

Immediate-hypersensitivity reaction to glucosamine sulfate

V. Matheu*, M. T. Gracia Bara, R. Pelta, E. Vivas, M. Rubio

Key words: glucosamine; immediate hypersensitivity; nonallergy.

• OSTEOARTHRITIS (OA) is the most common of the rheumatic diseases. About 10% of the population over the age of 60 suffer from symptoms of OA, and its incidence is increasing (1). Several agents are used in the disease-modifying therapy of OA, among them, the so-called "chondroprotective" agents. Some of them inhibit cyclooxy-

genase and prostaglandin biosynthesis, in which case they should be more properly classified

as mild NSAIDs (2). Only two of them, namely, diacerein and D-glucosamine sulfate, have true chondroprotective effects with anti-inflammatory and antireactive properties which are not based on inhibition of cyclooxygenase. Drug eruption or immediate-hypersensitivity reactions to these drugs have not been described. We report a patient with angioedema induced by glucosamine sulfate (GS).

A 76-year-old woman with arterial hypertension and OA was referred for evaluation of a recent episode of urticaria after drug intake. She was prescribed GS one dose per day for osteoarthritis. She suffered erythematous lesions and facial swelling within several hours after oral GS. The next day, 5 min after a new dose, she developed tongue, facial,

and throat swelling with facial erythema. She was treated in the emergency department with antihistamines and corticosteroids, and her symptoms resolved in 4 h.

After a washout period, the skin prick test and the intradermal test with GS prepared in our laboratory were performed. The skin prick test was negative. The intradermal test with a concentration of 1.5 mg/ml was positive with a papule of 36 mm². Positive control with histamine chloride (168 mm²) and negative control with saline serum (no papule) were also performed. The intradermal test in 10 healthy volunteers was negative. The ELISA, designed and performed for specific IgE against GS, was negative.

GS is the salt of D-glucosamine with sulfuric acid. The molecular mass of GS is 456.42 Da. In solution and in the human body, GS dissociates into the D-glucosamine ion (D-G), the active principle, and the sulfate ion. D-G is a chondroprotective agent with chondrometabolic, antireactive, and antiarthritic effects (2). D-G administered as sulfate (GS) has been proven to be effective in OA in double-blind, controlled clinical studies, improving mobility and relieving pain (3-5). The relief of pain under GS appears after 2-3 weeks of treatment, while under ibuprofen the pain is relieved already in week 1 of treatment (6).

Since its therapeutic effect is not due to inhibition of prostaglandin synthesis, treatment is not accompanied by the usual unwanted side-effects. Gastrointestinal discomfort and nausea have been reported, but the incidence was no higher than with placebo (7). This is the first case described of a patient with symptoms of immediate hypersensitivity induced by ingestion of GS. In view of the patient's history and the intradermal test, an IgE-mediated mechanism is possible. Failure to demonstrate IgE antibodies against GS is not surprising, given the small size of this molecule

and the problems arising with regard to linkage. In conclusion, GS appears to be a safe drug.

*Sección de Alergia
Hospital General Universitario Gregorio
Marañón
C/Dr. Esquerdo, 46
28007 Madrid
Spain
Tel. 34-91-5868268
Fax: 34-91-5868018

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Sensitization to pistachio is common in *Parietaria* allergy

G. Liccardi*, M. Russo, G. Mistrello, P. Falagiani, M. D'Amato, G. D'Amato

Key words: food allergy; *Parietaria*; pistachio nut; respiratory allergy.

Table 1. Results of diagnostic procedures in patients sensitized to both *Parietaria* and pistachio nut*

