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Effectiveness of lacosamide in children and young adults previously treated with other sodium channel blockers

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ABSTRACT

Purpose: This multicenter study examined the effectiveness and tolerability of lacosamide (LCM) for children and young adults with epilepsy, particularly in patients who had previously been treated with other sodium channel blockers (SCBs) and the difference in effectiveness and tolerability when using other concomitant SCBs.

Methods: We retrospectively studied the clinical information of patients aged <30 years given LCM to treat epilepsy. The effectiveness and adverse events (AEs) of LCM and the other SCBs were investigated. Factors related to the effectiveness and AEs of LCM, such as the number of antiepileptic drugs (AEDs) tried before LCM and concomitantly used SCBs, were also studied.

Results: We enrolled 112 patients (median age = 11 years). One year after starting LCM, 29% of the patients were seizure free, and 50% had a ≥50% seizure reduction. Of the patients, 17% experienced AEs, the most common being somnolence. A ≥50% seizure reduction was observed for LCM in 30% of patients in whom other SCBs had not been effective. Lacosamide produced a ≥50% seizure reduction in 35% of the patients taking one concomitant SCB. By contrast, no patients had ≥50% seizure reduction, and 33% developed AEs, when LCM was administered concomitantly with two SCBs.

Conclusions: Lacosamide was effective in 30% of children and young adults in whom other SCBs had not been effective. The effectiveness of LCM may differ from that of other SCBs, and it is worth trying in patients with epilepsy resistant to other AEDs.

1. Introduction

Lacosamide (LCM) is a new antiepileptic drug (AED) that exerts its effect by selectively enhancing the slow inactivation of voltage-gated sodium channels [1]. Similar to other sodium channel blockers (SCBs), such as carbamazepine (CBZ), lamotrigine (LTG), and phenytoin (PHT), LCM is effective and sufficiently tolerated by children and adults with focal onset epilepsy [2–4].

Lacosamide poses less risk of severe adverse events (AEs), such as skin rash (Stevens–Johnson Syndrome or toxic epidermal necrolysis), and has fewer drug interactions, compared to other SCBs [5,6]. However, the clinical effectiveness of LCM for patients in whom other SCBs were not effective is not clear. Lacosamide and other SCBs block sodium channels via different mechanisms: Lacosamide selectively enhances slow inactivation of sodium channels, while other SCBs enhance fast inactivation more preferably [7]. One randomized controlled trial on newly diagnosed epilepsy in adults and adolescents reported that LCM is not inferior to controlled-release CBZ [8]. However, the relative effectiveness and tolerability of LCM and other SCBs has not been clarified in children. The effectiveness and tolerability of LCM concomitantly administered with other SCBs also remains unclear, because the

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results of previous reports are inconsistent [2,9,10]. This multicenter, retrospective study aimed to describe the effectiveness and tolerability of LCM in children and young adults with epilepsy, particularly focusing on its effectiveness in patients who had ever been treated with other SCBs, and the effectiveness and tolerability when administered concomitantly with other SCBs.

2. Methods

2.1. Patients

We enrolled patients aged <30 years with childhood-onset epilepsy who were treated with LCM between August 2016 and October 2019 in the Department of Pediatrics or Department of Pediatric Neurology of eight hospitals (Nagoya University Hospital, Aichi Medical University Hospital, Aichi Developmental Disability Center, Anjo Kosei Hospital, Okazaki City Hospital, Hekinan City Hospital, Tokoname City Hospital, and Tosei General Hospital). In all patients, epilepsy onset was at ≤15 years of age. We excluded patients with insufficient data, for example due to transfer to another hospital within 12 months of starting LCM. Patients with no seizures during the three months before starting LCM were also excluded. All clinical data were collected retrospectively from the medical records. This study was approved by the ethics committee of Nagoya University Graduate School of Medicine. Informed consent from patients or families was not required because of the retrospective nature of the study.

