

Nonsteroidal antiinflammatory drug desensitization using flurbiprofen (Ansaid)

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Nonsteroidal antiinflammatory drug (NSAID) and aspirin reactions remain commonplace. Specific recommendations and standardized approaches to the use of NSAIDs in patients with known hypersensitivity to these agents are evolving. Cross reactivity and sensitization are frequent within this group of agents. The advent of newer synthetic nonsteroidal antiinflammatory drugs may offer a means of lowering reaction rates. Flurbiprofen (Ansaid) is a new NSAID for the treatment of rheumatoid arthritis and osteoarthritis. We report successful flurbiprofen desensitization with incremental oral challenge in a patient using this agent.

CASE REPORT

A 32-year-old white woman with severe inflammatory arthritis presented to the allergy clinic for evaluation of aspirin (ASA) and nonsteroidal antiinflammatory drug (NSAID) allergy. She reported experiencing a reaction in 1981 consisting of periorbital swelling, generalized itching with hives, followed by a sensation of throat tightness, dysphagia, cough, and wheezing. This reaction occurred within 20 to 30 minutes of tolmetin (Tolectin) ingestion. She recalls similar reactions with zomepirac (Zomax) and ibuprofen (Motrin) ingestion. She furthermore reports exactly the same reaction with aspirin ingestion in 1974. She denies using any aspirin or nonsteroidal antiinflammatory drugs since 1981. She had known allergic rhinitis but there was no personal history of asthma, sinusitis, or nasal polyposis. Because of the severity of her arthritis and

the patient's reluctance to use other classes of antiarthritic agents, her primary care physician desired to use a nonsteroidal antiinflammatory agent in her treatment regimen. We therefore planned to perform a NSAID desensitization/challenge procedure.

The patient was electively admitted to the medical intensive care unit to undergo this procedure because of her past history of life threatening signs and symptoms with ASA/NSAID ingestion. She was not taking any other medications at the time of administration. She had no other medication nor drug allergy history. The challenge was performed using flurbiprofen (Ansaid). (This was the agent preferred by the patient and rheumatologist.) The oral challenge procedure was performed as follows: flurbiprofen at dosages of 1, 10, 25, 50, 100, and 200 mg was given at 30-minute intervals. The patient was observed at the bedside by a physician throughout the procedure. She was monitored continuously for blood pressure, heart rate, respirations, oxygen saturation through pulse oximetry, and cardiac rhythm by telemetry. Flurbiprofen was administered as a 1 mg/mL suspension, 25 mg/mL suspension, and 100 mg/tablet.

The challenge was marked by a mild to moderate macular erythematous rash on her face, neck, and upper trunk, and a sensation of

throat itchiness with a cough within ten minutes following administration of the 25-mg dose. This had completely resolved by the time the 100-mg dose was given (except for mild throat itchiness). The final dose of 200 mg was administered without any symptoms or signs noted. Throughout the challenge and during her reaction at 25 mg the vital signs, oxygen saturation by pulse oximetry, and electrocardiogram remained within normal limits. Following the procedure the patient was observed in the intensive care unit for 24 hours. The remainder of her hospital course was uneventful. She was discharged on flurbiprofen, 200 mg/day.

DISCUSSION

Flurbiprofen was recently released for the long-term treatment of rheumatoid arthritis and osteoarthritis. Its long half-life and convenient twice daily dosing make it potentially useful in improving patient compliance. It was chosen for that reason in our patient.

ASA/NSAID intolerance or idiosyncratic reactions remain commonplace. Although the actual prevalence of ASA/NSAID reactions in the general population remains unknown, in patients with asthma, Stevenson¹ estimates the incidence at 8% to 20%.

The pathogenetic mechanism involved in ASA/NSAID reactions remains unknown. Following the dis-

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covery that aspirin inhibits prostaglandin synthesis, Vane² hypothesized that a mechanism for hypersensitivity reactions to aspirin and aspirin-like drugs particularly in subjects with asthma, was that the type of prostaglandin predominantly released in the lung was a bronchodilator and aspirin selectively inhibited its formation thereby promoting bronchoconstriction. Parker³ suggested the possibility that the arachidonic acid metabolism pathway is involved with ASA/NSAIDs providing a preferential diversion of metabolites from the cyclooxygenase enzymatic to the lipoxygenase enzymatic pathway with subsequent production of leukotrienes.

Szczeklik⁴ recently reported on the cyclooxygenase theory of aspirin-induced asthma mentioning that "the idea that the attacks might result from specific inhibition of a single enzyme, namely cyclooxygenase, has gained both experimental and clinical support."

It is well known that not all patients who ingest ASA/NSAIDs will develop adverse reaction, implying that other factors may be important in the development of reactions to these agents. Certain patient groups are associated with an increased risk of adverse ASA/NSAID reactions such as asthmatic patients, or patients with nasal polyposis. Stevenson¹ has noted the existence of a quadrad of ASA sensitivity, nasal polyposis, rhinosinusitis, and asthma. This complemented the classic observations by Samter and Beers⁵ of the

"aspirin triad," which consisted of ASA sensitivity, nasal polyposis, and asthma. Our patient had a history of allergic rhinitis only. Mathison and Stevenson⁶ published recommendations on the indications and methods for oral challenges with NSAIDs in 1979.

With regards specifically to flurbiprofen, Bosso⁷ recently reported on the use of a flurbiprofen provocative challenge to confirm a suspected flurbiprofen reaction in a patient with perennial rhinitis and asthma. He and his colleagues were able to demonstrate an aspirin cross sensitivity/desensitization mechanism in their patient with flurbiprofen.

We have demonstrated that desensitization to a specific NSAID, such as flurbiprofen, can be performed utilizing a slow incremental challenge technique. Our patient did not experience any significant adverse reaction during the challenge. Our challenge was performed in the intensive care unit setting due to the severity of prior ASA/NSAID reactions experienced by our patient and the known existence of cross sensitization among these agents.^{6,8}

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