Alergologia Polska – Polish Journal of Allergology 2022; 9, 4: 250–255
DOI: https://doi.org/10.5114/pja.2022.122005
Received: 29.08.2022, Accepted: 15.10.2022.

Alergologia POLSKA
Polish Journal of Allergology

ORIGINAL PAPER

The safety of celecoxib in cutaneous hypersensitivity reactions with nonsteroidal anti-inflammatory drugs: a single-center care experience

Bezpieczeństwo celekoksybu u pacjentów ze skórną postacią nadwrażliwości na niesteroidowe leki przeciwzapalne: jednoośrodkowe doświadczenia

Mehmet Erdem Cakmak

Department of Allergy and Clinical Immunology, Başakşehir Çam and Sakura City Hospital, Istanbul, Turkey

ABSTRACT

Introduction: Aspirin/non-steroidal anti-inflammatory drugs (NSAIDs) are frequently prescribed, and hypersensitivity reactions to these drugs are frequently observed in clinical practice.

Aim: To evaluate the safety of celecoxib in patients with a history of cutaneous hypersensitivity reactions to NSAIDs.

Material and methods: A retrospective evaluation was made of a total of 113 patients with a history of cutaneous hypersensitivity reactions to NSAIDs who underwent a drug challenge test with celecoxib. The diagnosis of NSAID hypersensitivity was based on a positive oral aspirin challenge test result or a recorded and significant clinical hypersensitivity reaction to aspirin and/or other NSAID-induced reaction.

Results: A total of 113 patients (40 (35.4%) male, 73 (64.6%) female) with a mean age of 39.64 ±12.65 years underwent the drug challenge with celecoxib. Atopy was determined in 40 (35.4%) patients. The most common accompanying allergic diseases were asthma in 46 (40.7%) patients and allergic rhinitis in 37 (32.7%) patients. The most common NSAIDs responsible for the allergic reaction were diclofenac (48.7%), flurbiprofen (47.8%), ketoprofen (47.8%), and aspirin (45.1%). No allergic reaction to celecoxib was observed in any of the 113 patients who underwent the drug challenge testing.

Conclusions: Celecoxib is a safe alternative drug in patients with a history of cutaneous hypersensitivity reactions to NSAIDs.

KEY WORDS

aspirin, celecoxib, drug allergy, drug hypersensitivity, non-steroidal anti-inflammatory agents.

ADDRESS FOR CORRESPONDENCE

Mehmet Erdem Cakmak, Department of Allergy and Clinical Immunology, Başakşehir Çam and Sakura City Hospital, Başakşehir Olimpiyat Bulvarı Street, 34480 Başakşehir, Istanbul, Turkey, phone: 0505 486 97 50, fax: +90 (212) 909 60 00, e-mail: mehmeterdemcakmak@gmail.com

INTRODUCTION

Aspirin/non-steroidal anti-inflammatory drugs (NSAIDs) are frequently prescribed, and hypersensitivity reactions to these drugs are frequently observed in clinical practice [1]. Hypersensitivity reactions to NSAIDs occur in approximately 0.6% to 2.5% of the general population, but the risk is higher in patients with asthma and chronic urticaria [2].

In recent years, classifications have been developed to define hypersensitivity reactions to NSAIDs based on the time of onset (early/late), the target organ (skin, airway, or other organs), or the severity of the reaction (from mild dyspnea to anaphylaxis and death) [3–5]. In the current classification, NSAID-related hypersensitivity reactions are considered "early" or "late" according to the time of onset, while they are also defined as "allergic" or "non-allergic" according to the underlying mechanism (Table 1) [3, 4]. NSAID intake and the time of occurrence of the reaction enable differentiation between immune and non-immune mechanisms. Reactions to more than one NSAID, which are chemically dissimilar but pharmacologically inhibit the cyclooxygenase (COX)-1 enzyme, occur early and are referred to as "cross-reaction" type NSAID sensitivity [3]. In some patients, a hypersensitivity reaction occurs with a single NSAID or a NSAID belonging to the same chemical group and other NSAIDs can be taken by the patient without any problems. This group of reactions occurs through immune mechanisms and is defined as "allergic" type hypersensitivity. The reactions occur early (IgE-mediated) or late (T lymphocyte-mediated) depending on the immune mechanism involved [3].