2.2. Seizure types and other clinical data

The seizure type of each patient was classified according to the 2017 ILAE Classification of Seizures [11]. We investigated seizure frequency within three months before starting LCM (pre-LCM), three months after starting LCM (post-LCM), and between months nine and 12 after starting LCM (1 year after starting LCM) by reviewing the clinical charts. We also obtained the basic characteristics of the patients, including age, sex, diagnosis of epilepsy, presence or absence of an abnormality on brain magnetic resonance imaging (MRI), number of AEDs administered before LCM, and AEDs concomitantly prescribed with LCM, the initial dose and average increase thereof of LCM, and AEs such as skin rash, somnolence, dizziness, and aggression. According to the previous report, we defined drug-resistant epilepsy as failure of adequate trials of two tolerated, appropriately chosen, and used AED schedules to achieve sustained seizure freedom [12]. The initial daily dose of LCM, and the average increase thereof, were determined by the attending physician; the doses are described in mg (in patients with bodyweight ≥50 kg) or mg/kg (in patients with bodyweight <50 kg). A dose of 2 mg/kg or 100 mg was the most commonly used in previous randomized-controlled trials. Based on the above, we categorized the doses as follows: low dose, ≤1.5 mg/kg; standard dose, >1.5 mg/kg and <2.5 mg/kg; high dose, ≥2.5 mg/kg (in patients with a bodyweight <50 kg); and low dose, ≤75 mg; standard dose, >75 mg and <125 mg; high dose, ≥125 mg (in patients with a bodyweight ≥50 kg) [2–4].

2.3. Effectiveness and tolerability

We evaluated the effectiveness of LCM based on the change in seizure frequency before and after LCM administration. The effectiveness was classified as 'effective' when seizure reduction was ≥50% compared to the baseline (including seizure-free patients), and as 'ineffective' when seizure reduction was <50% compared with to the baseline. Short- and long-term efficacies were defined as a reduction in seizure frequency from the pre- to post-LCM period, and from the pre-LCM period to 1 year after starting the LCM, respectively. We calculated the short- and long-term seizure-free rates and 50% responder rates. The primary outcome was the long-term 50% responder rate (rate of effective LCM). The secondary outcomes were the long-term seizure-free rate, and short-term seizure-free and 50% responder rates. We also investigated whether seizure type, number of AEDs administered before LCM, concomitant use of other SCBs, and initial LCM dose and daily increase thereof were associated with effectiveness and tolerability.

For patients who had received other SCBs (CBZ, LTG, or PHT) before starting LCM, the effectiveness of the other SCBs was studied in the same way as for LCM. Oxcarbazepine has not been approved in Japan.

In addition, we investigated the factors associated with differences in effectiveness between LCM and the other SCBs. Patients who had received at least one SCB before LCM, and for whom all SCBs except LCM were judged as ineffective, were classified as 'other SCBs ineffective'. We also obtained demographic (age when starting LCM, sex) and clinical (seizure type, age at seizure onset, number of AEDs before starting LCM, etiology of epilepsy) data for patients in both the 'other SCBs ineffective' and 'LCM effective' categories.

2.4. Statistical analysis

Fisher's exact test was used to compare categorical variables. The Mann–Whitney *U* test was used to compare continuous variables. SPSS 27.0 software (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. A p-value <0.05 was considered significant.

3. Results

Lacosamide was administered to 119 patients in the eight pediatric departments during the study period. Five patients with insufficient information, and two without seizures during the pre-LCM period, were excluded. The remaining 112 patients were included in the final analysis (Fig. S1).

Demographics, seizure types, and information about AED use are shown in Table 1.

1. Our cohort consisted of 61 males and 51 females with a median age of 11 years (range: 0–28 years). Of the 112 patients, 109 (97%) had at least one type of focal onset seizure. The other three patients exhibited generalized onset tonic seizure, generalized onset tonic-clonic seizure, or epileptic spasms. The median number of AEDs administered before LCM was three (range: 0–15), and two or more AEDs were tried in 72 patients (64%) before starting LCM. CBZ, LTG, and PHT were administered to 40, 29, and 17 patients, respectively, before initiating LCM. Twenty-three patients (21%) started LCM concomitantly with one SCB, and six patients (5%) started LCM with two SCBs. The mean initial LCM dose, and average increase thereof, were 1.77 and 1.64 mg/kg/day for patients with a bodyweight <50 kg and 84.1 and 81.9 mg/day for patients with a bodyweight ≥50 kg, respectively. Lacosamide was administered at a low initial daily dose, with a small average daily increase, in 48 (43%) and 55 (49%) patients, respectively.

