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## Rofecoxib as an alternative in aspirin hypersensitivity

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**Key words:** aspirin intolerance; cyclooxygenase-2 inhibitor; NSAID; rofecoxib; urticaria.

• THE mechanism underlying intolerance reactions to nonsteroidal anti-inflammatory drugs (NSAID) is not well understood. The clinical picture resembles a type I reaction (Coombs and Gell) including conjunctivitis, rhinitis, shortness of breath, angioedema, hypotension, and, in severe cases, even shock. It is assumed that the pathogenetic mechanism is IgE-independent, since intolerance reactions can be induced by NSAIDs of different chemical structures, and specific IgE directed against NSAIDs is only rarely detectable. Inhibition of the central enzyme in the arachidonic acid pathway, cyclooxygenase (COX), by several NSAIDs may be essential for the development of an intolerance reaction, since it leads to an increased synthesis of leukotrienes (LT) with bronchoconstrictory capacities (LTC<sub>4</sub>, LTD<sub>4</sub>, and LTE<sub>4</sub>) (1). Unfortunately, only a limited number of alternative anti-inflammatory pain

medications can be offered to aspirin-intolerant patients. Accordingly, the selective COX-2 inhibitors celecoxib and nimesulid have been conclusively reported to prevent pulmonary symptoms in aspirin-sensitive asthmatics. We here report the first case of an aspirin-intolerant patient who, upon oral challenge with aspirin, but not with the selective COX-2 inhibitor rofecoxib, developed severe cutaneous and extrapulmonary mucosal symptoms.

A 39-year-old patient was referred to our department with a history of rhinitis, swelling of the nasal mucosa, conjunctivitis, and shortness of breath 30 min after ingestion of 25 mg dexketoprofen. The patient denied having asthma, drug intolerance, or other allergies in the past. Acetylsalicylic acid (aspirin)- or pyrazolone-specific IgE antibodies in the serum could not be detected. Prick testing of a standard series with different NSAIDs in addition to dexketoprofen was negative. On the first day of the study, oral challenge with increasing amounts of the selective COX-2 inhibitor rofecoxib (suspensions of 1.2, 3, and 6 mg) given every 30 min was well tolerated, and 2 days later, oral challenge with 20, 50, and 125 mg of aspirin given at 30-min intervals was tolerated without complications. However, 20 min after challenge with aspirin at a dose of 250 mg, the patient developed itching of the eyelids and nasal mucosa, conjunctivitis, and generalized urticaria. Drug intolerance to aspirin was diagnosed and intravenously treated with 250 mg methylprednisolone and 2 mg clemastine hydrochloride.

Although the pathogenetic mechanism of NSAID intolerance is still incompletely understood, there are several reasons supporting the hypothesis that the enzyme COX and leukotrienes may play a crucial role. First, a mutation in the gene encoding the LTC<sub>4</sub> synthase results in increased levels of bronchoconstrictory LTC<sub>4</sub> in the

bronchoalveolar lavage of aspirin-intolerant asthmatics (2). Secondly, bronchospasm due to NSAID intolerance in asthmatics can be successfully treated with leukotriene receptor antagonists and lipoxygenase inhibitors (3). Third, it has been recently reported that the selective COX-2 inhibitor celecoxib did not induce bronchospasm in 27 aspirin-intolerant asthmatic patients (4).

We here provide evidence that the selective COX-2 inhibitor rofecoxib is well tolerated in a patient with aspirin intolerance and mainly extrapulmonary symptoms such as urticaria, rhinitis, and conjunctivitis. Thus, the new class of selective COX-2 inhibitors may be a useful alternative in the anti-inflammatory treatment for patients with arthritis and NSAID intolerance.

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Accepted for publication 5 April 2001  
Allergy 2001; 56:789  
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ISSN 0105-4538

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