Usefulness of montelukast to prevent adverse reactions to COX-2 selective inhibitors: a case report

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Summary. Nonsteroidal anti-inflammatory drug (NSAID)-sensitivity is a frequent condition in patients with chronic urticaria and/or asthma. The physiopathologic process underlying respiratory and cutaneous reactions probably involves an increased production of cysteinyl leukotrienes. Cyclooxygenase 2 (COX-2) selective inhibitor, has been proposed as the main alternative to control pain and inflammatory diseases in these patients. However, a small percentage of patients with NSAID-induced skin reactions does not even tolerate COX-2 selective inhibitors. We report a very infrequent case of a patient with NSAID, paracetamol and COX-2 selective inhibitors sensitivity in whom we induced tolerance to paracetamol and celecoxib using the leukotriene receptor antagonist montelukast prior to oral challenges.

Key Words: celecoxib, montelukast, NSAID sensitivity, paracetamol

Introduction

Nonsteroidal anti-inflammatory drug (NSAID)-sensitivity is defined as the presence of cutaneous (urticaria and/or angioedema) and/or respiratory reactions (rhinitis and/or bronchospasm) after administration of NSAID with different chemical structure. Its prevalence is low in the general population, but it can reach 30% in patients with chronic urticaria or asthma. Although the physiopathologic process underlying these reactions has not been completely elucidated, an increased production of cysteinyl leukotrienes appears to be involved in NSAID-induced nasal, bronchial and cutaneous reactions [1].

Cyclooxygenase 2 (COX-2) selective inhibitors, have been proposed as the main alternative to control pain and inflammatory diseases in these patients. However, a small percentage of patients with NSAID-induced skin reactions, does not even tolerate COX-2 selective inhibitors [2, 3]. These patients represent a difficult-to-manage therapeutical problem.

Case report

A 52-year-old woman was referred to our unit because she had suffered a generalized urticaria and angioedema one hour after being treated with 600 mg of ibuprofen. Some years ago she had had a similar reaction precipitated by 500 mg of aspirin. The patient tolerated paracetamol. An oral test with rofecoxib was performed. After the first dose of 5 mg the patient developed generalized urticaria. Two weeks later an oral test with celecoxib was carried out in two consecutive days. On day 1, we gave her placebo, 20 and 80 mg, with good tolerance. On day 2, we gave her placebo, 200 and 200 mg. After the second 200-mg dose, she developed generalized urticaria. On the basis of these results and the history of the patient, paracetamol was recommended in the event that analgesia would be required. Six months later, the patient was referred to our service for generalized urticaria after paracetamol (500 mg) treatment. We administered her 10 mg of montelukast daily for 3 days and we performed an oral
Challenge with 500 mg of paracetamol with good tolerance. Two months later, we repeated the oral challenge with celecoxib (400 mg cumulative dose) after 3 days of 10 mg of montelukast, and the patient tolerated the COX-2 inhibitor without problems.

Discussion

We report a very infrequent case of NSAID, paracetamol and coxibs sensitive patient. Coxibs tolerance in NSAID-sensitive patients with a history of respiratory reactions is 100% in the published series. However, the percentage of patients who tolerate coxibs is lower in subjects with isolated skin reactions (urticaria and/or angiodema) [2, 3]. It is unknown what determines that an NSAID-sensitive patient may be more or less susceptible to COX-2 selective inhibitors. Some authors suggest that asthmatic NSAID-sensitive patients could have overexpression of the enzyme leukotriene C4 synthase [4], whereas others have found downregulation of the cyclooxygenase pathway, with a low production of prostaglandin E2 [5]. Both theories have a common end: a high leukotriene production.

Pérez et al [6], reported that montelukast is able to inhibit skin reactions partially in 60% and totally in 30% of patients with skin reactions caused by NSAID. To our knowledge there are no case reports on the usefulness of montelukast in the prevention of reactions to paracetamol or coxibs.

In conclusion, selective COX-2 inhibitors have good tolerance in 100% of NSAID-intolerant patients with respiratory reactions. The tolerance is lower in those with skin reactions. For the first time we report the usefulness of the antileukotriene montelukast to induce tolerance to paracetamol and coxibs in a patient sensitive to all these drugs.

References


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