The effectiveness data for LCM are shown in Table 2. Seizure reduction of ≥50% and seizure-free status were achieved in 58 (52%) and 35 (31%) patients, respectively, over the short term. In 56 patients (50%), long-term seizure reduction of ≥50% was achieved, and 32 patients (29%) were seizure free over the long term. Of the 112 patients, LCM was terminated in 14 due to ineffectiveness, in three because of AEs, and in four following remission of seizures 12 months after starting LCM. No significant difference in

Table 1
Demographics, seizure types, and information about the antiepileptic drugs taken by patients.

	Numbers and median of patients (n = 112)
Age when starting LCM (years)	11 [0–28]
<4	8 (7%)
4–18	91 (81%)
>18	13 (12%)
Males	61 (54%)
Follow-up period (months)	18 [12–56]
Age at seizure onset (years)	5 [0–15]
Seizure types	
Focal aware seizure	15 (13%)
Focal impaired awareness seizure	28 (25%)
Focal to bilateral tonic-clonic seizure	46 (41%)
Combination of various types of focal seizures	12 (11%)
Combination of focal and generalized seizures	8 (7%)
Other	3 (3%)
Seizure frequency during the pre-LCM period (per month)	4 [0.33–3000]
Number of AEDs before starting LCM	
0	22 (20%)
1	18 (15%)
2 or more	72 (65%)
Number of SCBs before starting LCM	
None	63 (56%)
CBZ	40 (36%)
LTG	29 (26%)
PHT	17 (15%)
Number of concomitant AEDs with LCM	
0	28 (25%)
1	29 (26%)
2	34 (30%)
3	20 (18%)
4	1 (1%)
Number of concomitant SCBs with LCM	
0	83 (74%)
1	23 (21%)
2	6 (5%)
MRI findings	
Normal	55 (49%)
Abnormal	50 (45%)
No data	7 (6%)
Initial daily dose of LCM	
Low dose (1.5 mg/kg or ≤75 mg)	48 (43%)
Standard dose (1.5–2.5 mg/kg or 75–125 mg)	54 (48%)
High dose (2.5 mg/kg or ≥125 mg)	10 (9%)
Average increase in daily dose of LCM	
Low dose (1.5 mg/kg or ≤75 mg)	55 (49%)
Standard dose (1.5–2.5 mg/kg or 75–125 mg)	48 (43%)
High dose (2.5 mg/kg or ≥125 mg)	6 (5%)

Data are numbers (%) or medians [range].
LCM: lacosamide, AED: antiepileptic drug, SCB: sodium channel blocker, MRI: magnetic resonance imaging

the 50% responder rate was found by seizure type, or by the initial LCM dose or average daily increase thereof, over the short or long term.

Patients with no or only one previous AED treatment before LCM were more likely to be seizure- free than those with two or more previous AED treatments before LCM; the 50% responder rate was also higher in the former group ($p < 0.001$) (Table 2). Nine patients (13%) achieved seizure-free status among the seventy-two with two or more AED treatments before LCM, and twenty-seven patients (38%) achieved ≥50% seizure reduction in the short term. Eleven (15%) patients with two or more AED treatments before LCM were seizure free over the long term, and 26 (36%) patients were 50% responders.

Patients who were not taking any other SCBs concomitantly had a significantly higher likelihood of seizure-free status than those who with concomitant SCBs ($p < 0.001$) and a higher likelihood of being a 50% responder, over both the short and long term ($p = 0.002$ and $p = 0.004$, respectively). Among the 23 patients taking one concomitant SCB, 8 (35%) achieved a ≥50% seizure reduction over the short and long terms. None of the patients taking two concomitant SCBs was a 50% responder over the short or long term (Fig. 1).

AEs associated with LCM were seen in 19 (17%) patients. Somnolence was the most common AE in 11 patients (10%), followed by dizziness (4%), aggression (2%), nausea (1%), and headache (1%). Lacosamide was stopped in three patients (3%) for AEs (somnolence, dizziness, or aggression). No patient exhibited a skin rash, cytopenia, or hyponatremia. Table 3 shows the associations between the clinical characteristics and AEs. Patients who were not taking concomitant AEDs had significantly fewer AEs than those taking AEDs ($p = 0.021$). Patients with two concomitant SCBs and a higher initial and increasing daily dose of LCM tended to experience more AEs, although none of these differences reached statistical significance.

