

extracts of *E. arvense* and *Betula* whose band, although weaker, is also visible, are found in lanes 3 and 4.

We do not believe that the symptoms have been caused by sensitization to birch in our patient, as it does not exist in our environment (6), but rather that the use of carrot and its handling would have been responsible for her symptoms, first cutaneous and then respiratory, possibly maintained, and increased if possible, by the use of a product such as *E. arvense*, with a similar protein to that existing in carrot and BetV1. As a result of the scarcity of specific IgE to *Betula*, it is technically very difficult to be able to discern which of the 18–20 kDa molecules has greater sensitizing power in this patient. We are corroborated the bronchial inflammation by the quantification of ECP in IS after bronchial exposure to the suspected allergen. This would be the first case in which this technique is used as a diagnostic tool and in a nonprofessional patient (7).

*Servicio de Alergia

Hospital Clínico San Carlos
C/ Martín Lagos S/N, 28040
Madrid
Spain

Tel: 00 34 91330 3012

E-mail: mmartinez.hcsc@salud.madrid.org

Accepted for publication 16 June 2003

Allergy 2004; 59:786–787

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Acute urticaria induced by hyoscine butylbromide

R. González-Mendiola*, C. Sánchez Fernández,
P. Prieto Montañó, M. Cuevas, M. Ceña Delgado,
M. Sánchez Cano

Key words: antispasmodic; Buscapina®; hyoscine butylbromide; urticaria.

Hyoscine butylbromide (Buscapina®; Boehringer Ingelheim, Barcelona, Spain) is an anticholinergic antispasmodic agent with quaternary ammonium structure. Although it is widely used, reports of immediate hypersensitivity reactions after hyoscine administration are scarce (1, 2). The mechanism implicated is still unknown. We describe a probable IgE-mediated case of acute urticaria after administration of hyoscine butylbromide.

A 23-year-old atopic woman was diagnosed of an acute appendicitis. Before the operation, the patient was treated symptomatically with intravenous Buscapina® 20 mg once. Twenty minutes later, developed urticarial lesions on trunk and

extremities. Lesions disappeared within an hour after the administration of a parenteral antihistaminic and a corticosteroid. The patient did not remember previous ingestion of Buscapina® or Buscapina Compositum® (hyoscine butylbromide and metamizol). Afterwards, she tolerated Nolotil® (metamizol).

After informed consent was obtained, skin prick test (SPT) was performed using Buscapina® for parenteral administration (20 mg/ml). Histamine phosphate (10 mg/ml) was used as positive control and NaCl (0.9%) as negative control. Five non-atopic and five atopic subjects served as controls. A 4 mm wheal was obtained in the patient and was negative in control subjects. NaCl was negative and histamine was 11 mm in the patient.

A single-blind placebo-controlled oral challenge was performed with increasing doses of Buscapina®, starting with 2.5 mg with an hour interval. One hour after the administration of 5 mg, she presented headache, pruritus and rash in face, neck and upper area of thorax. Lesions disappeared in an hour after parenteral administration of 40 mg of prednisone. No late response was detected.

SPTs with a battery of commercially available common inhalant allergens and latex were also performed. The result was positive for grass and tree pollens and negative for the rest of allergens.

Histamine releasing test (HRT) according to Siraganian method (3) gave a negative result.

Tolerance to a different antispasmodic agent was needed to give the patient an alternative of treatment. Therapeutic doses (135 mg) of mebeverine were well tolerated.

On the one hand, the short period of latency added to the result of SPT, guide us to consider it an IgE-mediated reaction to hyoscine butylbromide. On the other hand, the result of HRT does not confirm this mechanism. However, some studies reveal a rate of 19% false negatives in HRT (4).

The patient was not sure she had taken this drug before. Quaternary ion ammonium might be the epitope responsible of the IgE-mediated reaction, as it happens with muscle relaxants used in general anesthesia. The ubiquity of the quaternary ion ammonium group could be the reason of previous sensitization in our patient.

A probable IgE-mediated case of acute urticaria after administration of hyoscine butylbromide (Buscapina®) is described.

The union to specific IgE and the consequent release of mediators, takes place when there are at least two quaternary ion ammonium groups. Hyoscine butylbromide has only one quaternary ion ammonium group in its molecule. For this reason, other antigenic structures might be implicated in the origin of the reaction.

