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Allergy to B12: two cases of successful desensitization with cyanocobalamin

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Key words: B12 vitamin allergy; cyanocobalamin; desensitization; hydroxycobalamin.

Allergy to vitamin B12 is uncommon. However, once diagnosed it presents difficult management problem in patients suffering from pernicious anemia, as there is no substitute (1).

The allergen involved in vitamin B12 reactions is likely to be a hapten.

We present two cases of desensitization with cyanocobalamin following a generalized reaction to B12 vitamin injections. Our two patients were nonatopic 45-year-old females, suffering from pernicious anemia. Both of them received quarterly cyanocobalamin injections for more than 3 years.

The first patient developed generalized urticaria 10 min after an injection of 1 mg of hydroxycobalamin. Symptoms subsided within 20 min after 10 mg chorpherniramine intramuscularly. She was tested with cyanocobalamin and hydroxycobalamin. Skin prick testing with solutions 1 mg/ml were negative. Intradermal testing with both preparations (1/100 dilutions) showed positive responses with a wheal of 8 × 9 mm surrounded by a flare.

The second patient developed anaphylaxis 5 min after injection of 1 mg of hydroxycobalamin. Symptoms included facial angioedema, swollen tongue, generalized urticaria, hypotension, dizziness and chest tightness. She was treated with intravenous methylprednisolone 80 mg and chorpherniramine 10 mg with good

response. Interestingly she remembered burning redness of her eyes, mild facial angioedema, 30 min after previous injection. Skin prick testing to cyanocobalamin and hydroxycobalamin were negative. Intradermal testing with one of 10 dilutions showed positive results to hydroxycobalamin and cyanocobalamin.

We desensitized both patients with cyanocobalamin. Our protocol comprised incremental subcutaneous injections every 15 min according to the following schedule (see Table 1).

At the end of the first day of our desensitization protocol intradermal tests to both cyanocobalamin and hydroxycobalamin with the following concentrations (1/100, 1/10, and neat) were negative. We continued with the above desensitization protocol with increasing intervals of 1, 2 and 4 weeks between the sessions. The persistence of negative results of intradermal testing was confirmed before each desensitization procedure. Loss of skin sensitivity appeared to be a good predictor of tolerance of the drug. Both patients continued receiving cyanocobalamin injections monthly with good tolerance.

Drug desensitization is time dependant and re-sensitization recurs after a while. We have little information about the length of time the drug tolerance persists. It is thought to be in the range of weeks. According to our experience, with the

above patients, it persists for at least 4 weeks. We did not assess a longer time interval and therefore would advise four weekly treatment with the therapeutic dose.

Our patients showed cross sensitivity between cyanocobalamin and hydroxycobalamin therefore we had no substitute drug available. Cross sensitivity has previously been described although it is not always found (2, 3). In a patient with hydroxycobalamin allergy and a negative result to cutaneous testing with cyanocobalamin, this latter preparation may be tolerated.

We have not been able to measure specific IgE in patients' serum, though the mechanism is likely to be IgE dependant. We suspect this to be true as both sensitizations occurred after a period of tolerance with increasing severity of the reaction after each injection. We were able to confirm positive skin test results in our patients as compared with negative test results in control subjects.

The preparation of cyanocobalamin we used did not contain benzyl alcohol preservative which has been involved in patient reacting to vitamin B12 injection (4). The allergen involved in vitamin B12 reactions is likely to be a hapten.

We are indebted to Lucy Riddington, allergy specialist nurse, for technical support.

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Table 1. Desensitization protocol with cyanocobalamin (1 mg/ml)

	Dilution	Amount (ml)
1st day	1/10000	0.1; 0.3; 0.6;
	1/1000	0.1; 0.3; 0.6;
	1/100	0.1; 0.3; 0.6;
	1/10	0.1; 0.3; 0.6;
	Neat	0.1
7th day	Neat	0.01; 0.03; 0.1
21th day	Neat	0.1
49th day	Neat	0.1

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Corrigendum

In (1), the following table was published on page 1341:

Table 1. Desensitization protocol with cyanocobalamin (1 mg/ml)

	Dilution	Amount (ml)
1st day	1/10 000	0.1; 0.3; 0.6;
	1/1000	0.1; 0.3; 0.6;
	1/100	0.1; 0.3; 0.6;
	1/10	0.1; 0.3; 0.6;
	Neat	0.1
7th day	Neat	0.01; 0.03; 0.1
21th day	Neat	0.1
49th day	Neat	0.1

This table was incorrect and should have read:

Table 1. Desensitization protocol with cyanocobalamin (1 mg/ml)

	Dilution	Amount (ml)
1st day	1/10 000	0.1; 0.3; 0.6;
	1/1000	0.1; 0.3; 0.6;
	1/100	0.1; 0.3; 0.6;
	1/10	0.1; 0.3; 0.6;
	Neat	0.1;
7th day	Neat	0.1; 0.3; 0.6
21th day	Neat	1
49th day	Neat	1

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2. Simons FER, Frew AJ, Ansotegui IJ, Bochner BS, Golden DBK, Finkelman FD et al. Practical allergy (PRACTALL) report: risk assessment in anaphylaxis. Allergy 2008;**63**:35–37.

In (2), the following words were duplicated on page 36, paragraph 3:

do not need to be differentiated with regard to clinical diagnosis and acute treatment.

This was incorrect and the sentence should have read:

Effector mechanisms in anaphylaxis do not need to be differentiated with regard to clinical diagnosis and acute treatment; nevertheless, it remains critically important to understand them with regard to long-term risk reduction measures, which are trigger- and mechanism-specific.