Forty-nine patients were treated with other SCBs before LCM, and seventeen of them experienced AEs associated with SCBs. The AEs most commonly seen with other SCBs were somnolence or skin rash with CBZ, skin rash with LTG, and somnolence or swollen gingiva with PHT. None of the four patients with a skin rash (1 of 40 patients on CBZ, 2 of 29 on LTG, and 1 on both CBZ and LTG), and five patients with somnolence from other SCBs (3 of 40 patients on CBZ and 2 of 17 on PHT), experienced the same AEs while taking LCM. One patient with dizziness taking CBZ was also dizzy after taking LCM. Patients who had experienced AEs with SCBs tended to experience more AEs while taking LCM than those with no prior AEs, although the difference was not significant.

All of the SCBs were ineffective in 33 patients who tried them before LCM, and 10 (30%) and 6 (18%) of them achieved a >50% seizure reduction over the short and long terms, respectively (Fig. S2). Table 4 shows the clinical features of the 11 patients in whom LCM was effective in the short or long term, but for whom other SCBs were ineffective. All 11 of those patients had tried two or more AEDs before LCM and fulfilled the criteria for drug-resistant epilepsy. MRI revealed various abnormal findings in all patients except cases 3 and 7, such as cortical malformation (ectopic gray matter or focal cortical dysplasia) or peri/postnatal brain injury (periventricular leukomalacia, perinatal hypoxic-ischemic encephalopathy, or postnatal acute infectious encephalopathy). In the group of patients for whom SCBs other than LCM were ineffective, those with MRI abnormalities were more likely to improve with LCM (8/22, 36%) than those without MRI abnormalities (2/11, 18%) over the short term, although the difference was not significant ($p = 0.256$). Patients with MRI abnormalities were more likely to improve on LCM over the long term (5/22, 23%) than those without (1/11, 9%), but the difference was not significant ($p = 0.329$). No commonalities were detected among these patients, such as age when starting LCM, sex, age at epilepsy onset, seizure type, or AEDs concomitantly prescribed with LCM.

4. Discussion

In this retrospective, multicenter study, we demonstrated that LCM was effective and generally tolerable for Japanese children and young adults with epilepsy. Approximately half of the patients achieved a ≥50% seizure reduction, and AEs were rare during short -and long-term observations.

Lacosamide reduced or remitted seizures for 30% of the patients in whom other SCBs were ineffective before LCM administration, although the present study was not designed as a randomized trial

Table 2
Effectiveness of lacosamide over the short and long terms.

	Short-term effectiveness			Long-term effectiveness		
	Ineffective	50% responder	Seizure-free	Ineffective	50% responder	Seizure-free
Total (n = 112)	54 (48%)	58 (52%)	35 (31%)	56 (50%)	56 (50%)	32 (29%)
Seizure types						
Focal aware seizure (n = 15)	5 (33%)	10 (67%)	3 (20%)	8 (53%)	7 (47%)	4 (27%)
Focal impaired awareness seizure (n = 28)	18 (64%)	10 (36%)	6 (21%)	13 (46%)	15 (54%)	8 (29%)
Focal to bilateral tonic-clonic seizure (n = 46)	17 (37%)	29 (63%)	23 (50%)	19 (41%)	27 (59%)	16 (35%)
Combined some types of focal seizures (n = 12)	7 (58%)	5 (42%)	2 (17%)	8 (67%)	4 (33%)	3 (25%)
Combined of and generalized seizures (n = 8)	5 (63%)	3 (37%)	0	6 (75%)	2 (25%)	0
Other (n = 3)	2 (67%)	1 (33%)	1 (33%)	2 (67%)	1 (33%)	1 (33%)
Number of AEDs before starting LCM						
0 (n = 22)	6 (27%)	16 (73%)	15 (68%)	7 (32%)	15 (68%)	11 (50%)
1 (n = 18)	3 (17%)	15 (83%)	11 (61%)	4 (22%)	14 (78%)	10 (56%)
$\geq$ 2 (n = 72)	45 (63%)	27 (38%)	9 (13%)	46 (64%)	26 (36%)	11 (15%)
Number of concomitant SCBs with LCM						
0 (n = 83)	33 (40%)	50 (60%)	34 (41%)	35 (42%)	48 (58%)	31 (37%)
1 (n = 23)	15 (65%)	8 (35%)	1 (4%)	15 (65%)	8 (35%)	1 (4%)
2 (n = 6)	6 (100%)	0	0	6 (100%)	0	0
Initial daily dose of LCM						
Low dose (1.5 mg/kg or $\leq$75 mg) (n = 48)	20 (42%)	28 (58%)	14 (29%)	22 (46%)	26 (54%)	14 (29%)
Standard dose (1.5–2.5 mg/kg or 75–125 mg (n = 54)	28 (52%)	26 (48%)	17 (31%)	27 (50%)	27 (50%)	15 (28%)
High dose (2.5 mg/kg or $\geq$125 mg) (n = 10)	6 (60%)	4 (40%)	4 (40%)	7 (70%)	3 (30%)	3 (30%)
Average increase in daily dose of LCM						
Low dose (1.5 mg/kg or $\leq$75 mg) (n = 55)	23 (42%)	32 (58%)	18 (33%)	25 (45%)	30 (55%)	16 (29%)
Standard dose (1.5–2.5 mg/kg or 75–125 mg) (n = 48)	27 (56%)	21 (44%)	13 (27%)	26 (54%)	22 (46%)	12 (25%)
High dose (2.5 mg/kg or $\geq$125 mg) (n = 6)	3 (50%)	3 (50%)	3 (50%)	3 (50%)	3 (50%)	3 (50%)

