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ORIGINAL

Are Cox-2 drugs the second line option in indomethacin responsive headaches?

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Abstract Paroxysmal hemicrania and hemicrania continua are both indomethacin-responsive headaches. Although indomethacin use to be well tolerated, some patients developed gastrointestinal side effects. We report four cases of hemicrania continua and a patient suffering chronic paroxysmal hemicrania completely responsive to celecoxib. In our experience celecoxib is a good option treatment for patients suffering from hemicrania continua or chronic paroxysmal hemicranea that presents indomethacin adverse effects.

Keywords Hemicrania continua · Chronic paroxysmal hemicrania · COX-2 · Celecoxib

Introduction

Paroxysmal hemicrania and hemicrania continua are both indomethacin-responsive headaches. Although indomethacin is usually well tolerated, some patients developed gastrointestinal side effects, specially those patients who require long term therapy [1]. Therefore, the use of cyclooxygenase-2 specific inhibitors could reduce secondary effects and they are essentially equipotent to indomethacin in vitro and in vivo [2]. Indeed, some reports in the literature indicate the usefulness of the COX-2 inhibitors in the treatment of indomethacin-responsive headaches [3–8]. We report four cases of hemicrania continua and a patient suffering chronic paroxysmal hemicrania completely responsive to COX-2 inhibitors.

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Case reports

Case 1

A 42 years-old woman had sudden onset of short-lived pains on the left side of her head. She described the pain periorbital in localisation. She suffers for a month an intense headache with short attacks (about 5−10 min) but high frequency (10−18 attacks per day). The pain associated with lacrimation and nasal congestion, but not pupil changes. Intensity was 8/10 in VAS. Her physical and neurological examinations and a head MRI were absolutely normal. We put her on indomethacin 25 mg 3 times a day, and in 24 h her hemicranial pain completely disappears. Because of legs oedema we discontinued indomethacin and 1 week later the pain returned. We introduced celecoxib 200 mg per day with total recovery. After 12 months of follow up she is still pain free.

Case 2

A 56 years-old man present with an 8 month history of a continuous left-sided headache strictly unilateral. The pain was moderate in intensity but fluctuating (between 2 and 7/10 VAS). The pain exacerbations were associated with lacrimation but not phono, photofobia, nausea or vomiting. An MRI was normal and indomethacin 25 mg 3 times a day was started with completely recovery. Two-month later he started to have gastric symptoms, indomethacin was

discontinued and the hemicrania return. With celecoxib 200 mg twice a day the hemicrania disappears. After 10 month the patient is still asymptomatic.

Case 3

A 78 years-old woman with 1 year history of continuous and strictly left-sided headache, fluctuating in intensity (3−9 in VAS) and accompanied by conjuntival injection and nasal congestion during exacerbation time. A cranial MRI was normal. With indomethacin 50 mg 3 times a day the hemicrania disappear, however, she developed disabling subjective tinnitus 1 month later. We discontinued indomethacin and introduced celecoxib 200 mg twice a day with completely recovery that persists 18 month later.

Case 4

A 64 years-old woman with 3 years history of right-sided headache, fluctuating in intensity (2−8 in VAS). She referred rhinorrhea and lacrimation only during headache exacerbation time. A cranial MRI was normal. With indomethacin 25 mg 3 times a day the hemicrania disappear, however, the patient suffer gastrointestinal disturbances. We discontinued indomethacin and introduced celecoxib 200 mg twice a day with completely recovery that persists 10 month later.

Case 5

A 76 years-old man with 6 month history of continuous left-sided headache and facial pain. He scored the pain between 4−9 in VAS. The pain exacerbations were associated with lacrimation. A cranial MRI was normal. With indomethacin 25 mg 3 times a day the hemicrania disappear. After 2 weeks on indometacina he complaint about pyrosis, that persists after omeprazol 40 mg per day. We decided to discontinue indomethacin and introduced celecoxib 200 mg twice a day with completely recovery that persists 6 month later.

Discussion

We present five patients suffering indomethacin-responsive headache case 1 suffering from paroxysmal hemicranias and cases from 2 to 5 from hemicranias continua (Table 1). All of them have absolutely response to indomethacin, but the presence of adverse reactions or intolerability let us discontinued and introduce celecoxib with completely recovery of the symptoms.

Indomethacin is consider the first-choice drug for the treatment of "indomethacin-responsive headaches", and the headache resolution is consider as a diagnosis criteria in some of theses headaches. Sometimes patients develop side effects that require us to look for other therapeutic options. Although other drugs have been reported as useful treatment, most of them are anecdotic or single cases [9–15]. Other anti-inflammatory drugs that have been demonstrated as alternative drugs, in particular piroxicam, however, their efficacy is lower when compared with indomethacin [16]. The pathophysiology of theses "indomethacin-response headache" are still unknown, but the cyclo-oxygenase (COX)-2 should be implicated in the pathogenesis.

Celecoxib have been previously reported to be effective in the treatment of other indomethacin-responsive headache [3–11], however, there was no absolutely response in all patients [4]. Anyhow, in our experience celecoxib is a good option treatment for patients suffering from hemicrania continua or chronic paroxysmal hemicranea that presents indomethacin adverse effects.

Table 1 Clinical characteristics of the patients

Case	Age	Gender	Headache type	Side	Doses (mg)	Time in month
1	42	F	HP	Left	200	12
2	56	M	HC	Left	400	10
3	78	F	HC	Left	400	18
4	64	F	HC	Right	400	10
5	76	M	HC	Left	400	6

All doses correspond to celecoxib

F female, *M* male, *HC* hemicrania continua, *HP* hemicrania paroxistica

Conflict of interest None.

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