Among antispasmodic agents with anticholinergic action, there are compounds with quaternary ion ammonium structure, as hyoscine butylbromide and compounds with tertiary amine structure, like mebeverine. The tolerance of mebeverine could rule out the existence of *in vivo* cross-reactivity between both drugs.

In conclusion, we describe a rare case of urticaria due to hyoscine butylbromide. Positive SPT and oral provocation with this drug suggest an allergic IgE-mediated mechanism. However, more evidences are necessary to corroborate such mechanism.

*Rosario González-Mendiola
c/ Villaamil 5, 2^oC
28039 Madrid
Spain
Tel: + 34 679 99 77 62
E-mail: chargomendi@excite.com

Accepted for publication 9 September 2003
Allergy 2004: 59:787–788
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Tolerance induction to rofecoxib in a patient with Bartter's syndrome

E. Nucera, D. Schiavino, E. Pollastrini, R. Manna, M. De Lillo, A. Buonomo, C. Roncallo, G. Patriarca*

Key words: Bartter's syndrome; desensitization; drug intolerance; rofecoxib.

Bartter's syndrome is a group of inherited diseases, because of a defective salt reabsorption in the thick ascending limb of the Henle's loop. It

is also called hyperprostaglandin E syndrome, because of excessive renal and systemic

production of prostaglandin E₂ (1). Nonsteroidal anti-inflammatory drugs (NSAIDs) are known to be useful in the management of Bartter's syndrome because of their inhibiting action on cyclooxygenase (COX), with consequent decrease in prostaglandins synthesis. A long-term therapy with a nonselective NSAID, such as indomethacin, is often associated with the occurrence of important side effects (such as gastric ulcers and prolonged bleeding time). As renal induction of COX-2 seems to play an important role in the Bartter's syndrome pathogenesis, selective COX II-inhibitors are particularly effective. We report the case of a 28-year-old woman with Bartter's syndrome and multiple drug intolerance, who experienced adverse reactions (generalized erythema and

Patient became clinically tolerant to rofecoxib.

itching) to rofecoxib despite a preventive antireactive therapy (loratadine 10 mg, cromolyn sodium 500 mg). Avoidance of NSAIDs was recommended. As rofecoxib resulted particularly suitable for the management of our patient, after a preliminary evaluation (negative prick and patch tests), we attempted a desensitization to rofecoxib, according to a new original protocol, on the basis of our encouraging previous experiences with tolerance induction to other drugs (heparin, cotrimoxazole, spiramycin, etc) (2–4). Oral 8-day desensitizing treatment was performed with increasing doses of rofecoxib, starting with 1 ml of a rofecoxib solution (2.5 mg/ml) diluted 1 : 10⁵ and reaching the final daily dose of 50 mg (Table 1). Antihistamine medication (loratadine 10 mg/day) was administered during the treatment. After the rush phase, our patient perfectly tolerated rofecoxib (50 mg/day). A personal history of adverse reactions to a drug can preclude its use, but if it is necessary for the management of a patient, tolerance induction can represent an useful tool. Our results confirm desensitization safety and effectiveness: it was well tolerated, rapidly reaching the therapeutic daily dose.

*Department of Allergology
Università Cattolica del Sacro Cuore
Policlinico 'A. Gemelli'
Largo F. Vito, 1 – 00168 Rome
Italy
Fax: + 39 06 3051343
E-mail: allergologia@hotmail.com

Accepted for publication 24 September 2003
Allergy 2004: 59:788–789
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Table 1. Protocol of tolerance induction to rofecoxib

Rofecoxib	Days	Dilution	Final dose (ml)	Final daily amount (mg)
Solution (2.5 mg/ml)	1	10 ⁻⁵	10	2.5 × 10 ⁻⁴
	2	10 ⁻⁴	10	2.5 × 10 ⁻³
	3	10 ⁻³	10	2.5 × 10 ⁻²
	4	10 ⁻²	10	2.5 × 10 ⁻¹
	5	10 ⁻¹	10	2.5
	6	Pure solution	10	25
Tablet (1 = 25 mg)	7	–	1 + 1/2	37.5
	8	–	2	50