■ Clinical vignette

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Perampanel is effective against Lance-Adams syndrome

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The development of persistent intention or action myoclonus as a sequela of hypoxic injury was described in detail by Lance and Adams in 1963 [1]. Lance-Adams syndrome (LAS) is a rare chronic post-hypoxic condition characterized by action myoclonus within days to weeks after resuscitation and persists in patients who have recovered consciousness [2-4]. There are no large controlled trials available for guiding treatment for LAS. Among anti-seizure medications, treatment response has been reported with valproate, clonazepam, levetiracetam, and lacosamide. We report four patients with LAS treated with add-on perampanel (PER) with dramatic improvement in myoclonus (*table 1*).

Case 1: A 28-year-old African American woman with end-stage renal disease, suffered an asystolic arrest with hypoxic injury but subsequent return of normal circulation after resuscitation. Several days later, she developed daily, repetitive myoclonus affecting the head, torso, and bilateral extremities, consistent with LAS. Myoclonic events were so pervasive that they prevented her from performing activities of daily living or moving independently. Her bilateral upper extremity and torso myoclonus had no EEG correlate. However, she also developed bilateral tonic-clonic seizures. Levetiracetam, lorazepam, valproate, clobazam, lamotrigine, and phenytoin failed to control myoclonus. Eventually, she was started on PER, 4 mg twice daily, with extra dose post dialysis, then 4 mg three times daily, with near cessation of myoclonus. She was also maintained on clobazam, valproate, and phenytoin. Only occasional myoclonus was present at follow-up.

Case 2: A 75-year-old male suffered a hypoxic injury due to pulseless electrical activity arrest. Post arrest, he had persistent non-epileptic multifocal action myoclonus affecting the head, torso, and extremities, consistent with LAS. Myoclonus made him unable to feed himself, walk, or participate in therapy. Levetiracetam, valproate, and clonazepam failed to control myoclonus. He was then started on PER, at 4mg nightly, with dramatic and near-full abatement of myoclonic jerks. His medication regimen was simplified to PER 4mg nightly and valproate, with complete resolution of myoclonus at two weeks of follow-up.

Case 3: A 29-year-old male with no past medical history was involved in a high-speed motor collision and experienced hypoxic injury due to brief cardiac arrest at the scene of the accident. The patient was noted to have near-continuous jerking of the mouth, torso, and extremities, four days post arrest. Continuous EEG captured stimulus-induced multifocal myoclonic jerks without EEG correlate, consistent with LAS. The patient received four doses of IV lorazepam, and was loaded and maintained on levetiracetam, without improvement of myoclonic jerks. Clobazam produced minimal improvement in myoclonic jerks. PER was then initiated at a dose of 4 mg nightly, with complete resolution of myoclonus. The patient was weaned off levetiracetam and maintained on PER 4 mg nightly and clobazam. The patient remained free of myoclonus at follow-up.

▼ **Table 1.** Demographic and clinical data of Lance-Adams syndrome patients responding to perampanel.

Age/ gender	Cause of arrest	Time to return of spontaneous circulation	Time to myoclonus*	Time to PER administration	Time to myoclonus control	Duration of follow-up
28/ F	Septic shock/ asystole	~15 minutes	~15 days	4 months	1 day	6 months
75/ M	Mucous plug/ pulseless electrical activity	~5 minutes	~3 days	18 days	1 day	2 weeks
29/ M	Trauma and massive blood loss	~5 minutes	~4 days	10 days	1 day	10 weeks
36/ M	Found unresponsive-unknown initial insult	Unknown	~9 days	~3 weeks	2 days	7 months

*Onset may have been delayed by sedation.

Case 4: A 36-year-old male with a history of hypoxic events, developed non-epileptic myoclonus involving the trunk, extremities, head, and neck, consistent with LAS. He was trialed on levetiracetam, carbamazepine, and lamotrigine, with limited benefit. Significant improvement was seen after addition of PER, titrated to 4 mg twice daily. There was marked worsening of myoclonus after stopping PER, then marked improvement upon restarting it and additional benefit when PER was increased to 4 mg, three times daily. Carbamazepine and lamotrigine were stopped and not restarted. There was no EEG evidence for co-existent epilepsy. At follow-up, myoclonus occurred occasionally with motor activity, predominantly during transfers from the bed to the wheelchair, and speech.

Perampanel is a non-competitive antagonist of a-amino-3-hydroxy-5methyl-4 isooxazoleproprionic acid (AMPA) glutamate receptor. It was first approved by the USA Food and Drug Administration (FDA) in 2012 and is currently indicated as adjunctive therapy and monotherapy for focal seizures, as well as adjunctive treatment for primary generalized tonic-clonic seizures. Although there is no FDA indication for myoclonic seizures, several case reports and case series suggest its efficacy against progressive myoclonic epilepsies, which are usually resistant to therapy, as well as non-epileptic myoclonus [5-8]. Several reports also support efficacy against refractory status epilepticus, including post-anoxic myoclonic status epilepticus [9-11]. Even though perampanel has a long half-life, we administered it in divided doses in some instances in order to reduce peak concentration when exceeding the recommended starting dose. Perampanel was tolerated in our patients. While Patients 1, 2, and 4 did not complain of adverse effects, Patient 3 was too cognitively impaired to report adverse effects. It is possible that the benefit of perampanel outweighed adverse effects to the point that patients did not report them.

These cases help justify add-on perampanel for difficult-to-treat Lance-Adams syndrome, to control myoclonic jerks and improve functionality. Future controlled studies examining perampanel's efficacy for myoclonic disorders in general and Lance-Adams syndrome in particular are needed. ■

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

Disclosures.
None of the authors have any conflicts of interest to declare.

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TEST YOURSELF

(1) What type of myoclonus is most characteristic of Lance Adams syndrome?

(2) What is perampanel's regulatory approval and spectrum of efficacy?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.