

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.

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Accepted for publication 9 September 2003
Allergy 2004: 59:787–788
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References

1. ROBINSON ACR, TEELING M. Angioneurotic oedema and urticaria induced by hyoscine butylbromide. *Postgrad Med J* 1982;**58**:316.
2. WATANABE T, FUNAYAMA M, MORITA M. Fatal anaphylactic shock to hyoscine and diphenhydramine. *J Toxicol Clin Toxicol* 1994;**32**:593–594.
3. SIRAGANIAN RP, BRODSKY MJ. Automated histamine analysis for *in vitro* allergy testing I. A method utilizing allergen-induced histamine release from whole blood. *J Allergy Clin Immunol* 1976;**57**:525–540.
4. SIRAGANIAN RP, HOOK WA. Histamine release and assay methods for the study of human allergy. In: ROSE NR, de MACARIO EC, FAHEY JL, FRIEDMAN H, PENN GM, editors. *Manual of clinical laboratory immunology*, 4th edn. Washington DC: American Society for Microbiology, 1992:709–716.

Tolerance induction to rofecoxib in a patient with Bartter's syndrome

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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.

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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

References

1. REINALTER SC, JECK N, BROCHHAUSEN C, WATZER B, NÜSING RM, SEYBERTH HW et al. Role of cyclooxygenase-2 in hyperprostaglandin E syndrome/antenatal Bartter syndrome. *Kidney Int* 2002;**62**:253–260.
2. PATRIARCA G, ROSSI M, SCHIAVINO D, SCHINCO G, FAIS G, VARANO C et al. Rush desensitization in heparin hypersensitivity: a case report. *Allergy* 1994;**49**:292–294.
3. NUCERA E, SCHIAVINO D, BUONOMO A, DEL NINNO M, SUN JY, PATRIARCA G. Tolerance induction to cotrimoxazole. *Allergy* 2000;**55**:681–682.
4. NUCERA E, RONCALLO C, MASINI L, BUONOMO A, DE PASQUALE T, POLLASTRINI E et al. Successful tolerance induction to spiramycin in pregnancy. *Scand J Infect Dis* 2002;**34**:550–551.

Delayed reaction urticaria due to trimebutine

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Key words: delayed type reaction; Proctolog®; trimebutine; urticaria.

A 40-year-old nonatopic woman presented with generalized pruritic and erythematous hives without angioedema, 7 days after initiating a therapy with Nolotil® (Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany) and Proctolog® (Juste, Madrid, Spain) cream for hemorrhoids.

Nolotil® and Proctolog® cream were stopped and the patient was successfully treated with intramuscular corticosteroid (6-Metil-prednisolone).

Proctolog® cream contains trimebutine and ruscogenin.

We present a case of delayed reaction urticaria induced by trimebutine.

Patch tests were performed on the upper back with the European Standard

Urticaria reaction due to trimebutine confirmed by patch and oral provocation test.

Series, Proctolog® cream and its components (trimebutine and ruscogenin).

Oral provocation tests were realized with Nolotil® and trimebutine

European Standard Series were all negative, but the patch tests with Proctolog® cream and trimebutine were positive at 48 (++) and 96 h (+++) (Fig. 1). Twenty controls were entirely negative.

Seventy-two hours after oral provocation test with trimebutine the patient presented generalized urticaria. Oral provocation test with Nolotil® was negative

Trimebutine [2-dimethylamino-2-phenylbutyl 3,4,5-trimethoxybenzoic acid], is an antispasmodic used orally to treat functional bowel disorders (1), and rectally and topically for anal fissures and hemorrhoids (2).

The first adverse effects from topical application were reported by Maffioli et al. in 1975 (3) and Chebanon in 1976 (4), both reports being erythema and/or burning. There is only one article published in the literature about contact allergic dermatitis caused by trimebutine (5).

To our knowledge, delayed-type hypersensitivity urticaria from trimebutine has not previously been reported. The patch test has been demonstrated as a good way for the diagnostic of a type

IV hypersensitivity reaction to trimebutine.

We would like to thank our nurse Ms Rosa García for her valuable collaboration.

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Accepted for publication 6 October 2003

Allergy 2004; 59:789–790

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References

1. KAMIYA T, NAGAO T, ANDOU T, MISU N, KOBAYASHI Y, HIRAKO H et al. Effects of trimebutine maleate on gastric motility in patients with gastric ulcer. *J Gastroenterol* 1998;**33**:823–827.
2. HO YH, SEOW-CHOEN F, LOW JY, TAN M, LEONG APKF. Randomized controlled trial of trimebutine (and sphincter relaxant) for pain after hemorrhoidectomy. *Br J Surg* 1977;**84**:377–379.
3. MAFFIOLI G, BRUNETAUD JM, GEOFFROY H. Utilisation de l'association ruscogenines-trimebutine en pathologie anale. *Ann Med de Reims* 1975;**12**:361–363.

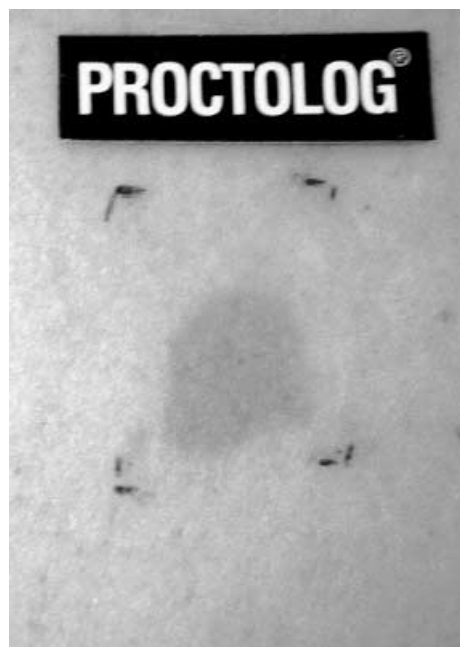


Figure 1. A positive result was found with Polibutin® cream.