailed list was compiled of products used and occupational exposure and an internet search was conducted on each product reported by the patient.

Patients who had facial eczematous eruptions, the most frequently affected site, reported exposure to cosmetics, and those with a perianal/vulval dermatitis reported recent or current use of topically applied medicaments (antifungal and hemorrhoidal creams), which contained SMB. In the retrospective arm, 14 patients had possible past relevant exposure, but this was difficult to define with certainty because SMB in products is sometimes missed of potential cross reaction to sulfites (Table 2), as well as exposure to other relevant preservative and fragrance allergens.^{4,7} Ten of the patients in the prospective study had concomitant allergens, often to fragrances and preservatives that are present in many cosmetic products containing sulfites. Vena et al⁶ reported that 12 of 50 positive reactions to SMB were relevant and prick tests, intradermal tests, and oral challenge in these cases were negative. We were unable to explain the significance of the result in 32 patients (46%) overall, but this reduced to 4 of 14 patients in the prospective study because of a more detailed inventory of potential exposure. These 4 patients were asymptomatic, and it was a coincidental finding. This is not unusual.^{1–8} Relevance may be easier to determine in cases of occupational exposure, in particular, the hairdressing and food industry, and further patch testing to the

appropriate sulfite should be performed in these cases.^{1,2,6,9} Patients who have a positive patch test result to SMB should avoid exposure to other sulfites,^{7,8} and it should prompt a detailed review of cosmetic, topical medicament, occupational exposure, and, where possible, patch testing to own products.

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