In general, patients who are NSAID-sensitive are sensitive to all NSAIDs that inhibit COX-1. Celecoxib, a selective COX-2 inhibitor, is known to be a relatively safe therapeutic alternative for patients intolerant to NSAIDs [6].

AIM

The aim of the present study was to evaluate the safety of celecoxib in patients with a history of cutaneous hypersensitivity reactions to NSAIDs.

MATERIAL AND METHODS

STUDY DESIGN, PARTICIPANT SELECTION, AND DATA COLLECTION

A retrospective evaluation was made of 113 patients with a history of cutaneous hypersensitivity reactions to NSAIDs who underwent a drug challenge test with celecoxib between January 2021 and January 2022. The demographic data, comorbidities, and laboratory data of the patients were obtained from the medical records.

Atopy was evaluated using a skin prick test (Allergopharma/Germany). The test was performed using a panel consisting of *Dermatophagoides pteronyssinus*; *Dermatophagoides farinae*; grass, tree, and weed pollen; and cat, dog, *Alternaria*, *Cladosporium*, and cockroach allergens. The positive control was histamine (10 mg/ml) and the negative control was saline. The skin prick test was performed using the puncture method. A mean wheal diameter of 3 mm or greater from the control solution (saline) was defined as a positive result.

CLASSIFICATION OF CUTANEOUS NSAID HYPERSENSITIVITY

Patients with a history of cutaneous hypersensitivity reactions to NSAIDs were divided into four groups [3]. NSAID-induced urticaria/angioedema (NIUA): $n = 48$ (42.5%), NSAID-exacerbated cutaneous disease (NECD): $n = 34$ (30.1%), single NSAID-induced urticaria/angioedema and anaphylaxis (SNIUAA): $n = 18$ (15.9%) and single NSAID-induced delayed reactions (SNIDR): $n = 13$ (11.5%).

DRUG CHALLENGE TESTS

The diagnosis of NSAID hypersensitivity was based on a positive oral aspirin challenge test result or a recorded and significant clinical hypersensitivity reaction to aspirin and/or other NSAID-induced reaction. In patients with a history of suspected or a single group NSAID hypersensitivity, a challenge test with the potent COX-1 inhibitor, aspirin, was performed to confirm NSAID hypersensitivity or to confirm or exclude a cross-reaction. Drug challenge tests with aspirin or celecoxib were not performed in patients who had taken antihistamines, systemic corticosteroids, cromolyn, or β-blocker drugs in

TABLE 1. Classification of hypersensitivity reactions to NSAIDs according to the underlying mechanism

Non-immunological (cross-reaction type) hypersensitivity reactions
Airway disease exacerbated by NSAIDs (NERD)
Skin diseases exacerbated by NSAIDs (NECD)
Urticaria/angioedema triggered by NSAIDs (NIUA)
Immunological hypersensitivity reactions
SNIUAA
SNIDR

NSAID – nonsteroidal anti-inflammatory drug, NERD – NSAID-exacerbated respiratory disease, NECD – NSAID-exacerbated cutaneous disease, NIUA – NSAID-induced urticaria/angioedema, SNIUAA – single NSAID-induced urticaria/angioedema and anaphylaxis, SNIDR – single NSAID-induced delayed reactions.

the previous week; had a history of sensitivity to lactose or sulfonamides; or had active urticaria and/or rash. In patients with concomitant asthma, drug challenge tests were performed if their asthma had been stable for at least 2 weeks and the forced expiratory volume (FEV) 1 value was greater than 70% predicted. Drug challenge tests were not performed in patients with a medical history of drug hypersensitivity reactions in the previous 4–6 weeks. Written informed consent was obtained from all patients before the drug challenge tests.