Data are numbers (%).
LCM: lacosamide, AED: antiepileptic drug, SCB: sodium channel blocker.

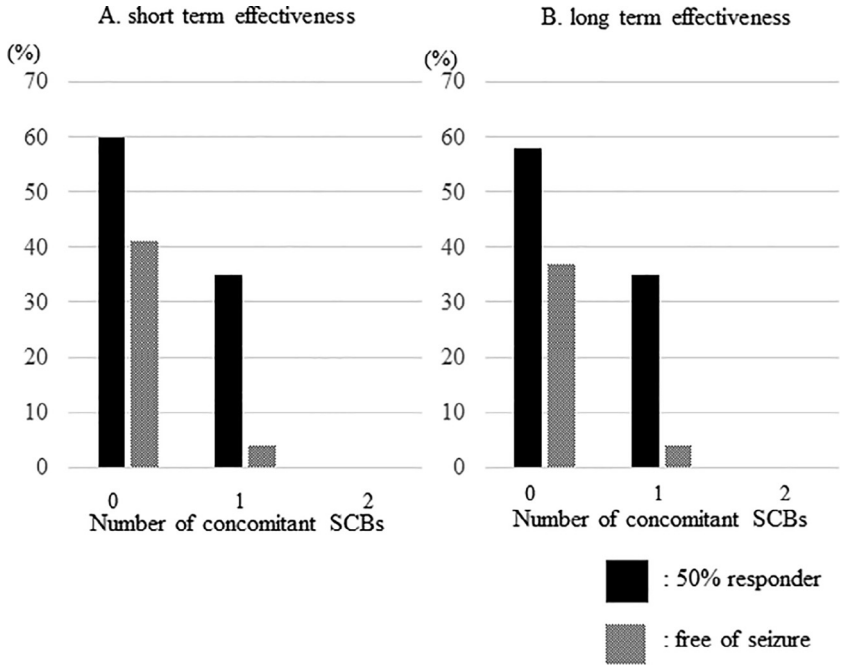

Fig. 1. Short- and long-term effectiveness of lacosamide concomitantly administered with other sodium channel blockers. The 50% responder and seizure-free rates over the short term (A) and long term (B) after starting lacosamide. Patients taking more concomitant sodium channel blockers were less likely to be 50% responders and seizure free. SCB: sodium channel blocker.

to compare LCM with other SCBs. We identified no characteristics, such as age, sex, or seizure type, clearly distinguishing patients in whom LCM was effective. All of the patients had taken two or more ineffective AEDs before LCM (drug-resistant epilepsy) [12]. One way in which LCM is different from the other SCBs concerns the mechanism of sodium channel blockade; LCM enhances the slow inactivation of sodium channels more selectively. Another reason is the different mechanism of glial inactivation. Lacosamide suppresses the gliotransmitter release associated with astroglial hemichannel activation, while CBZ does not [13]. The decreased glial activation induced by LCM, and its neuroprotective effects, have also has been reported in a gerbil model [14]. Reactive astrogliosis is present in structural epileptic lesions, such as cortical dysplasia, and leads to epileptic hyperexcitability [15,16]. In the present study, 9 of 11 patients in whom LCM, but not other SCBs, was effective exhibited abnormalities on brain MRI. In the group

Table 3
Associations between adverse events from lacosamide and clinical information.