Patient	Sex	Age (years)	After exposure to <i>Parietaria</i>			<i>In vivo</i> tests (wheal areas as mm ²)				<i>In vitro</i> tests			
			Clinical symptoms	Pattern of symptoms	Duration of disease (years)	SPT		PPT		Total IgE (U/ml)	IgE Specific classes		Allergic oral/systemic symptoms After eating p.n.
						P	p.n.	H	p.n.		P	p.n.	
CM	M	15	R+A	Per.	8.3	22.5	12.6	19.8	19.8	60	2	0	+
CE	F	8	R+A	S	1.6	38.5	28.7	28.5	20.6	150	3	1	+
PF	F	37	R+C	S	10.3	62.6	9.1	12.5	7.8	44	3	1	+
UL	M	20	R+C	S	4.5	50.2	8.2	19.5	8.3	364	4	1	+
SA	M	26	R+A	S	8.4	28.7	27.6	29.3	19.6	276	2	1	+
DPD	M	28	R+C+A	S	10.1	63.9	38.5	19.2	12.8	114	4	1	–
HG	F	23	R	S	5.7	18.5	19.8	28.8	12.5	38	2	0	–
FO	F	52	R+A	Per.	7.2	132.7	12.8	63.6	20.6	148	4	0	–
MA	M	26	R+C+A	S	6.8	63.8	19.6	38.7	13.5	173	4	0	–
FD	M	14	R+C	S	11.6	50.2	15.5	28.2	7.6	125	4	0	–
DNA	M	9	R+A	S	1.9	60.6	12.5	19.3	7.9	198	3	1	–

P: *Parietaria*; R: rhinitis; A: bronchial asthma; C: conjunctivitis; Per.: perennial; S: seasonal; H: histamine (positive control).

*All these subjects occasionally ate pistachio.

● **PISTACHIO** nuts (the anacardiaceous species *Pistacia vera*) are widely used in the catering industry to produce ice creams, cakes, and mortadella; they are also eaten roasted. Very few cases of pistachio nut sensitization have been reported

(1, 2), whereas sensitization to other dried fruits is well established. We previously described two patients, sensitized to *Parietaria* allergens, who were affected by severe oral allergy syndrome after the ingestion of pistachio nut (3). Using SDS-PAGE and immunoblotting techniques, we also found a slight degree of cross-reactivity between *Parietaria* and pistachio nut allergens in these two cases (3).

This study aimed to evaluate the frequency of allergic sensitization to pistachio nut in atopic and nonatopic individuals, and to determine whether sensitization to pistachio nut is more frequent in patients with *Parietaria* pollinosis.

Patients with *Parietaria* pollinosis should undergo allergy testing for pistachio nut if they frequently eat this food.

A total of 1529 subjects, who were examined at our allergy center from 1 February 1996 to 31 January 1998 for nasal and/or bronchial symptoms that seemed to be IgE-mediated, were enrolled in the study. Exactly 564 individuals were monosensitized to *Parietaria* allergens, and 490 to other allergens (e.g., house-dust mites, Gramineae, and animal dander). The remaining 475 were nonallergic. Patients underwent anamnestic data collection, physical examination, and cutaneous and serologic diagnostic tests. Skin prick tests (SPT) were administered according to a standardized method with commercially available allergenic extracts for the common inhalant allergens and the most frequently offending foodstuffs such as hazelnut, peanut, walnut, and pistachio nut (Lofarma Laboratories, Milan, Italy). Only patients with a positive SPT to pistachio nut underwent the prick-prick test (PPT), administered, according to Dreborg & Foucard (4), with fresh foods (pistachio nut and other Anacardiaceae foods, i.e., cashew nut and mango). Wheal areas (expressed as mm²) were measured after SPT and after PPT. Total and specific IgE was measured in serum

samples from patients SPT-positive to pistachio nut (Sferikit, System Lofarma Laboratories, Milan, Italy).

Of the 1529 atopic and nonatopic individuals enrolled in the study, 11 (0.72%) were SPT-positive to pistachio nut (Table 1). All 11 patients were from the *Parietaria*-sensitized group. No evidence of cutaneous or serologic sensitization to pistachio nut was detected in patients allergic to other allergens or in SPT-negative subjects. Finally, no patient sensitized to both *Parietaria* and pistachio nut had a positive SPT to other dried fruits and/or other anacardiaceous nuts. All patients who were SPT-positive to both *Parietaria* and pistachio nut had ingested moderate or low quantities of roasted pistachio nuts or of food containing pistachio nut (ice cream, cake, and mortadella). No subjects of this study frequently consumed large amounts of pistachio nut.