Aspirin challenge test

The aspirin (acetylsalicylic acid 100, 300, 500 mg, Bayer, Germany) challenge test was performed under strict medical surveillance in the adult allergy clinic. It was performed as a single-blind and placebo-controlled oral drug challenge on two separate days. The aspirin challenge scheme makes it easy to discriminate from the placebo challenge by patients. On the first day, 1/4 and 3/4 divided doses of placebo (lactose) were given at 2-hour intervals. On the second day, the active drug, aspirin, was given. Basal blood pressure and FEV_1 were measured before the aspirin challenge. For the oral aspirin challenge, 25, 50, 100, 300, and 500 mg was administered at 1-hour intervals. Blood pressure and FEV1 were measured 30 min after each dose was administered. The patients were carefully observed and the observation was carried out until 4 h after administration of the last aspirin dose. The test result was considered negative if there was no significant objective change in clinical symptoms and signs. If bronchospasm, dyspnea, chest tightness, wheezing, a significant decrease in FEV_1 (> 20% of baseline FEV1), nasal symptoms (such as rhinorrhea and nasal congestion), cutaneous symptoms (urticaria, erythema, angioedema, and other skin rashes), hypotension (if systolic blood pressure was measured below 90 mm Hg or more than 30% decrease from baseline), or gastrointestinal symptoms (abdominal pain, diarrhea, nausea, vomiting) were observed, the aspirin challenge test was considered positive. When patients developed these symptoms, the aspirin challenge test was stopped and medications such as antihistamines, systemic steroids, short-acting beta-2 agonist, and epinephrine were administered to treat and alleviate their symptoms.

Celecoxib challenge test

The celecoxib (Celebrex 200 mg, Pfizer, Turkey) challenge test was performed under strict medical surveillance in the adult allergy clinic. It was performed as a single-blind and placebo-controlled oral drug challenge on two separate days. On the first day, 1/4 and 3/4 divided doses of placebo (lactose) were given at 2-hour intervals. On the second day, the active drug was administered at 2-hour intervals as 1/4 and 3/4 divided doses of celecoxib. Basal blood pressure and FEV_1 were measured before the celecoxib challenge. Blood pressure and FEV_1 were measured 30 min after each dose was administered. The patients were carefully observed and the observation was carried out until 4 h after administration of the last celecoxib dose. Similar to the aspirin challenge test, the test was considered positive if respiratory, nasal, gastrointestinal, or skin symptoms or hypotension occurred. If the patient developed symptoms, appropriate treatment was given as in the aspirin challenge test. To evaluate NSAID-induced delayed reactions, the patients were re-examined 48 h after the celecoxib challenge.

ETHICS STATEMENT

The study protocol was approved by the Hospital Ethics Committee (Approval no. 2021-258). The study was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the nature of the study and written informed consent was obtained.

STATISTICAL ANALYSIS

The data were analyzed with IBM SPSS Statistics for Windows v. 20.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov or Shapiro-Wilk test was used to test the normality of the distribution of the data. Descriptive analyses were presented using median values for non-normally distributed variables, and mean and standard deviation values for normally distributed variables. One-way ANOVA was used if the numerical data were normally distributed to compare the means of more than two groups, and the Kruskal-Wallis test was used if the numerical data were not distributed normally. The homogeneity of variances was evaluated with the Levene test. Pearson's χ^2 test and Fisher's exact test were used to compare the proportions of two or more than two independent groups. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

The drug challenge with celecoxib was administered to 113 patients (40 (35.4%) male, 73 (64.6%) female) with a mean age of 39.64 ±12.65 years. Atopy was determined in 40 (35.4%) patients. The most common accompanying allergic diseases were asthma in 46 (40.7%) patients and allergic rhinitis in 37 (32.7%) patients. The demographic data and general characteristics of the patients are shown in Table 2.

TABLE 2. Demographic data and general characteristics of the patients ($n = 113$)

Parameter	Value
Age [years] (mean ± SD)	39.64 ±12.65
Sex male, *n* (%)	40 (35.4)
Total IgE [kU/l] median (min.–max.)	96 (18–1900)
Eosinophil (cells/µl) median (min.–max.)	160 (30–760)
Atopy (skin prick test +) *n* (%)	40 (35.4)
Underlying diseases	*n* (%)
Asthma	46 (40.7)
Allergic rhinitis	37 (32.7)
Other drug allergy	37 (32.7)
Nasal polyp	34 (30.1)
Atopic dermatitis	10 (8.8)
Food allergy	9 (8)
Metal allergy	5 (4.4)
Bee allergy	4 (3.5)
Classification of cutaneous NSAID hypersensitivity:	*n* (%)
NECD	34 (30.1)
NIUA	48 (42.5)
SNIUAA	18 (15.9)
SNIDR	13 (11.5)

SD – standard deviation, min. – minimum, max. – maximum, NSAID – nonsteroidal anti-inflammatory drug, NECD – NSAID-exacerbated cutaneous disease, NIUA – NSAID-induced urticaria/angioedema, SNIUAA – single NSAID-induced urticaria/angioedema and anaphylaxis, SNIDR – single NSAID-induced delayed reactions.