	AEs from LCM use		
	Patients without AEs	Patients with any AE	Discontinuation due to AE
Total (n = 112)	93 (83%)	19 (17%)	3 (3%)
Number of concomitant AEDs prescribed with LCM			
0 (n = 28)	27 (96%)	1 (4%)	0
1 (n = 29)	23 (79%)	6 (21%)	1 (3%)
2 (n = 34)	27 (79%)	7 (21%)	1 (3%)
3 (n = 20)	15 (75%)	5 (25%)	1 (4%)
4 (n = 1)	1 (100%)	0	0
Number of concomitant SCBs prescribed with LCM			
0 (n = 83)	69 (83%)	14 (17%)	2 (2%)
1 (n = 23)	20 (87%)	3 (13%)	0
2 (n = 6)	4 (67%)	2 (33%)	1 (17%)
Initial daily dose of LCM			
Low dose (1.5 mg/kg or ≤75 mg) (n = 48)	42 (88%)	6 (12%)	2 (4%)
Standard dose (1.5–2.5 mg/kg or 75–125 mg) (n = 54)	43 (80%)	11 (20%)	1 (2%)
High dose (2.5 mg/kg or ≥125 mg) (n = 10)	8 (80%)	2 (20%)	0
Average increase in daily dose of LCM			
Low dose (1.5 mg/kg or ≤75 mg) (n = 55)	48 (87%)	7 (17%)	1 (2%)
Standard dose (1.5–2.5 mg/kg or 75–125 mg) (n = 48)	40 (83%)	8 (17%)	0
High dose (2.5 mg/kg or ≥125 mg) (n = 6)	4 (67%)	2 (33%)	0
History of any AEs with other SCBs			
(−) (n = 32)	28 (88%)	4 (12%)	1 (3%)
(+) (n = 17)	12 (71%)	5 (29%)	2 (12%)

Data are numbers (%).
LCM: lacosamide, AED: antiepileptic drug, SCB: sodium channel blocker, AE: adverse event.

of patients for whom the other SCBs were ineffective, those with MRI abnormalities were more likely to be 50% responders to LCM over the short (36% vs. 18%) and long term (23% vs. 9%), although the differences were not significant. The different effects on glial inactivation (in epileptic lesions with astrogliosis) of LCM compared to other SCBs may explain the greater effectiveness of LCM in patients for whom other SCBs are ineffective.

In this study, LCM and the other SCBs were not always associated with the same AEs. Four patients developed skin rashes and five had somnolence while using SCBs other than LCM. AEs specific to some drugs were also seen, such as swollen gingiva caused by PHT. None of the patients with AEs due to SCBs other than LCM experienced the same AEs while taking LCM. Although LCM seems to be associated with fewer AEs than the other SCBs, the data should be interpreted with caution because we included patients in whom treatment with other SCBs failed due to severe AEs.

Previous studies have reported inconsistent results regarding the difference in effectiveness and tolerability of LCM between patients concomitantly using and not using an SCB. A randomized controlled trial conducted by Farkas et al. showed that LCM has similar effectiveness, but was associated with more AEs, in patients taking a concomitant SCB compared to those who were not [2]. McGinnis et al. also reported that concomitant SCB use resulted in more AEs and was an independent predictor of discontinuation of LCM [17]. In contrast, in an observational study, Hmaimess et al. reported that LCM was less effective, and had a similar incidence of AEs, in patients with versus without concomitant use of SCB [10]. A prospective observational study by Runge et al. found similar effectiveness and tolerability between patients with and without a concomitant SCB when LCM was added to one baseline AED [9]. In the present study, the 50% responder rate was significantly lower in the group concomitantly using versus not using an SCB, and tolerability was not different between the groups similarly to the result reported by Hmaimess. The dissociable changes in effectiveness and tolerability among studies may be due to the differences in the background of the patients and the study designs. Another possible reason why AEs were similar between the patients with and without concomitant SCBs in the present study is the relatively small dose of LCM. The initial daily dose, and daily increase thereof, of LCM were fixed at 100 mg (patients ≥50 kg body weight) or 2 mg/kg (patients <50 kg body weight) in most previous studies [2–4]. In our study, the mean initial daily dose, and mean daily increase thereof, were lower than 100 mg or 2 mg/kg, which may explain the lower rate of AEs (17%) than in previous studies (31–84%) [2–4]. The lower dose and fewer AEs may also have reduced the difference in the number of AEs between patients with and without concomitant SCB use.

