

## The Efficacy of Lacosamide in Children with Drug-Resistant Epilepsy: Three Cases in Pediatric Patients

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Lacosamide is a relatively new anti-seizure medication (ASM) that is classified as a sodium channel blocker (SCB). Unlike conventional SCBs, such as carbamazepine, phenytoin, and oxcarbazepine, lacosamide stabilizes hyperexcitable neuronal membranes by selectively enhancing the slow inactivation of voltage-gated sodium channels [1-3]. In addition, it exhibits relatively little interaction with other ASMs and has high utility because it has both oral and intravenous (IV) formulations. In recent years, IV lacosamide has increasingly been recognized as a useful treatment for status epilepticus [4,5]. Lacosamide has shown efficacy and safety not only in adults, but also in children [2]. As such, lacosamide has been approved for use as monotherapy and adjunctive therapy for the treatment of focal-onset seizures in adults, adolescents, and children aged  $\geq 4$  years with epilepsy in the European Union and the United States [3,6-8]. However, further research on the efficacy and safety of lacosamide in children is still needed. In particular, in South Korea, lacosamide has not yet been approved for use in patients with epilepsy among children under 16 years of age. Here, we report three cases of pediatric intractable focal epilepsy that were effectively treated with lacosamide add-on therapy. This study was approved by the Institutional Review Board of the Gangnam Severance Hospital, Yon-

sei University College of Medicine for the study of ASMs, including lacosamide, in refractory childhood epilepsy (3-2022-0135). The review board waived the need for informed consent for this retrospective study.

**Case 1:** A 10-year-old girl with normal development without a specific birth history had intractable focal seizures at 24 months of age. After the seizures, she began experiencing cognitive decline. She took several ASMs, but they had no significant effect on seizure control, and her condition progressed to intractable epilepsy. In the pre-surgical evaluation, brain magnetic resonance imaging (MRI) was normal; however, focality was found in the right frontal area on fluorodeoxyglucose-positron emission tomography (PET) and electroencephalography (EEG) (Fig. 1A). Hence, she qualified for epilepsy surgery on her right frontal lobe. Her full-scale intelligence quotient (FSIQ) at that time was 69 and she weighed 31 kg. While awaiting epilepsy surgery, she was administered lacosamide as an add-on therapy. She became seizure-free after the titration of lacosamide up to 200 mg/day. Her seizures stopped for more than a year after the treatment, with no major side effects, and her EEG normalized considerably more than it had in the earlier study (Fig. 1B). As a result, her scheduled epilepsy surgery was canceled, and her seizures are now well



**Fig. 1.** Electroencephalography (EEG) findings of three pediatric patients with intractable epilepsy before and after treatment with lacosamide. (A) EEG findings of a 10-year-old girl before treatment with lacosamide. Frequent sharp wave discharges, predominantly in the right frontal area, were observed. (B) Eight months after lacosamide treatment, the background of the EEG was stabilized, and the epileptiform discharge was almost eliminated. (C) EEG findings of a 13-year-old girl before treatment with lacosamide. Focal slowing was observed, admixed with frequent sharp wave discharges from the right frontotemporal areas. (D) Six months after lacosamide treatment. The background of the EEG had stabilized, and the epileptiform discharge was almost eliminated. (E) EEG findings of a 32-month-old boy with an sodium voltage-gated channel alpha subunit 2 (SCN2A) pathogenic variant before treatment with lacosamide. A slow and disorganized background with nearly continuous multifocal sharp wave discharges, mainly found in both the frontal and temporal areas, was observed. (F) Five months after lacosamide treatment. The background of the EEG had somewhat stabilized, and the left-side dominant multifocal sharp wave discharges were greatly reduced.

controlled.

**Case 2:** A 13-year-old girl with no specific birth history experienced intractable focal seizures and status epilepticus from the age of 26 months. Her seizures seemed to be under control after taking several ASMs; however, they recurred. Brain MRI and PET showed focal abnormalities in the right temporal lobe. In addition, frequent epileptic discharges on the right temporo-parietal region were observed on EEG (Fig. 1C). Thus, the decision was made to

perform resective epilepsy surgery on the right temporo-parietal areas. Her FSIQ at that time was 84 and she weighed 48 kg. However, while awaiting the surgery, lacosamide was added to her treatment, and the dosage was gradually increased to 400 mg/day. She became seizure-free for more than 8 months, and her EEG improved to the point where her epileptic discharge was barely detectable (Fig. 1D). Other than slight dizziness, she had no particular side effects of lacosamide, and her seizures have been well

controlled so far.

**Case 3:** A 32-month-old boy with a *de novo* heterozygous pathogenic variant of sodium voltage-gated channel alpha subunit 2 (SCN2A), c. 4426T>A (p.Phe1476Ile) (NM\_001040142.1), experienced intractable focal seizures and was diagnosed with early infantile epileptic encephalopathy at 3 months of age. Several ASMs, a ketogenic diet, and steroids were administered, but the daily intractable seizures persisted. His brain MRI findings showed diffuse atrophy and thinning of the corpus callosum. He had a profound intellectual disability and was bed-ridden. The EEG findings before lacosamide add-on therapy were slow and disorganized, with nearly frequent multifocal sharp wave discharges, mainly in both the frontal and temporal areas (Fig. 1E). Based on a genetic mutation involving sodium channelopathy, lacosamide was added and titrated gradually to 10 mg/kg/day. After 5 months, the seizure frequency decreased by more than 90%, and the EEG findings significantly improved (Fig. 1F). Moreover, no serious side effects were observed.

For pediatric patients with intractable focal epilepsy, epilepsy surgery or a ketogenic diet may be considered. However, strong rejection and low compliance are often observed with these treatments. Therefore, there is an increasing demand for safe and effective ASMs for such patients [2,6]. The side effects of lacosamide include dizziness, vomiting, and headache, and serious adverse events have rarely been reported [2,6]. Lacosamide add-on therapy not only showed favorable outcomes even when there was an obvious focal abnormality on EEG, such as in case 1 and case 2, but also for targeted therapy in a patient who had intractable epilepsy with sodium channelopathy. Lacosamide shows promise as a new treatment option for children with refractory epilepsy [9]. A study on the strong association between lacosamide treatment failure and the concomitant use of other SCBs together with lacosamide in children has recently been reported, and the findings could be useful for pediatric epileptologists [10]. We found that lacosamide could be safely and effectively used as an add-on therapy for patients with pediatric intractable epilepsy based on these three cases. Therefore, lacosamide is considered to be a promising drug for patients with intractable focal epilepsy. Large cohort studies on the effectiveness and safety of long-term lacosamide treatment in children are needed. Additionally, more data on the use of lacosamide in pediatric patients are needed to determine the drug efficacy, and these efforts may provide better treatment options for patients with pediatric intractable focal epilepsy.

## Conflicts of interest

Hoon-Chul Kang is an associate editor, Heung Dong Kim is an ed-

itorial board member of the journal, but They was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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Conceptualization: JHN, HCK, and HDK. Data curation: JHN, HCK, and HDK. Formal analysis: JHN. Methodology: HDK. Project administration: HDK. Visualization: HCK and HDK. Writing-original draft: JHN. Writing-review & editing: JHN.

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