The most common NSAIDs responsible for the allergic reaction were diclofenac (48.7%), flurbiprofen (47.8%), ketoprofen (47.8%), and aspirin (45.1%) (Table 3).

The NECD, NIUA, SNIUAA, and SNIDR groups were compared. The frequency of nasal polyps was significantly higher in the NECD and NIUA groups ($p = 0.002$). In total, 113 patients underwent drug challenge testing with celecoxib and no allergic reaction was observed in any patient (Table 4).

DISCUSSION

The results of the present study demonstrated that celecoxib was well tolerated in patients with cutaneous hypersensitivity reactions to NSAIDs. No allergic reaction was observed as a result of the drug challenge test with celecoxib in a total of 113 patients with both immunological and non-immunological (cross-reaction type) cutaneous hypersensitivity reactions to NSAIDs. The tolerability of celecoxib was 100%. There are studies in the literature evaluating the safety of COX-2 inhibitors in patients with hypersensitivity reactions to NSAIDs. Çelik *et al.* [7] found the tolerability of selective and partially selective COX-2 inhibitors in patients with cross-reactive NSAID hypersensitivity as follows: nimesulide 91.9%, meloxicam 90.2%, rofecoxib 94.9%, and celecoxib 94.9%. In a study of 75 patients with analgesic intolerance, no patient allergic reaction was observed as a result of oral challenge testing with celecoxib [8]. In a study that examined 62 articles concerning patients with a history of hypersensitivity reactions to NSAIDS and who underwent drug challenge tests with selective COX-2 inhibitors, the reaction rate was reported as 3.29% [9]. In another study of 92 patients with a history of cutaneous hypersensitivity reactions to NSAIDs, the tolerability to celecoxib was 98.9%. Urticaria developed in only 1 patient as a result of oral challenge testing with celecoxib [10]. In a study with another COX-2 inhibitor, etoricoxib, all patients with chronic urticaria tolerated etoricoxib well [11].

TABLE 3. NSAIDs responsible for allergic reactions in patients

Drug	*n*	%
Diclofenac	55	48.7
Flurbiprofen	54	47.8
Ketoprofen	54	47.8
Aspirin	51	45.1
Naproxen	48	42.5
Metamizole	46	40.7
Ibuprofen	42	37.2
Propyphenazone	34	30.1
Paracetamol	34	30.1
Etodolac	32	28.3
Indomethacin	20	17.7
Meloxicam	18	15.9
Nimesulide	17	15
Tenoxicam	12	10.6

NSAID – nonsteroidal anti-inflammatory drug.

The partially selective COX-2 inhibitors, nimesulide and meloxicam, and the weak COX-1 or COX-2 inhibitor, paracetamol, are generally safe alternative drugs in patients with cross-reactive NSAID hypersensitivity [7]. In the present study, celecoxib was seen to be safe in patients with a history of cutaneous allergic reactions to drugs such as nimesulide, meloxicam, and paracetamol. There was a history of allergic reactions to paracetamol in 34 (30.1%) patients, to meloxicam in 18 (15.9%), and to nimesulide in 17 (35%). No allergic reaction was observed in any of these patients as a result of the drug challenge test with celecoxib.

TABLE 4. Comparison of clinical characteristics of cutaneous NSAID intolerant patients and results of the celecoxib challenge test

Parameter	NECD ($n = 34$)	NIUA ($n = 48$)	SNIUAA ($n = 18$)	SNIDR ($n = 13$)	*P*-value
Age [years] mean ± SD	27.56 ±12	38.51 ±11.96	39.62 ±16.97	46.09 ±13.63	0.308*
Sex (male), *n* (%)	11 (32)	18 (37.5)	5 (27.8)	6 (46.2)	0.718†
Total IgE [kU/l]	100	89	100	74	0.617§
Median (min.–max.)	(34–1135)	(18–1900)	(30–1200)	(23–1100)	
Eosinophil [cells/µl]	160	200	130	160	0.334§
Median (min.–max.)	(50-450)	(80-760)	(44-450)	(30-410)	
Atopy (+), *n* (%)	15 (44)	15 (31.3)	5 (27.8)	5 (38.5)	0.572†
Underlying diseases, *n* (%):					
Asthma	16 (47.1)	21 (43.8)	5 (27.8)	4 (30.8)	0.470†
Allergic rhinitis	13 (38.2)	15 (31.3)	5 (27.8)	4 (30.8)	0.864†
Other drug allergy	11 (32.4)	14 (29.2)	6 (33.3)	6 (46.2)	0.718†
Nasal polyp	15 (44)	18 (37.5)	1 (5.6)	–	0.002¶
Atopic dermatitis	4 (11.8)	2 (4.2)	1 (5.6)	3 (23.1)	0.160¶
Food allergy	4 (11.8)	2 (4.2)	2 (11.1)	1 (7.7)	0.602¶
Metal allergy	2 (5.9)	2 (4.2)	–	1 (7.7)	0.720¶
Bee allergy	3 (8.8)	–	1 (5.6)	–	0.156¶
Challenge results with celecoxib	N: 34	N: 48	N: 18	N: 13	
	P: 0	P: 0	P: 0	P: 0	

