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Letter to the Editor

Urticaria by thiamine (vitamin B1)

Dear Editor,

Vitamin B1 or thiamine hydrochloride is the most allergenic vitamin. However, type I hypersensitivity reactions are unusual, but a few cases have been reported until the date.¹ Although delayed reactions may occur (like systemic allergic dermatitis),² immediate reactions after intravenous administration are mostly related with thiamine (like anaphylaxis).^{3–5}

We present a 50-year-old woman who was referred to our Allergy Unit for drug allergy study. She developed a generalized urticaria, edema and facial erythema after 30 min of intramuscular administration of Inzitan®-cyanocobalamin, dexamethasone, pyridoxine, thiamine (50 mg; 25 mg/ml) and lidocaine-(Kern Pharma, Barcelona, Spain). No other symptoms were associated. Previously she had good tolerance to this drug, as well as to oral dexamethasone and other oral and topic corticosteroids (prednisone, betamethasone). The reaction resolved with intramuscular (IM) dexchlorpheniramine in 60 min. Epinephrine or other treatments were not necessary at this moment.

After obtaining informed consent from the patient, an allergy study was realized.

Skin tests were performed in prick test with a negative result for all compounds of Inzitan. Due to lower sensitivity of the prick test to intradermal test (IDT), and therefore a greater number of false negatives, we performed IDT with all types of vitamins B: vitamin B12-cyanocobalamin-(1 mg/ml); vitamin B6-pyridoxine-(1 mg/ml); vitamin B1-thiamine-(1 mg/ml); and with the other culprit drugs: dexamethasone (0.04 and 0.4 mg/ml) and lidocaine (0.2 mg/ml and 2 mg/ml) with immediate readings at 15 min. To calculate the concentration of the thiamine IDT we performed dilutions with healthy controls. Histamine was used as positive control test and physiological serum as negative control. The IDT with vitamin B1-thiamine was positive, and negative with all the rest of drugs tested (Fig. 1). Ten healthy controls were negative.

A drug provocation test (DPT) was performed with oral vitamin B12, vitamin B6, dexamethasone and subcutaneous, lidocaine with gradually increasing doses of 30 min intervals, following the protocol of the European Academy of Allergy and Clinical Immunology (EAACI) drugs committee,⁶ all with good tolerance.

We diagnosed the patient of an acute urticaria-angioedema due to sensitization to vitamin B1-thiamine, confirmed by skin tests, which suggests a type I hypersensitivity mechanism.

Vitamin B1-thiamine-is found in many foods like yeast, integral cereal, oatmeal, nuts and meat. It's used for treating vitamin deficiency syndromes such as Beriberi and Wernicke's encephalopathy.

In addition, its recommended in patients with vitamin deficiency due to malnourished, chronic alcoholics and in some kind of patients as a supplement to reduce the number of infectious diseases.³

Although type I hypersensitivity reactions are uncommon, a few cases have been reported in the literature but most of them are poorly documented (Table 1). Most of the severe reactions related to vitamin B1-thiamine, like anaphylaxis, occur by intravenous administration.^{4,5} It seems like oral intake is less frequent related with hypersensitivity reactions. Some authors suggest that the reason might be due to phosphorylation of thiamine hydrochloride at the resorption site in the intestinal mucosa.⁵

Only a few cases of skin test have been reported.^{3,5} In addition, these tests have shown a high sensitivity,^{7–9} as we can observe in our patient. Proebstle *et al.*⁵ reported an anaphylactic reaction with positive prick test, specific IgE and IgG antibodies to thiamine hydrochloride. Fernandez *et al.*³ reported another case of anaphylaxis to thiamine, diagnosed by positive prick test (1 mg/ml) and *in vitro* histamine release assay with purified basophils of the subject and 4 negative controls. Histamine release was observed with vitamin B1 (a dose response curve was obtained between 100 and 0.001 pg that did not appeared in the negative controls).

We present an acute urticaria-angioedema due to sensitization to vitamin B1-thiamine diagnosed by positive IDT. We would like emphasize the value of skin tests for diagnosis of vitamin B1-thiamine allergy and the importance of a complete and detailed allergy study.



Fig. 1. IDT with vitamin B1-thiamine.

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Table 1

Review of the literature: immediate reactions to thiamine.

Author	Clinical symptoms	N° cases	Skin test	In vitro test
Proebstle <i>et al.</i> (1995)	Anaphylaxis	1	- Prick test (undetermined concentration): positive	IgE (ELISA): positive
Fernandez <i>et al.</i> (1996)	Anaphylaxis	1	- Prick test (1 mg/ml): positive	BAT: positive
Fernandez <i>et al.</i> (1997)	Anaphylaxis	1	- IDT (0.5 mg/ml): positive	- IgE (ELISA): positive - HR: positive
Juel <i>et al.</i> (2013)	Anaphylactic shock	1	NP	NP

NP, not performed; BAT, basophil activation test; HR, non specific histamine release.

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The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article.

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Conflict of interest

The authors have no conflict of interest to declare.

Ana Rodríguez-Fernández *, Marcos Sánchez-Domínguez, Blanca Noguerado-Mellado, Patricia Rojas-Pérez-Ezquerro

Allergy Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

* Corresponding author. Allergy Department, Hospital General Universitario Gregorio Marañón, 46th Dr Esquerdo St., 28007, Madrid, Spain.
E-mail address: anarf@me.com (A. Rodríguez-Fernández).

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