

healthy controls tolerating omeprazole and with negative skin test results.

Up to now, hypersensitivity reactions to lansoprazol, omeprazole and pantoprazole have been described, and their diagnosis was confirmed by *in vivo* tests.

In previous cases in which *in vitro* detection of specific IgE was attempted, it turned out to be negative. This is the first case in which basophil activation test was used to confirm the existence of the specific IgE.

As a conclusion, FAST, also called basophil activation test, is a quick new diagnostic test, that requires no prior antigenic coupling technique and can be easily used with new drug antigens.

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Accepted for publication 31 January 2003
Allergy 2003; 58:538–539
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ISSN 0105-4538

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Delayed-type hypersensitivity rash from ibuprofen

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Key words: exanthematous eruption; ibuprofen; patch testing.

Nonsteroidal anti-inflammatory drugs (NSAIDs) vary considerable in chemical structure but they all share the ability to block the cyclo-oxygenase (COX) enzyme that catalyzes the conversion of arachidonic acid to prostaglandins. Ibuprofen is a NSAID that belongs to the group of propionic acid derivatives (1, 2). It is widely used to treat a variety of conditions, including headache and musculoskeletal disorders, and now, there are many drugs containing ibuprofen – suspensions, creams, and oral medicine. With regard to the safety of ibuprofen, much is known about the possible adverse effects. Here we describe a patient with an exanthematous eruption of eczematous and urticarioid type, to ibuprofen (Brufen®, Abbott, Latina, Italy). A study was carried out in order to examine the amount of ibuprofen in this skin reaction and to investigate cross-reactions between naproxen, ketoprofen, and ibuprofen.

A 21-year-old man, without any personal or familiar history of atopy, 11 h after taking 200 mg of ibuprofen (Brufen®) p.o. on day 2 of treatment for headache, was referred to our department for generalized erythematous-vesicular rash and some urticarioid lesions, with labial oedema associated with nausea, and a fever of 38–39°C. Mucous membranes were spared and there was no lymphadenopathy, hepato- or splenomegaly and arthralgia. At the same time, other drugs were not used. Complete blood count, viral serologies, erythrocyte sedimentation rates, urinalysis, biochemistry including liver, thyroid and renal function tests, electrolytes, C-reactive

A patient with an exanthematous eruption of eczematous and urticarioid type, to ibuprofen.

protein, studies of humoral immune function including serum immunoglobulins and circulating immune complexes, C3–C4, antinuclear antibodies, and chest X-rays were all normal with the exception of an increase in erythrocyte sedimentation rates, 45 mm/h (normal values 0–15 mm/h) and a leukocytosis with neutrophilia (12 200 leukocytes/ μ l, 80.5% neutrophils).

The patient was treated with oral administration of corticosteroids and antihistamines, with resolution in 2 weeks.

One and a half year before, he had presented an eczematous acute dermatitis that had appeared after 10 days of continuous topical application of an ointment, containing ibuprofen (Brufen®), localized at the primary sites of contact with the drug.

Six months after his visit to our clinic and a written consent, an allergy study was carried out.

Skin prick tests (SPT) with common inhalant allergens (Stallergènes, Paris, France) were negative. Total IgE in patient's serum were measured with the paper radio immunosorbent test (PRIST; CAP system fluorescence enzyme immunoassay) and the result was 51.1 kU/l.

A patch test with immediate and delayed reading was performed with the Società Italiana di Dermatologia Allergologica, Professionale e Ambientale (SIDAPA) standard series (Chemotecnique Diagnostics AB, Uppsala, Sweden) and a series of phenylpropionic acid derivatives, comprising ibuprofen, naproxen and ketoprofen (each 2% and 5% petrolatum). The patch preparations were applied with Finn Chambers® on Scampor® (Epitest, Tuusula, Finland) following the International Contact Dermatitis Research Group recommendations. Immediate reading of the patch test was negative, while the delayed reading was positive at day (D)2 and D3 for ibuprofen 2% (+/++) and ibuprofen 5% (++/++).

SPT and intradermal (ID) test with ibuprofen, diluted in 0.9% NaCl, starting with a concentration of 0.05 mg/ml and continuing with 10-fold increases of concentration every 20 min, were performed. Histamine chloride (0.1%) and NaCl (0.9%) were used as a positive and negative controls; wheals of 4 mm or

greater were regarded as positive in the absence of reaction to normal saline. SPT and ID test for ibuprofen were negative after 20 min, but after 36 h, infiltrated erythema appeared at the site of the ID test (maximum diameter: 14 mm).