SD – standard deviation, min. – minimum, max. – maximum, (+) – positive, NSAID – nonsteroidal anti-inflammatory drug, NECD – NSAID-exacerbated cutaneous disease, NIUA – NSAID-induced urticaria/angioedema, SNIUAA – single NSAID-induced urticaria/angioedema and anaphylaxis, SNIDR – single NSAID-induced delayed reactions, *One-way ANOVA, †Pearson's χ^2 test, ¶Fisher's exact test, §Kruskal-Wallis test, N – negative, P – positive.

Of the hypersensitivity reactions that occur after taking NSAIDs, 30% are immunogenic hypersensitivity reactions. In this group, reactions occur with a single NSAID or with NSAIDs from the same chemical group. The most frequently responsible NSAIDs are pyrazolones, ibuprofen, diclofenac, aspirin, and paracetamol. Patients tolerate other NSAIDs.

These reactions are divided into two subgroups: early-type (IgE-mediated, SNIUAA) or late-type (T-lymphocyte-mediated, SNIDR) reactions [3, 12]. In the current study, no allergic reaction was observed after oral challenge testing with celecoxib in any of these patients who had early-type (IgE-mediated, SNIUAA) or late-type (T-lymphocyte-mediated, SNIDR) hypersensitivity reactions to NSAIDs. An allergic reaction was not expected in these patients as a result of the oral challenge test with celecoxib, and the drug challenge test with celecoxib was performed to find a safe alternative NSAID that they could take.

In this study, the oral provocation test was performed with celecoxib at a dose of 200 mg. Although there is no consensus in the literature regarding the challenge protocol for celecoxib, it has been reported that 200 mg celecoxib has a better analgesic effect than a placebo and aspirin [8]. However, higher doses (such as 400 mg) of celecoxib can be used in the treatment of diseases such as osteoarthritis and rheumatoid arthritis [13, 14]. In the current study, none of the patients had a history of osteoarthritis or rheumatoid arthritis. Therefore, a 200 mg dose was used as the maximum provocation dose for the challenge test.

Of the patients in the current study, 34 (30.1%) had a history of concomitant nasal polyps and a history of NSAID-exacerbated respiratory disease (NERD). The rate of patients with nasal polyps and NERD was significantly higher in the patient group with NECD and NIUA. This was expected as the underlying pathophysiological mechanism (non-immunological, cross-reaction type) was similar in these three patient groups (NERD, NECD, and NIUA) in hypersensitivity reactions to NSAIDs. As the underlying pathophysiology is similar, patients with cutaneous hypersensitivity reactions to NSAIDs may have concomitant NERD and may develop respiratory problems during drug challenge testing with NSAIDs. No respiratory problem was observed after the oral challenge test with celecoxib in any of these patients. Previous studies have also shown that celecoxib is a safe alternative drug in patients with NERD [15–19].

The current study had some limitations. First, it was a retrospective study. Second, it was not possible to per-

form aspirin challenge or culprit drug challenge testing for the diagnosis of hypersensitivity reactions to NSAIDs in some patients. In some patients, the diagnosis of hypersensitivity reactions to NSAIDs was based on proven clinical history. The drug challenge test is the gold standard in the diagnosis of hypersensitivity reactions to NSAIDs [3]. Despite these limitations, the significance of this study can be considered to be that it evaluated the safety of celecoxib in different groups of patients who had a history of cutaneous hypersensitivity reactions (NECD, NIUA, SNIUAA and SNIDR) to NSAIDs. The results showed that the safety of celecoxib was 100% in patients with a history of cutaneous hypersensitivity reactions to NSAIDs.

