Brief Communication

Hemicrania Continua Responds to Cyclooxygenase-2 Inhibitors

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Background.—Hemicrania continua is a primary headache disorder defined by its absolute responsiveness to indomethacin. We report the treatment response to two cyclooxygenase-2 inhibitors, celecoxib and rofecoxib, in a series of patients with hemicrania continua.

Methods.—Fourteen patients were treated, 9 with rofecoxib and 5 with celecoxib.

Results.—Three patients in each group had a complete response to treatment.

Conclusion.—The cyclooxygenase-2 inhibitors may represent an alternative to indomethacin in the treatment of hemicrania continua. Their mechanism of action for this potential indication is unknown.

Key words: hemicrania continua, celecoxib, rofecoxib, indomethacin, COX-2 inhibitors

Abbreviations: HC hemicrania continua, COX cyclooxygenase

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Hemicrania continua (HC) is an indomethacin-responsive headache disorder characterized by continuous, moderate to severe, unilateral headache that fluctuates in intensity. Exacerbations of pain often are associated with autonomic disturbances (eg, ptosis, miosis, tearing, and sweating). Migrainous symptoms such as photophobia, phonophobia, nausea, and vomiting may also be present.

The cardinal feature of HC is its indomethacin responsiveness, but indomethacin often is poorly tolerated. Other nonsteroidal anti-inflammatory drugs (NSAIDs) reported to be helpful in HC include ibuprofen, piroxicam beta-cyclodextrin, and rofecoxib, a selective cyclooxygenase (COX)-2 inhibitor.[1-3] Celecoxib, another selective COX-2 inhibitor, has been reported to be beneficial in another indomethacin-responsive headache disorder, chronic paroxysmal hemicrania.[4]

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We report our experience with celecoxib and rofecoxib in the treatment of HC.

METHODS

We evaluated 14 patients with HC whose headaches were absolutely responsive to indomethacin and otherwise met diagnostic criteria for HC proposed by Goadsby and Lipton.[5] These patients were unable to tolerate chronic treatment with indomethacin, and a selective COX-2 inhibitor, either celecoxib or rofecoxib, consequently was prescribed.

Patients were directed to discontinue indomethacin and start the selective COX-2 inhibitor if the headaches returned. All 14 patients had headache recurrence when indomethacin was stopped. Rofecoxib 50 mg per day was administered to 9 patients (7 women, 2 men) and celecoxib to 5 (all women), starting with 200 mg twice a day, increasing to 400 mg twice a day, if necessary (Table). Treatment response was rated by patients as none, mild, moderate, or complete.

RESULTS

Of the 9 patients who received rofecoxib 50 mg, relief was complete in 3 patients, moderate in 2, mild in 3, and absent in 1. Of the 5 patients who received

Clinical Response to Cyclooxygenase-2 Inhibitors*

Response	Rofecoxib	Celecoxib
None	1 (11)	1 (20)
Mild	3 (33)	—
Moderate	2 (22)	1 (20)
Complete	3 (33)	3 (60)

*Values are number (percentage).

celecoxib, 1 patient failed to improve (despite sequential dose increase to 800 mg daily), 1 patient had a moderate response on 600 mg that did not increase on 800 mg, 1 patient had complete response to 400 mg, and 2 patients had complete responses to 600 mg. Patients who failed one COX-2 inhibitor were not treated with the other.

Thus, 60% of patients who received celecoxib and 33% who received rofecoxib experienced a complete response, while 20% receiving celecoxib and 55% receiving rofecoxib had a partial response (mild to moderate), and 20% on celecoxib and 11% on rofecoxib had no response (Table).

COMMENTS

Hemicrania continua is not as rare as previously believed. The hallmark of the disorder is its absolute, often dramatic response to indomethacin. The physiology underlying indomethacin responsivity are still unknown. Theories proposed have included a drug-related decrease in cerebral blood flow, reduction in cerebrovascular permeability, decrease in cerebrospinal fluid pressure, effect on melatonin pathway, and an antagonist effect on nitric oxide.[6-10]

Indomethacin often is not well tolerated and its adverse effects and potential complications limit its use in conditions such as renal failure, gastric ulcers, and bleeding disorders.

Other drugs have been tried to treat HC. Sumatriptan is not effective, but nonselective NSAIDs such as ibuprofen (800 mg three times a day) and piroxicam beta-cyclodextrin (20 to 40 mg a day) have been reported to be effective.[1,2] One of us (M.P.) recently reported a patient with HC who responded completely to rofecoxib.[3] A patient with another indomethacin-responsive disorder, chronic paroxysmal hemicrania, was reported to respond to celecoxib, suggesting that the COX-2 inhibitors may be effective in treating the so-called indomethacin-responsive headaches.

The number of patients reported here is too small to allow one to draw firm conclusions regarding the efficacy of the COX-2 inhibitors in the treatment of HC. A placebo-controlled trial evaluating these medications at various doses will be required to confirm their effectiveness.

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