Migraine effectively using candesartan-hydrochlorothiazide combination (ECARD® Combination Tablets LD) as prophylaxis

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Introduction

The Japanese Clinical Guidelines for Chronic Headache recommend anti-hypertensive, anti-epileptic, anti-depressant and non-steroidal anti-inflammatory drugs (NSAIDs) to prevent migraine. Among the anti-hypertensive drugs, β blockers, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II type 1 receptor blockers (ARB) can be used to prevent migraine, but the effectiveness of the ARB candesartan cilexetil (candesartan) combined with diuretic hydrochlorothiazide (ECARD® Combination Tablets LD; ECARD®) against migraine has not been reported.

This case report is the first to describe that ECARD® taken as a prophylactic therapy decreased the frequency of migraine without aura accompanied by premonitory fluid retention in the legs.

Case report

A 26-year-old woman who worked at a pharmaceutical company attended our hospital with severe, throbbing headaches that had persisted daily and had increased in intensity over the past year to the point where she had obtained a leave of absence from work. She had no specific personal history or family history of headache, occasionally consumed alcohol and was a nonsmoker. Temporal profiles of the headache revealed that fluid retention in both legs was a premonitory symptom and that an aura was absent. Pain that radiated over the whole head from the middle of the forehead, becoming a throbbing headache with vomiting and photophobia, was not associated with menstruation, and the patient was forced to retire to bed due to the severity of the pain. Loxoprofen was initially effective, but the effect slowly attenuated and she had recently started to use triptans such as eletriptan, sumatriptan, or naratriptan on a daily basis.

At the first presentation, her blood pressure was 116/68 mmHg and her pulse was regular at 77 beats/min. General physical findings were normal except for hypertonic muscles in both shoulders and a neurological examination revealed that she was alert and free of dysarthria, cortical signs and neurological abnormalities. Blood and urine values were within normal limits, and chest X-ray and ECG findings were also normal. Plain MRI and MRA of the head revealed no intracranial abnormality, vascular malformation and sinusitis. She had no heart failure, liver dysfunction, nephrotic syndrome or renal dysfunction, and no remarkable laboratory findings were associated with the leg edema.

Figure 1 shows the clinical features of the patient whom we diagnosed as having migraine without aura, accompanied by fluid retention in both legs as premonitory symptoms according to the second edition of the International Headache Classification (ICHD-II). Because of the frequency of the headache and the fact that she had never been prescribed with preventive therapy for migraine, we started her on lomerizine (10 mg/day) as preventive therapy from the day of the first examination. She stopped using loxoprofen, and reduced the sumatriptan frequency to twice weekly. She returned to work two months later as the frequency of the headaches had gradually decreased. We then changed sumatriptan to zolmitriptan because sumatriptan was not sufficiently effective, and increased the dosage of lomerizine to 20 mg/day after four months. However, lomerizine was also insufficiently effective so we added candesartan cilexetil (2 mg/day) from month 5 followed by candesartan cilexetil (4 mg) plus hydrochlorothiazide (6.25 mg; ECARD®; half tablet daily) at 16 months from the start of the preventive therapy. Six months thereafter, leg edema followed by migraine disappeared, and we gradually tapered off the lomerizine and ECARD®. She has only developed one very slight migraine over the past seven months. We started ECARD® again because she developed severe migraines with premonitory fluid retention in both legs at eight months after ECARD® cessation. At three months after restarting ECARD® (half tablet daily), the migraines and fluid retention had disappeared. No side effects including hypotension developed either before or after ECARD® administration.

Conclusions

Migraine attacks are considered to have already started at the time of premonitory symptoms. We described a patient in whom the appearance of migraines was controlled from the premonitory phase of leg edema using ECARD®. Thus, the combination of candesartan cilexetil with a low dose of hydrochlorothiazide in ECARD® might be useful for controlling the frequency of migraines in patients with the premonitory migraine symptom of leg edema.

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