CONCLUSIONS

The results of the current study demonstrated that celecoxib is a safe alternative drug in patients with a history of cutaneous hypersensitivity reactions to NSAIDs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Jenkins C, Costello J, Hodge L. Systematic review of prevalence of aspirin induced asthma and its implications for clinical practice. BMJ 2004; 328: 434.
2. Szczeklik A, Niżankowska-Mogilnicka E, et al. Hypersensitivity to aspirin and non-steroidal antiinflammatory drugs. In: Middleton's Allergy: Principles and Practice. 7th ed. Adkinson NF Jr, Bochner BS, Busse WW, et al. (eds). Mosby/Elsevier, London 2009; 43.
3. Kowalski ML, Asero R, Bavbek S, et al. Classification and practical approach to the diagnosis and management of hypersensitivity to nonsteroidal anti-inflammatory drugs. Allergy 2013; 68: 1219-32.
4. Gollapudi RR, Teirstein, Donald DD, et al. Aspirin sensitivity: implications for patients with coronary artery disease. JAMA 2004; 292: 3017-23.
5. Szczeklik A. The cyclooxygenase theory of aspirin-induced asthma. Eur Respir J 1990; 3: 588-93.
6. Li L, Laidlaw T. Cross-reactivity and tolerability of celecoxib in adult patients with NSAID hypersensitivity. J Allergy Clin Immunol Pract 2019; 7: 2891-3.
7. Çelik GE, Erkekol FÖ, Aydın Ö, et al. Are drug provocation tests still necessary to test the safety of COX-2 inhibitors in patients with cross-reactive NSAID hypersensitivity? Allergol Immunopathol 2013; 41: 181-8.
8. Celik G, Paşaoğlu G, Bavbek S, et al. Tolerability of selective cyclooxygenase inhibitor, celecoxib, in patients with analgesic intolerance. J Asthma 2005; 42: 127-31.
9. Li L, Laidlaw T. Cross-reactivity and tolerability of celecoxib in adult patients with NSAID hypersensitivity. J Allergy Clin Immunol Pract 2019; 7: 2891-3.
10. Viola M, Quaratino D, Gaeta F, et al. Celecoxib tolerability in patients with hypersensitivity (mainly cutaneous reactions) to nonsteroidal anti-inflammatory drugs. Int Arch Allergy Immunol 2005; 137: 145-50.
11. Asero R. Etoricoxib challenge in patients with chronic urticaria with NSAID intolerance. Clin Exp Dermatol 2007; 32: 661-3.
12. Kowalski ML, Makowska JS, Blanca M, et al. Hypersensitivity to nonsteroidal antiinflammatory drugs (NSAIDs)-classification, diagnosis and management: review of the EAACI/ENDA and GA2LEN/HANNA. Allergy 2011; 66: 818-29.
13. Burns KA, Robbins LM, LeMarr AR, et al. Celecoxib significantly reduces opioid use after shoulder arthroplasty. J Shoulder Elbow Surg 2021; 30: 1-8.
14. McCormack PL. Celecoxib: a review of its use for symptomatic relief in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Drugs 2011; 71: 2457-89.
15. Umemoto J, Tsurikisawa N, Nogi S, et al. Selective cyclooxygenase-2 inhibitor cross-reactivity in aspirin-exacerbated respiratory disease. Allergy Asthma Proc 2011; 32: 259-61.
16. Gyllfors P, Bochenek G, Overholt J, et al. Biochemical and clinical evidence that aspirin-intolerant asthmatic subjects tolerate the cyclooxygenase 2-selective analgetic drug celecoxib. J Allergy Clin Immunol 2003; 111: 1116-21.
17. Martın-Garcıa C, Hinojosa M, Berges P, et al. Celecoxib, a highly selective COX-2 inhibitor, is safe in aspirin-induced asthma patients. J Investig Allergol Clin Immunol 2003; 13: 20-5.
18. Szczeklik A, Nizankowska E, Bochenek G, et al. Safety of a specific COX-2 inhibitor in aspirin-induced asthma. Clin Exp Allergy 2001; 31: 219-25.
19. Morales DR, Lipworth BJ, Guthrie B, et al. Safety risks for patients with aspirin-exacerbated respiratory disease after acute exposure to selective nonsteroidal anti-inflammatory drugs and COX-2 inhibitors: meta-analysis of controlled clinical trials. J Allergy Clin Immunol 2014; 134: 40-5.