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Case Report

Add-on perampanel in Lance–Adams syndrome

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ABSTRACT

Perampanel (PER) is the first-in-class selective, noncompetitive α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor antagonist that has been licensed and marketed as antiepileptic drug (AED) indicated for patients with partial-onset and primary generalized tonic–clonic seizures. A positive effect was reported in some patients with epileptic myoclonic jerks in idiopathic generalized epilepsy and in progressive myoclonic epilepsy. We treated a male patient with posthypoxic nonepileptic myoclonus (Lance–Adams syndrome) with add-on PER and achieved an almost complete cessation of jerks. This effect was reproducible and, therefore, we suggest that it might be worth trying PER in comparable cases.

1. Introduction

Perampanel (PER) is the first-in-class orally active antagonist of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors [1,2]. Perampanel was licensed in Europe and the US for the add-on treatment of patients with epilepsy with partial-onset seizures after three phase III trials that assessed the clinical efficacy and tolerability of PER as adjunctive antiepileptic drug (AED) in patients with difficult-to-treat partial-onset epileptic seizures [3–6]. In addition, PER was approved for the treatment of patients with primary generalized tonic–clonic seizures because superiority over placebo was shown in a randomized controlled trial [7]. In this trial, at least some patients reported a beneficial effect on additional myoclonic jerks. Furthermore, single reports indicated a potential beneficial effect of PER when used in an off-label manner in Lafora disease, a form of progressive myoclonic epilepsy [8,9]. Experience in other indications is very limited. However, our own clinical experience beyond the label and one report on convincing efficacy of PER in a case of superrefractory acute posthypoxic myoclonus [10] encouraged us to start add-on PER in a chronic case of drug-resistant posthypoxic myoclonus (Lance–Adams syndrome).

2. Case report

This 36-year-old male had suffered from drug-resistant posthypoxic myoclonus for one year after a cardiac arrest and reanimation because of cardiologically proven Brugada syndrome.

On admission, he presented with almost continuous stimulus-sensitive polytopic myoclonic jerks that required the permanent use of a wheelchair. Electroencephalography recordings were repeatedly normal and showed no epileptiform discharges during myoclonic jerks. We did not perform magnetic resonance imaging (MRI) because a pacemaker with defibrillator had been implanted. Previous computed cerebral tomography (CCT) had not shown clinically relevant abnormalities. His medication consisted of 2000 mg of levetiracetam, 1500 mg of valproic acid, 2 mg of clonazepam, and 7600 mg of piracetam. In addition, 100 mg of lacosamide had been added few weeks prior to admission in our hospital.

Perampanel was initiated at a dose of 2 mg and increased to 4 mg once daily in the evening after three days. Myoclonic jerks were suppressed almost completely after the dose increased to 4 mg. It was possible to discontinue lacosamide and piracetam without complications. Since the patient complained about PER-related somnolence, he wished to try a withdrawal. The next day, myoclonus was very prominent again and remained over the following five days before we decided to reintroduce PER (4 mg per day). Myoclonus was suppressed again and has not been reported for the follow-up of 4 weeks. Somnolence decreased and is tolerable now.

3. Discussion

Myoclonic jerks are frequent symptoms in several central nervous diseases and conditions. They may not only be part of various epilepsy syndromes but also occur as the result of nonepileptic pathogenesis as a cerebellar phenomenon in patients with posthypoxic brain damage which is well-known as so-called Lance–Adams syndrome. Although the action myoclonus in Lance–Adams syndrome is usually not of epileptic origin, antiepileptic drugs are recommended for its treatment [11–15]. In addition, piracetam has been recommended [16]. Because of the nonepileptic origin of the myoclonus, other therapeutic approaches addressed the idea of a movement disorder and suggested

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the use of L-5-hydroxytryptophan [17], levodopa, and GABAergic drugs [18] including alcohol [19], sodium oxybate [20], baclofen [21], or deep-brain stimulation [22,23]. The prognosis is bad; the efficacy of AEDs is usually limited.

In our patient, most recommended AEDs had already been tried in vain. Therefore, it was tempting to speculate if PER might be a suitable option since beneficial effects have been reported in single patients with juvenile myoclonic epilepsy [7] and Lafora disease [8,9] as well as in an acute myoclonic status after severe hypoxia [10].

Somnolence and dizziness belong to the most common adverse events under add-on PER [6,24]. The rather fast up-titration to 4 mg was performed more quickly than generally recommended because we wanted to estimate the potential efficacy of PER in this severe case with numerous myoclonic jerks as fast as possible. Therefore, somnolence might have been partly caused by this titration regimen. In patients with epilepsy, a more cautious titration is useful in order to avoid adverse events [25]. We discontinued PER in our case in spite of the apparent beneficial effect against the myoclonic jerks because of the sedating effects the patient complained about. After discontinuation, myoclonus exaggerated and was suppressed almost completely again when we reintroduced PER. Interestingly, this time tolerability was better, and so, we assume that a sort of adaptation had happened. Because of the reproducible effect of add-on PER after reintroduction, we are convinced about its efficacy in our patient and recommend trying it in comparable cases. Since patients with Lance–Adams syndrome suffer from very frequent myoclonus, one should be able to judge the efficacy of PER rather promptly in spite of the long elimination half-life and the considerable delay until plasma steady state is reached [25]. We hope that our patient will be able to cope with the sedating profile of PER. Long-term follow-up is not yet available.

4. Conclusion

This observation justifies trying add-on PER beyond the labeling in difficult-to-treat cases of Lance–Adams syndrome on an individualized basis.

Conflict of interest disclosure

BJS has received speaker's honoraria from Desitin, Eisai, Med Update, Omnia Med, UCB, and Viropharma. He was a member of advisory boards of or has consultancy agreements with Actelion, B.Braun, Eisai, Shire, and UCB.

CK has received speaker's honoraria from Desitin, Eisai, and UCB. He was a member of advisory boards of Eisai and UCB.

AMS has received speaker's honoraria from Desitin, Eisai, and UCB. She was a member of advisory boards of Eisai and UCB.

MB and RK have nothing to declare.

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