As far as we are aware, apart from our earlier study (3), there are no reports of a correlation between *Parietaria* sensitization and pistachio nut sensitization in patients with respiratory allergy. The interesting finding to emerge from our data is that all patients with

pistachio nut sensitization suffered from *Parietaria*-related respiratory symptoms. The other finding is that sensitization to pistachio nut allergens rarely induces severe clinical symptoms. In fact, symptoms were mild in the five patients sensitized to pistachio nut. Unlike our two earlier patients, who frequently ate large amounts of pistachio nuts and had severe symptoms (3), the subjects described herein reported sporadic ingestions of these nuts and had mild symptoms. Thus, it is conceivable that a high intake of this food (be it as roasted nuts or as an ingredient of other foods) is related to a higher risk of developing allergic symptoms.

Because of the low degree of serologic sensitization to pistachio nut in our patients, we did not do SDS-PAGE, immunoblotting, or RAST-inhibition studies.

In conclusion, given the high frequency of *Parietaria* pollinosis in the Mediterranean area (5, 6) and the increasing consumption of pistachio nut, we suggest that patients affected by this disorder undergo SPT for pistachio.

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*Division of Pneumology and Allergology
Hospital "A. Cardarelli"
Piazza Arenella n° 7/h
80128 Naples
Italy
Tel. +39. 081. 7473335-4-3
Fax: +39. 081 7473331

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Skin tests of steroid allergy

H. Asakawa*, T. Araki, I. Imai, Y. Tsutsumi, F. Kawakami

Key words: adverse reaction; bronchial asthma; hydrocortisone sodium succinate; methylprednisolone sodium succinate.

● We present a case of bronchospasm worsened by the administration of drip intravenous (d.i.v.) hydrocortisone sodium succinate and methylprednisolone sodium succinate. A 31-year-old man with bronchial asthma was referred to our hospital because of an asthma attack worsened by methylprednisolone sodium succinate administered by d.i.v. in February 1998. He had been under medication for 10 years and had a previous history of aspirin shock. Recently, his disorder had been controlled with theophylline, ozagrel, oral betamethasone, and inhalations of beclomethasone dipropionate and procaterol HCL. When his bronchial asthma could not be controlled by the usual medication 3 years previously, he had received hydrocortisone sodium succinate d.i.v. for the first time. The treatment was effective. Recently, he did not need steroid d.i.v. therapy. Three weeks before admission, he

was administered hydrocortisone sodium succinate d.i.v. by his family doctor. Ten minutes later, his dyspnea, wheezing, and stupor worsened. His doctor stopped d.i.v. and considered the possibility of allergy to steroids. His dyspnea was relieved by aminophyllin d.i.v. at that time. This time, he received methylprednisolone sodium succinate d.i.v. for an asthma attack, but his dyspnea worsened. He was immediately admitted to our hospital. Laboratory data showed that his serum IgE level was 2050 U/ml (normal range: 27.5–138.3 U/ml), and his peripheral eosinophil count was 868/μl. His dyspnea was relieved by aminophyllin d.i.v., and we conducted an intradermal test the next day. Intradermal tests were performed with a 26-gauge hypodermic needle, and results were read at 15 min. Prednisolone sodium succinate, methylprednisolone sodium succinate, and hydrocortisone sodium succinate were positive (Table 1). On the other hand, betamethasone disodium phosphate was negative. Two weeks later, we conducted the same intradermal tests to confirm the results. Next, we attempted to challenge d.i.v. betamethasone disodium phosphate to confirm the safety. Moreover, we administered d.i.v. betamethasone disodium phosphate to him when he had an asthma attack. The treatment was very effective. Three months later, skin prick tests and patch tests were performed in a standard fashion, and the results were read at 15 min, 48 h, and 72 h. The results are summarized in Table 1. Solvent of Solu-Cortef containing paraben was positive in both skin prick and patch tests. Hydrocortisone sodium phosphate was also positive.

It is known that i.v. therapy with hydrocortisone and methylprednisolone is sometimes associated with adverse reactions (1–5). Corticosteroid-induced adverse effects are more common in patients with aspirin intolerance. Our patient had a previous history of aspirin shock. He showed

Skin tests can predict the safe administration of alternative steroid agents for patients with steroid allergy.