

Short Communication

Adverse skin reactions to vitamin K₁: report of 2 cases

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Key words: vitamin K₁; positive intradermal test; negative patch test; phytomenadione; delayed hypersensitivity; medicaments; drug reactions. © Munksgaard, 1998.

Vitamin K is essential to the biosynthesis of prothrombin and other clotting factors (VII, IX and X), and is mostly used for the prophylaxis of bleeding disorders, mainly in patients with hepatic disfunction (1). 4 different pharmacological forms exist: the natural form K₁ (phytomenadione); K₂ (menaquinone), which is derived from intestinal bacterial action; K₃ (menadione); and K₄ (menadiol). The latter 2 are synthetic products. In Italy, only vitamin K₁ is marketed (2).

Adverse cutaneous reactions to vitamin K are rare; 2 are mainly reported: an erythematous plaque (3, 4) or pseudo-scleroderma (5) at the injection site. Contact dermatitis and localized urticarial lesions have also been described (2).

Case Report

Case no. 1

A 49-year-old woman began pre-operative treatment with intramuscular (i.m.) folic acid (Prefolic[®], 15 mg/day) and vitamin K₁ (Konakion[®], 10 mg/day). 5 days later, she developed at the site of the injections (right buttock) a large erythematous, slightly itchy plaque. At

the same site, 2 years earlier, she had received 30 mg (10 mg/day) of i.m. vitamin K₁ for a haemorrhage.

The tests performed gave results shown in Table 1.

Histopathologic examination of 2 biopsy specimens (from the lesion and the intradermal (i. d.) test site) showed epidermal hyperkeratosis and focal spongiosis, in addition to a perivascular infiltrate consisting mainly of lymphocytes and eosinophils.

Administration of vitamin K₁ was stopped. Topical betamethasone was applied 2×daily for 20 days, but was almost ineffective. The lesion persisted for about 4 months and then healed spontaneously.

Case no. 2

A 59-year-old man had been treated with i.m. vitamin K₁ (Konakion[®]) 10 mg/day for 3 years and then orally for 2 years. For 1 year, he had had a sclerotic plaque extending from the upper half of both buttocks to the lateral aspects of the thighs, with the typical "cowboy gunbelt and holster" pattern.

Histopathology showed a scleroderma-like picture: thinning of the epithelial outline and reduction of adnexal structures; thickening and packing of collagen

Table 1. Case no. 1

	Patch test (D3)	Scratch-patch test (20 min and D3)	Prick test (20 min and D3)	Intradermal test (20 min and D3)
GIRDCA standard series	—	NT	NT	NT
Konakion [®] as is	—	—	—	positive
Prefolic [®] as is	—	—	—	—

Table 2. Case no. 2

	Patch test (D3)	Scratch-patch test (20 min and D3)	Intradermal skin test (20 min and D3)	Intradermal skin test (D7)
GIRDCA standard series	—	NT	NT	NT
Konakion [®] as is	—	—	—	positive
Prefolic [®] as is	—	—	NT	NT

bundles in the reticular dermis and replacement of fat cells with collagen in the subcutaneous tissue were also noted.

The tests performed gave results shown in Table 2.

The i.d. test with Konakion® as is 0.1 ml was negative at 20 min and D3: at D7, an erythematous, slightly indurated macule appeared. The efficacy of treatment with systemic pentoxifylline (1200 mg/day) and topical emollient creams for 1 year was poor.

Discussion

In earlier reports, most reactions to parenteral vitamin K₁ were found in patients with liver disease, thus suggesting that hepatopathy may play a rôle in determining an adverse reaction. However, since then, patients with no signs of liver disease have been described: therefore, the high prevalence of adverse reactions in patients with hepatic disease probably depends on the large number of hepatopathic patients needing treatment with vitamin K (2). To the best of our knowledge, no cases have been described in which orally administered vitamin K resulted in adverse reactions: only parenteral oil-soluble vitamin K seems to be able to react (1–10).

Our cases confirm previous observations: the 1st patient did not have any hepatopathy, and in both cases, a parenteral oil-soluble formulation had been used. The pathogenetic mechanism of these reactions still remains unknown, but in some reports, delayed-type hypersensitivity has been suggested (7). We found negative responses to patch tests with vitamin K₁. In a recent review, 7 out of 17 patients patch tested with vitamin K₁ were negative, but they had at least 1 positive intracutaneous test (2). However, several histopathologic studies, made on biopsies from both the lesion and the intracutaneous test site, have shown a histologic picture consistent with delayed-type hypersensitivity. Thus, it is advisable to perform both patch and intracutaneous tests in patients suspected of adverse reactions to vitamin K (10).

Acknowledgement

My special thanks to Mario Vaccaro for empathic consultation.

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