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Adverse reactions to vitamin B12 injections due to benzyl alcohol sensitivity: successful treatment with intranasal cyanocobalamin

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Key words: benzyl alcohol; cyanocobalamin; drug reaction; hydroxycobalamin; vitamin B12.

A 16-year-old female was referred for assessment of possible anaphylactic reactions following vitamin B12 injections. In March 2001, the patient received an intramuscular injection of vitamin B12 (cyanocobalamin 1000 µg) and experienced pain at the injection site. In May 2001, 1 h after her second injection, she reported a sensation of substernal burning and pleuritic pain that resolved over days. Within minutes of her third injection in June 2001, she felt similar chest discomfort and developed pruritus of the arms and legs, but no rash.

As the reactions to cyanocobalamin injections were becoming progressively

more serious, she was referred for assessment. A number of allergic reactions following parenteral administration of vitamin B12 have been described (1–4). Cobalamin is synthesized for therapeutic use as either cyanocobalamin or hydroxycobalamin. There are reports of patients with reactions to one form of cobalamin who have been able to tolerate the alternate formulation (4–7). Unfortunately, this management strategy was not available to us as the hydroxycobalamin preparation is not available in the United States.

She was skin tested to three commercial preparations of injectable cyanocobalamin and to the benzyl alcohol (0.9%) preservative found in each. Prick testing was negative (Table 1a), but intradermal testing to all cyanocobalamin preparations and benzyl alcohol was positive (Table 1b).

These results indicated that the patient was likely reacting to the benzyl alcohol preservative present in the cyanocobalamin injections. However, the data did not eliminate the possibility of sensitization to both the benzyl alcohol and cyanocobalamin. Hypersensitivity reactions to benzyl alcohol have been documented in patients treated with a variety of medications containing benzyl alcohol as a preservative (8, 9).

Although there was no commercially available parenteral formulation of vitamin B12 lacking the benzyl alcohol preservative, we were fortunate to identify Nascobal® (Questcor Pharmaceuticals

Intranasal administration of cyanocobalamin is an option for vitamin B12-deficient patients sensitive to benzyl alcohol.

Table 1. Skin test results

	Patient	Healthy control
(a) Skin prick testing results		
Cyanocobalamin brand no. 1 (1 mg/ml)	Negative	Negative
Cyanocobalamin brand no. 2 (1 mg/ml)	Negative	Negative
Cyanocobalamin brand no. 3 (1 mg/ml)	Negative	Negative
Benzyl alcohol (0.9%)	Negative	Negative
Histamine (6 mg/ml)	10 mm wheal + flare	10 mm wheal + flare
Normal saline	Negative	Negative
(b) Intradermal testing results		
Cyanocobalamin brand no. 1 (0.01 mg/ml)	7 mm wheal + flare	Negative
Cyanocobalamin brand no. 2 (0.01 mg/ml)	6 mm wheal + flare	Negative
Cyanocobalamin brand no. 3 (0.01 mg/ml)	10 mm wheal + flare	Negative
Benzyl alcohol (0.009%)	9 mm wheal + flare	Negative
Normal saline	Negative	Negative

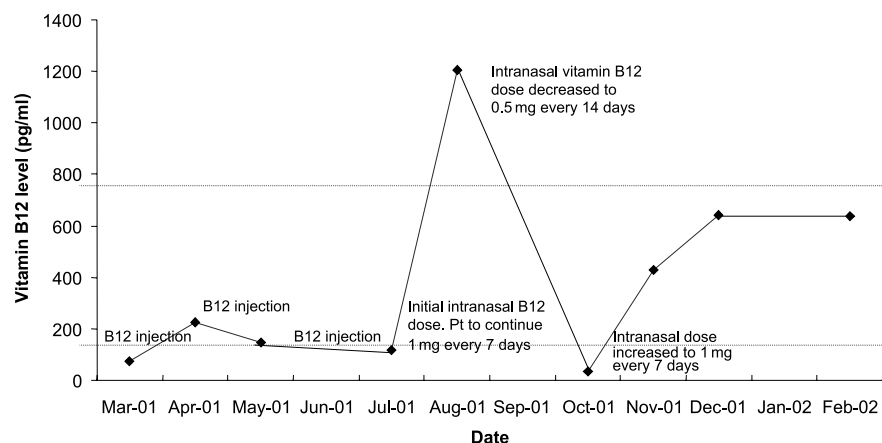


Figure 1. Serum vitamin B12 levels and replacement schedule.

Inc., Union City, CA, USA), a cyanocobalamin gel for intranasal administration that does not contain benzyl alcohol. The patient was skin tested to this nasal preparation at its full concentration and demonstrated no reaction. She was given a test dose of 500 µg, with no adverse reaction. Subsequently her vitamin B12 deficiency was successfully treated with the nasal preparation of cyanocobalamin as demonstrated by her relatively stable levels of vitamin B12 since beginning treatment (Fig. 1).

This patient's reactions to benzyl alcohol, along with previously reported cases, confirm the importance of considering benzyl alcohol as a cause of hypersensitivity reactions to parenteral medications. Intranasal administration of cyanocobalamin gel is an option for

vitamin B12-deficient patients who are sensitive to benzyl alcohol.

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