SPT and ID test for ibuprofen and the immediate and delayed patch tests for ibuprofen, naproxen and ketoprofen were also performed on a control group of 10 people with a negative history of adverse reactions to drugs and their results were negative.

Finally, oral tolerance exposure tests with naproxen and ketoprofen were performed. On the first day the patient received two placebo capsules, one every hour; after 7 days, divided doses of naproxen (125 mg initially and 375 mg 1 h later) and ketoprofen (50 mg initially and 150 mg 1 h later) were administered with negative results.

NSAIDs can elicit nonallergic hypersensitivity depending on the potency of the COX inhibition. Other reactions suggest immediate-type hypersensitivity, mediated by IgE, being reproduced in the skin, respiratory tract and cardiovascular system (3). Some cases of urticaria (4), anaphylaxis (5), and also fatal asthma (6) induced by ibuprofen have been described. Finally, NSAIDs also produce delayed-hypersensitivity reactions, like contact dermatitis, erythema multiforme, and Stevens-Johnson syndrome. In this case, clinical findings, patch and ID testing are suggestive of delayed-type hypersensitivity to ibuprofen. Our patient, presensitized by topical application, developed an exanthematous eruption of eczematous and urticarioid type, to oral ibuprofen, which has not been described in the literature, to our knowledge. Both patch and ID tests are useful in evaluating this delayed reaction and the drug challenge test can be avoided.

This drug-induced eruption may be with hardly distinguished from viral exanthema and, in order to verify this patient's probable viral diseases, viral serologies were carried out with negative results. Further investigations were carried out to differentiate this adverse drug reactions which are generally benign from a severe form of adverse reaction termed hypersensitivity syndrome (7) that includes a similar rash and fever, often

with hepatitis, arthralgia, lymphadenopathy, and eosinophilia.

Valsecchi and Cainelli showed that cross-reactivity between some chemically related NSAIDs was possible (8). Then, it was evaluated if this patient was also sensitized to naproxen and ketoprofen. Patch testing proved useful to rule out such cross-sensitivity and naproxen and ketoprofen tolerances were also reported. This estimation is important in that, persons with adverse reactions to ibuprofen can safely take other NSAIDs, although additional cases should have to be evaluated.

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Accepted for publication 18 February 2003

Allergy 2003; 58:539–540

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ISSN 0105-4538

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Rapid oral desensitization to isoniazid, rifampin, and ethambutol

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Key words: drug hypersensitivity; oral desensitization; tuberculosis.

Drug desensitization may be an effective tool of treatment in patients with drug allergy when

alternative drug is not available. Desensitizations have been reported in patients who have hypersensitivity reactions to

Rapid oral desensitization in a child with hypersensitivity to multiple antituberculous agents.

β-lactam/cephalosporin, vancomycin, and antituberculous agents. There have been two reports of desensitization to antituberculous agents in adults but the experience is limited in children (1, 2).

A 7-year-old girl presented with swelling and pain on the left ankle for 4 months. She was diagnosed with tuberculous osteomyelitis after incision and drainage in another hospital and was started on a regimen of isoniazid (INH), rifampin (RFP), kanamycin, and pyrazinamide (PZA). After 3 days of therapy, pruritus, fever, and elevation of serum levels of glutamic-oxaloacetic transaminase (GOT) and glutamate pyruvate transaminase (GPT) developed. She was referred for possible desensitization. She did not have a history of allergic disease or of hypersensitivity to drugs. A blood test showed elevation of SGOT and SGPT of 115/116 IU/l, leukocyte count of $10.2 \times 10^9/l$, and an erythrocyte sedimentation rate of 31 mm/h (normal < 20 mm/h). Her magnetic resonance imaging showed an abscess in the posterior aspect of the left calcaneus. Upon admission, all drugs were stopped and one drug was reintroduced at a time. After 1 h of taking 250 mg of INH and 750 mg of streptomycin (SM), she developed dyspnea, pruritus, and skin rash. A 250-mg dose of RFP was tried and the same symptoms occurred. Four days