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RESEARCH LETTERS

Sulfite sensitivity in a patient with allergic asthma

To the Editor:

Sulphites or sulphate agents (in the forms of sodium sulphite, sodium bisulphite, sodium metabisulphite, potassium bisulphite, and potassium metabisulphite) are agents widely used as preservatives in a long variety of foods, beverages and drugs.[1]

Sulphites have been used for centuries, mainly as food additives, but can also be present naturally in foods such as fermented beverages and wines.

Symptoms of sulphite sensitivity include asthma, urticaria, angio-oedema, abdominal pain, nausea, diarrhoea, seizures, and anaphylactic shock resulting in death.

Sulphites cause few to no problems in most people without allergies and asthma, even when large amounts are consumed.

It is not completely known how sulphites cause reactions in certain people.

The gases generated from sulphites might cause muscle spasms in the lungs of some asthmatics,[1] or could be related to the inability in some people to metabolise the sulphites appropriately.

There is no clear understanding of the mechanism by which inhaled sulphites trigger bronchospasm. It may be due to the formation of sulphur dioxide (SO2) within the airways that affects the airway mucosa, and to some extent this activates both the IgE mechanism and the cholinergic reflex resulting in bronchoconstriction.[1]

Adverse reactions to sulphites like urticaria, angio-oedema, abdominal pain, or diarrhoea could be due to the generation of sulphur dioxide in the stomach.[3]

The gases generated from sulphites might produce a cholinergic stimulation that would increase gastric motility.[3]

We present a case of sulphite-induced bronchospasm in a patient with previous allergic asthma. Sulphites were well tolerated after an adequate treatment of underlying asthma.

A 37-year-old female referred rhinoconjunctivitis and perennial asthma, with spring exacerbations. Several months before coming to our outpatient clinic, she presented acute asthma attacks after drinking red wine. (Crianza red wine). She also presented urticaria and acute asthma after the ingestion of hake fish and cod fish. She was treated in the Emergency Room with bronchodilators, antihistamines and corticosteroids, with clinical improvement several hours later. In the past history she denied allergy to hymenoptera.

Total serum IgE was 112.5 U/ml. Specific IgE antibodies (CAP-FEIA Pharmacia, Uppsala, Sweden) to dog dander were 5.88 kU/ml, *Alternaria alternate* 1.90 kU/ml, Anisakis simplex 1.81 kU/ml, and cod fish 1.30 kU/ml.

Specific IgE antibodies to cat dander, house dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae), Aspergillus fumigatus, Cladosporium herbarum, sardine, hake fish, shrimp, squid, Apis mellifera, Vespula spp, and Polistes spp, were all negative.

Skin prick tests with common inhalants (ALK-Abello, Madrid, Spain) were positive to grass pollens (8x8 mm), *Olea* (9 x 11 mm), *Cupressus arizonica* (5 x 10 mm), dog dander (6x6 mm), *Artemisia vulgaris* (6x6 mm), *Taraxacum* (6x6 mm), *Plantago Lanceolata* (5x7 mm), and *Anisakis simplex* (7x5 mm).

Skin prick tests to mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae)*, moulds, cat dander, cynodon, *Platanus Occidentalis*, hake fish, codfish, and sardine, were all negative.

Skin prick test with Crianza red wine was negative too.

Histamine at 10 mg/ml and glycerol phosphate buffer were used as positive and negative controls, respectively.

A single-blind placebo-controlled oral challenge test with sulphite[4–6] (adapted from Bush) was performed with a positive result. For a dose of 50 mg of sodium metabisulphite we found a FEV1 fall of 1.03 L (- 26%) and a FEV1/CV ratio of 72%.

The patient went on a free-sulphite diet (especially red wine). The underlying asthma was controlled after dog avoidance and she only presented asthmatic exacerbations from April to June. She was then treated with immunotherapy (Bial Aristegui, Bilbao, Spain) 100% grass pollens, perennially, with a good control of asthma and without new acute bronchospasm episodes.

