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Selective cyclo-oxygenase 2 inhibitor in patients with aspirin-induced asthma

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To the Editor:

Acetylsalicylic acid and other nonsteroidal anti-inflammatory agents (NSAIDs) with anticyclo-oxygenase (COX) activity induce severe, sometimes life-threatening asthmatic attacks in about 10% to 20% of adults with asthma.¹ Because the inhibitory effect of NSAIDs with nonselective anti-COX activity is thought to be blockade of the arachidonic cascade, the inhibition of constitutive COX (ie, COX-1) should play a pivotal role in the pathogenesis of aspirin-induced asthma (AIA).

Celecoxib, designated as 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzene sulfonamide, is an NSAID that exhibits inhibition of prostaglandin synthesis, primarily through specific inhibition of COX-2 at therapeutic concentrations in human beings, whereas celecoxib does not inhibit the COX-1 isoenzyme. If the inhibition of COX-2 is not involved in the mechanism of bronchoconstriction in AIA, celecoxib is available for patients with this disease. However, it has never been reported whether the selective inhibition of COX-2 is involved in AIA.

To examine this hypothesis, we performed oral challenge testing with a capsule of 200 mg celecoxib (Celebrex, Searle Ltd, Caguas PR) in 17 patients with AIA (Table I). A double-blind, randomized, crossover design was used. All patients were nonsmokers and had had mild or moderate asthma diagnosed according to the criteria of the American Thoracic Society.² All had stable conditions and had been free of respiratory infections for at least 6 weeks. Aspirin sensitivity was confirmed by aspirin, lysine-aspirin, and/or sulpyrine provocation testing. Patients using oral or inhaled corticosteroids, theophylline, any antileukotriene drug, or any other anti-inflammatory agents were excluded. All patients used metered-dose inhalers of β -stimulants to control their asthma on demand. The study was conducted according to the ethical standards of our medical center and required informed consent from each patient.

Table I. Patient data

Patient No.	Sex	Age (y)	Duration (y)	Atopy	Nasal polyp	FEV1 (% predicted)	FVC (% predicted)	Eosinophils (%)	IgE (RIST) (U/mL)	PC20-sulpyrine (mg/mL)	
										Placebo	Celecoxib
1	M	29	3	HD, Gr	–	76	97	9	466	10	10
2	M	42	8	Cd	+	70	96	4	132	10	10
3	M	35	5	HD, C, Gr	–	87	103	7	475	10	10
4	M	39	16	None	+	84	94	5	151	20	20
5	M	40	7	None	–	72	96	3	54	20	20
6	M	45	11	Cd	+	76	99	8	260	10	10
7	M	33	4	None	–	86	97	7	123	10	10
8	M	56	29	None	+	71	89	9	19	20	20
9	F	38	2	None	–	88	88	3	48	100	100
10	F	42	9	Gr, HD	+	70	97	5	133	10	10
11	F	29	25	C	+	76	89	4	37	20	20
12	F	38	3	None	–	70	91	6	116	10	10
13	F	46	15	Cd	+	69	101	4	245	20	20
14	F	30	5	None	–	88	88	4	89	250	250
15	F	50	6	None	+	70	97	6	63	10	10
16	F	42	9	HD, Cd	+	74	118	8	340	20	20
17	F	47	10	None	+	68	82	10	77	4	4

All patients used metered-dose inhalers of β -stimulants to control their asthma.

RIST, Radioimmunosolvent test; *FVC*, forced vital capacity; *HD*, house dust; *C*, cat; *Gr*, grass; *Cd*, *Candida*.

Patients were randomly assigned to receive orally a capsule of 200 mg celecoxib or a dose of placebo that was identical in appearance. After a washout period of at least 2 weeks, the subjects crossed over to receive alternative challenge testing. Measurements of FEV₁ were obtained before challenge as the baseline and serially for 60 minutes after the challenge testing. In addition, all patients' conditions were observed, and FEV₁ was measured every 60 minutes until 8 hours after challenge to detect the late asthmatic response.

Significant decreases in FEV₁ were not reproducible after the treatment with either celecoxib or placebo, even 8 hours after challenge testing. None of the subjects reported any adverse effect after celecoxib administration, nor could they discriminate between celecoxib and placebo.

Our results revealed that a specific COX-2 inhibitor, celecoxib, is safely available for patients with AIA. Furthermore, inhibition of COX-1 may play an important role in the pathogenesis of AIA, whereas COX-2

might not. However, inhaled sulpyrine is a relatively weak stimulus compared with oral or inhaled acetylsalicylic acid challenge. The difference between inhalation challenge with sulpyrine and challenge with a full therapeutic dose (650 mg) of acetylsalicylic acid should be made clear. Also, to determine the exact relationship between celecoxib and leukotriene production or release in AIA, additional studies will be required.

This is the first clinical report that the selective inhibition of COX-2 would not be involved in the mechanism of bronchoconstriction in AIA.

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Satoshi Yoshida, MD, FAAAAI
Yuko Ishizaki, MD
Kazuya Onuma, MD
Department of Medicine
Harvard Medical School Boston, MA
Tatsuhiko Shoji, MD, FACG
Hiroshi Nakagawa, DDS, BSc
Hideaki Amayasu, MD, FACAAI
AOKI International Medical Center and
Hirosaki University School of Medicine Hirosaki Japan

References

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1. Spector SL, Wangaard CH, Farr RS. Aspirin and concomitant idiosyncrasies in adult asthmatic patients. *J Allergy Clin Immunol* 1979;64:500-6.

MEDLINE

2. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary diseases (COPD) and asthma. *Am Rev Respir Dis* 1987;136:225-44.

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