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Occupational Allergic Contact Dermatitis With Secondary Spreading From Vitamin K₃ Sodium Bisulphite in a Pig Farmer

To the Editor:

Vitamin K is a group of 6 molecules derived from 2-methyl-1,4-naphthoquinone. Vitamin K₁ (phyloquinone or phytomenadione) is an anticoagulant; its oxidized isoform is used in cosmetics as a lightening against hyperpigmentation of the skin^{1,2} and to prevent and to treat Epidermal Growth Factor Receptor inhibitors-related papulo-pustular eruption.³ Vitamin K₂ (menaquinones) is synthesized by symbiotic bacteria in human gut flora. Vitamin K₃ (menadione) is a synthetic organic fat-soluble molecule; its water-soluble form (menadione sodium bisulphite) is widely used as food supplement and as a veterinary antihemorrhagic drug. Vitamin K₄ is used to treat neonatal hemorrhagic diseases and as an antifungal additive in animal feed, along with vitamin K₅ and vitamin K₆.^{1,2}

Case History

A nonatopic 42-year-old male pig farmer came presenting an itchy dermatitis lasting more than 1 month affecting his right forearm and hand. In the following days, the dermatitis progressed to a severe vesicular eczema involving the face, axillary

folds, abdomen, buttocks, upper and lower limbs, as well as feet (Fig. 1). Eczematous lesions developed a few hours after occupational exposure to veterinary powder containing vitamin K₃ sodium bisulphite (Kappavit). For the last decade, the patient usually prepared the antihemorrhagic drug by dissolving it into water (0.1%) using his right forearm. The eczema gradually cleared with oral prednisone and ebastine (an H1-blocker antihistamine) and an emollient cream; 1 month later, the patient restarted his job and immediately experienced a flare-up of the previous eczema. Three months before, he had started taking a food supplement containing vitamin K₁, which we stopped at the time of referral. Patch tests were performed on the upper back with Haye's Test Chambers (Haye's Service B.V., Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy) and removed after 2 days. The readings (D2 and D4) were performed according to International Contact Dermatitis Research Group criteria. Positive reactions to Kappavit (0.1%), vitamin K₃ (0.01 and 0.1%), and vitamin K₃ sodium bisulphite (0.01 and 0.1%) were reported (Table 1). Patch tests with these K vitamins in 20 healthy subjects were negative. Food supplement containing vitamin K₁ was restarted, without a relapse of skin lesions.

DISCUSSION

In the literature, only 4 cases of occupational allergic contact dermatitis (ACD) from vitamin K₃ sodium bisulphite are reported, all in the 80s.^{4–6} Two patients worked in a veterinary factory,^{4,6} whereas 2 patients were employed in a pharmaceutical laboratory.^{4,5} No cases have been reported in pig farmers. In 3 patients, eczematous dermatitis developed at the sites of contact with vitamin K₃.^{4,6} In 1 case, a widespread eczematous dermatitis was accompanied by gastrointestinal symptoms and giddiness, suggesting a systemic poisoning by inhalation or ingestion of the allergen in a sensitized patient.⁵



FIGURE 1. Eczematous dermatitis of the forearms (A), face (B), and lower limbs (C). The patient signed an informed consent for the publication photographs.

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TABLE 1. Results of Patch Test With K Vitamins

K vitamins	%	D2	D4
Kappavit	0.1 [*]	++	++
Vitamin K ₃	0.01 [†]	++	++
	0.1 [†]	+++	+++
Vitamin K ₃ sodium bisulphite	0.01 [*]	++	++
	0.1 [*]	+++	+++
Vitamin K ₁	0.01 [†]	---	---
	0.1 [†]	---	---
	1.0 [†]	---	---
Sodium bisulphite	5.0 [†]	---	---
Sodium metabisulphite	5.0 [†]	---	---
Konakion (vitamin K ₁)	1.0 [*]	---	---

*In saline solution.

[†]In pet.

The reported case shows that ACD from vitamin K₃ sodium bisulphite is not a forgotten problem but it continues. Clinical history of our patient shows that the eczema developed on the right upper arm, site of occupational exposure to water-soluble Kappavit, with subsequent symmetric spreading to nonexposed sites. This suggests that our patient developed ACD from vitamin K₃ sodium bisulphite with secondary spreading.

Vitamin K₃ sodium bisulphite is a well-known irritant compound. Patch tests are not easy to perform. According to published data,⁴⁻⁷ they should be carried out at 0.01% and 0.1%. In our patient, both 0.01% and 0.1% proved positive. We did not observe irritant patch tests with these concentrations, either in patients or controls.

In the literature, a single case of cross reactivity between vitamin K₁ and vitamin K₃ was reported.⁷ This was characterized by itching eczematous reaction in the site of an intramuscular injection of vitamin K₁, with subsequent spreading to the face, neck, and arms. The patient also presented positive patch test to vitamin K₃ sodium bisulphite 0.1%, suggesting possible cross

reaction. In our case, a cross reaction between vitamin K₁ contained in the food supplement and vitamin K₃ sodium bisulphite was excluded on the basis of a negative patch test for vitamin K₁. Moreover, subsequent re-administration of vitamin K₁-based food supplement did not result in flare-up of eczematous lesions. Finally, we highlight the oral tolerability of vitamin K₁ in a vitamin K₃ contact-sensitized patient. However, as proposed by Wong and Freeman,⁷ in a patient sensitized to K vitamins, both K₁ and K₃ vitamins should be tested.

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