

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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References

1. BIGBY M, STERN R. Cutaneous reactions to nonsteroidal antiinflammatory drugs. *J Am Acad Dermatol* 1985;**12**:866–876.
2. ALBERT KS, GERNAAT CM. The pharmacokinetics of ibuprofen. *Am J Med* 1984;**77**:40–45.
3. VIELUF D, PRZYBILLA B, SCHWERBROCK U, RING J. Oral provocation test in the diagnosis of anaphylactoid reactions to mild analgesic preparations. *Int Arch Allergy Immunol* 1995;**107**:268–271.
4. SHELLEY ED. Ibuprofen urticaria. *J Am Acad Dermatol* 1987;**17**:1057–1058.
5. TAKAHAMA H, KUBOTA Y, MIZOGUCHI M. A case of anaphylaxis due to ibuprofen. *J Dermatol* 2000;**27**:337–340.
6. ANTONICELLI L, TAGLIABRACCI A. Asthma death induced by ibuprofen. *Monaldi Arch Chest Dis* 1995;**50**:276–278.
7. ROUJEAU JC, STERN RS. Severe adverse cutaneous reactions to drugs. *N Engl J Med* 1994;**331**:1272.
8. VALSECCHI R, CAINELLI T. Contact dermatitis from ibuprofen. A case with cross-reactivity with ketoprofen. *Contact Dermatitis* 1990;**22**:51.

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

later, with a SM 750 mg, PZA 750 mg and cycloserin 250 mg regimen, there was no adverse reaction. However, the addition of ethambutol (EB) 500 mg, resulted in the development of skin rash and pruritus. The initial dosages of INH and RFP were determined by performing a skin prick test and an intradermal test before desensitization. She was kept in an intensive care unit and was premedicated with oral steroid and cetirizine. Six hours into desensitization, she developed facial flushing and chest discomfort, but they were well controlled by antihistamine administration. After desensitization, she completed the standard INH (10 mg/kg) and RFP (12 mg/kg) regimens for 18 months without adverse reactions.

The incidence of disease by *Mycobacterium tuberculosis* is decreasing in Korea but the risk of infectivity is high, up to 0.5%. This is higher than the published risk of 0.01–0.1% in developed countries. Hypersensitivity reactions that lead to discontinuance of antituberculous agents and to switch of therapy are rarely seen in 4–5% of the general population (1). In drug-allergic patients, drug desensitization converts a highly sensitive state to a tolerable one and makes it possible to administer the necessary drugs (3). In the past, acute drug desensitization was considered as an approach to the manage-

ment of IgE sensitivity only. However, it is possible that modified forms of desensitization can be used to manage the condition of patients with drug-induced allergic reactions thought to be immunological in nature but are not IgE mediated (4). The mechanism inducing desensitization is not yet known, but in studies of desensitization to penicillin, it may be due to the presence of blocking IgG antibodies, consumption of IgE by immune complexes, haptene inhibitors, desensitization of the antigen specific mast cells or exhaustion of mediated substances (3, 5). In this study, the modified penicillin protocols were used (1). Peak serum level and half-lives of INH, RFP and EB were three to six times that of penicillin, and so the dosing interval was increased, to 45 min.

In conclusion, this may be the first report of rapid oral desensitization in a child with hypersensitivity to multiple antituberculous agents. Rapid oral desensitization enables patients with hypersensitivity reactions to multiple antituberculous agents to access appropriate drugs immediately and continuously.

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References

1. HOLLAND CL, MALASKY C, OGUNKOYA A, BIELORY L. Rapid oral desensitization to isoniazid and rifampin. *Chest* 1990;**98**:1518–1519.
2. MATZ J, BORISH LC, ROUTES JM, ROSENWASSER LJ. Oral desensitization to rifampin and ethambutol in mycobacterial disease. *Am J Respir Crit Care Med* 1994;**149**:815–817.
3. GRUCHALLA RS. Acute drug desensitization. *Clin Exp Allergy* 1998;**28**(suppl 4):63–64.
4. GRUCHALLA R. Understanding drug allergies. *J Allergy Clin Immunol* 2000;**105**:S637–S644.
5. SULLIVAN TJ. Antigen-specific desensitization of patients allergic to penicillin. *J Allergy Clin Immunol* 1982;**69**:500–508.