

Fixed drug eruption from sodium benzoate

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We report a fixed drug eruption caused by a syrup containing sodium benzoate. Our patient gave a positive reaction to a patch test and to a provocation test after 15 h ingestion, but no patch test reaction in the interdigital area where the patient had previous lesions.

Key words: cutaneous adverse drug reactions; fixed drug eruption; positive patch test; provocation test; sodium benzoate. © Blackwell Munksgaard, 2004.

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Sodium benzoate is used to preserve certain products in the cosmetic, chemical and food industries, as well as a corrosion inhibitor and in antifreeze solutions. Its solubility in water is 556 g/l at 20° C.

It is used to treat acute hyperammonaemia (1), for local anaesthesia in association with other substances (2), to add flavour in oral drugs (3) and also to treat dental plaque (4).

In the opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers in a meeting held on 4 July 2002, sodium benzoate (C_6H_5COONa) could be used without danger at maximum concentrations of 2.5% in skin-cleansing cosmetic products and at 1.7% in dental hygiene. As food conservers, it can be used at 0.7%, and at 0.5% in oral and parenteral drugs.

We can consider safe its use for humans and experimental animals and WHO considers it acceptable to ingest daily 5 mg/kg, which means 375 mg/kg per day for an average adult (5).

It has been incriminated in acute leucocytoclastic vasculitis (6) and in asthmatic crisis, because it appears in some food (7) and drinks (8). It has also been described as causing anaphylactic reactions (9).

Referring to cutaneous reactions, it has been related to the following: immune urticaria with angioedema (8); 3 cases of airborne contact urticaria in a pharmaceutical manufacturing plant (10); flares of atopic eczema in sensitive patients (11); and 1 case of a patient who was sensitized from a toothpaste (12).

Case Report

A 64-year-old female teacher, with no personal or family history of any allergic or cutaneous disorders, had 2 years ago, a few days after suffering from a throat infection, presented with itching on the right side of the ring finger of the right hand and within 48 h developed erythema and oedema at that site. 4 days later, a blister appeared in the same site with symptoms of pain and burning. This blister resorbed in 10 days and a pigmented circular area then appeared which also disappeared a month later.

Our patient experienced similar episodes during the years 2000 and 2001, until she related them to the syrup that she was taking for respiratory infections, the qualitative composition of which is summarized in Table 1.

Table 1. Results of patch testing with syrup components

Component	% vehicle	D2	D4
Trimethoprim	5% petrolatum (pet.)	–	–
Sulfamethoxazole	5% pet.	–	–
Bromhexine hydrochloride	5% and 10% pet.	–	–
Sodium benzoate	5% pet.	+	+
Tolu balsam	1% alc.	–	–
Glycerol (E422)	10% aq.	–	–
Xanthan gum	1% pet.	–	–
Parabens mix.	6% pet.	–	–
Polysorbate 80	10% pet.	–	–
Dimethylpolysiloxane	2% pet.	–	–
Anise essence	25% o.o.	–	–
Saccharin sodium	As is	–	–
Saccharose	As is	–	–

The patient was admitted to a Medical Centre where she was prick tested to various medicines, dusts, mites, grass pollen, etc. All results were negative.

Eventually, in November 2002, her general practitioner referred her to our Allergic Unit for investigation. We carried out patch test on her with the Chemotechnique (Malmö, Sweden) drugs series, and, she was also patch tested with the components of the incriminated syrup (Table 1). Only 1 of these components, sodium benzoate, gave a positive result (+) at D2 and D4 (Table 1). 2 months later, the patient consented to a patch test being carried out in the interdigital area with sodium benzoate at 5% petrolatum. Results were negative at D2 and D4.

In February 2003, the patient consented again to a sodium benzoate provocation test which was carried out as follows. Firstly, we prescribed for her a sodium benzoate-free diet for 15 days before the test. The diet was based on the following foods: milk, cheese, vegetables, fresh fish and meat, bread and water (13). We prepared a solution of 750 mg of sodium benzoate in 100 cc of distilled water, all of which was orally administered. 15 h after ingestion, the patient noted lesions in right lateral zone of the first phalange of the right finger and also in the interdigital area between the right ring and middle fingers. 48 h later, she developed a bulla at the affected site in the same location and with the same intensity as she had shown previously.

Discussion

Sodium benzoate sensitized 1.9% of 465 patients who presented with a suggestive clinical history of allergic contact dermatitis due to cosmetics, drugs, textiles and industrial products (14,15). It has been described several times as aetiological agent in various dermatological reactions, but we have not found any reference to it being the aetiological agent of a fixed drug eruption with positive patch test results at D2 and D4, nor a positive reaction to a provocation test by oral administration of 750 mg of sodium benzoate in 100 cc of water.

Although a lesional patch test was negative, this does not undermine the diagnosis, because

only 1 of 12 patients gave a positive lesional patch test in a previous study (15).

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