Complementary exams performed in our outpatient clinic showed a normal lung function test. A methacholine bronchial challenge test was negative. We also carried out a single-blind placebo-controlled oral challenge test with sulphite up to 200 mg of sodium metabisulphite with a negative result. She also tolerated up to 200 cc of Crianza red wine without symptoms and with normal spirometric parameters.[7]

Currently the patient is asymptomatic, on a free diet, even tolerating wine. She has not referred any asthma

symptoms in the past two years. She also takes measure to avoid *Anisakis simplex*.

Wine is the alcoholic beverage most frequently involved in adverse reactions, most of them being due to the non-alcoholic components used as preservatives, such as sulphites.[2]

In asthmatic patients sulphite inhalation can cause bronchospasm depending on the amount of sulphur dioxide (S02) and the severity of the underlying asthma.[1,7]

It is also important to know the type of wine, and the possibility of allergy to hymenoptera.[8]

We report a female patient with poorly controlled asthma who developed bronchospasm after drinking wine. Once her underlying asthma was properly controlled, with immunotherapy and dog avoidance, sulphite sensitivity subsided. The patient does not have allergy to hymenoptera, corroborated by clinical history and specific IgE antibodies.

Some previous studies suggest that sulphite sensitivity in asthmatics could be related with poor asthma control. These patients might be susceptible to cholinergic stimulation, such as sulphite inhalation, which could trigger bronchospasm.[2]

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V. Marenco Arellano*, M. Reaño Martos, M. Rodriguez Cabreros, A. Bueso Fernández, J. Garcia Loria, M. Rodríguez Mosquera

Allergy Department, Hospital Puerta de Hierro Majadahonda, (Madrid)

* Corresponding author.
E-mail address: vmarenco75@hotmail.com
(V. Marenco Arellano).

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Antihistamines in chronic urticaria: threat or treat?

To the Editor:

Although antihistamines are the cornerstones for symptomatic treatment of urticaria,[1,2] sensitivity reactions to antihistamines in systemic administration have been rarely reported. In this sense, antihistamines may cause fixed drug eruptions, urticaria and other hypersensitivity reactions. Other than these reactions, in a limited number of cases with chronic urticaria, antihistamines may exacerbate the underlying disease, which eventually lead to a difficulty in treatment. Here, we report two cases of chronic urticaria exacerbated with antihistamines and discuss the way of finding therapeutic options for these cases.

In both cases, patients first had skin prick and intradermal tests with antihistamines. If the skin prick tests (SPT) and intradermal tests (IDT) are negative, drug provocation tests were performed. All tests were performed under strict medical surveillance and written signed consents were obtained prior to tests.

Briefly, SPT were performed with dilutions of 1/100, 1/10, undiluted and IDT with dilutions of 1/1000 and 1/100 of the tested drugs. A wheal diameter of 3 mm greater than negative control and accompanied by erythema after 20 minutes was considered positive. Histamine and saline served as positive and negative controls, respectively. The drug provocation tests were performed in a single-blinded, placebo-controlled design in which the patient was blinded. The doses of the drugs used for DPTs were ¼ and ¾ of the therapeutic doses. Tests were considered positive if any sign of hypersensitivity reactions such as urticaria; angio-oedema; laryngeal oedema; hypotension; dyspnoea; nasal symptoms; 20% fall in FEV1 value; anaphylaxis; or other rashes were observed during or after the test. The tests were considered negative if no adverse reaction occurred within 24 hours.

Case 1

The first patient was a 42-year-old woman who had chronic recurrent urticaria for three years. She experienced generalised urticarial lesions especially exacerbating with antihistamines like pheniramine maleate on several occasions. As she developed urticaria with the use of several other antihistamines of which she did not remember the names, there was a difficulty in treating the urticaria. On physical examination, she had generalised urticaria all around the trunk, arms and legs. No other pathological findings existed. Her routine blood and urine analysis were in normal range. Allergic work up with SPT with common aeroallergens and foods were negative. Other diagnostic work up such as thyroid autoantibodies, and immunological studies were in normal limits.