Patients with epilepsy who do not respond to the first two drug courses are considered drug-resistant [12,18,19]. In the present study, the group with drug-resistant epilepsy in which two or more AEDs had been tried had significantly lower 50% responder and seizure-free rates than the other groups. However, 36% of patients with drug-resistant epilepsy achieved a ≥50% seizure reduction and 15% were seizure free when taking LCM. Because the mechanism of the antiepileptic effect of LCM differs from traditional AEDs (including SCBs) and other new AEDs, LCM may be worth trying in patients with epilepsy resistant to other AEDs.

Our study had several limitations. First, the effectiveness of LCM could not be assessed relative to a control group not taking LCM because of the retrospective nature of the study; patient selection and the LCM doses were dependent on the clinician. However, we were able to identify a possible association between lower initial and increasing doses of LCM and fewer AEs because there was no predefined protocol. Second, because the timing and length of use differed between LCM and the other SCBs, the effectiveness and AE rates could not be compared directly. Prospective trials are needed to determine whether there is a difference in effectiveness between LCM and other SCBs. Despite these limitations, our results provide important information based on real-world clinical practice.

Table 4
Clinical features of 11 patients in whom lacosamide was effective but other sodium channel blockers were ineffective.

Case	LCM effectiveness (short-term)	LCM effectiveness (long-term)	Age at start of LCM (years)	Sex	Seizure type	SCBs administered before LCM	Age at epilepsy onset (years)	Number of AEDs before starting LCM	AEDs concomitantly prescribed with LCM	Etiology of epilepsy
1	Seizure free	Seizure free	16	Male	FBTCS	CBZ	7	4	CLB, LEV	Sequela of acute encephalopathy
2	Seizure free	Seizure free	16	Female	FIAS	CBZ	6	4	CLB, PER	Ectopic gray matter
3	Seizure free	Effective	4	Female	FIAS	CBZ	0	4	TPM, VPA, VGB	CDKL5 mutation (normal MRI)
4	Effective	Seizure free	11	Female	FAS	CBZ	6	3	PB	Periventricular leukomalacia
5	Effective	Effective	27	Female	FIAS	CBZ, LTG, PHT	0	8	CZP, VPA, CBZ, TPM	Unknown etiology, diffuse volume reduction of white matter on MRI
6	Effective	Ceased for AE	16	Male	FAS	LTG	3	2	LEV	Unknown etiology, multiple nodular lesions on MRI
7	Effective	Stopped, ineffective	4	Male	FBTCS	CBZ	4	2	LEV	childhood epilepsy with centrotemporal spikes
8	Effective	No change	17	Female	FAS	LTG	0	8	LTG, CLB, PER	Ectopic gray matter
9	Effective	No change	15	Male	FAS	LTG, PHT	0	11	VPA, LEV, PER	Perinatal HIE
10	Effective	No change	15	Male	FIAS	LTG	1	13	VPA, PER	Perinatal HIE
11	No change	Effective	3	Male	FBTCS	CBZ	2	7	CZP, PB	Perinatal HIE

LCM: lacosamide, SCB: sodium channel blocker, AED: antiepileptic drug, AE: adverse event, FAS: focal aware seizure, FIAS: focal impaired awareness seizure, FBTCS: focal to bilateral tonic-clonic seizure, CBZ: carbamazepine, LTG: lamotrigine, PHT: phenytoin, CLB: clobazam, LEV: levetiracetam, PER: perampanel, TPM: topiramate, VPA: valproic acid, VBG: vigabatrin, PB: phenobarbital, CZP: clonazepam, CDKL5: cyclin-dependent kinase-like 5, MRI: magnetic resonance imaging, HIE: hypoxic-ischemic encephalopathy.

5. Conclusions

In conclusion, our multicenter study showed good effectiveness and tolerability of LCM for Japanese children and young adults with epilepsy. The effectiveness of LCM may be different from that of other SCBs, and it is worth trying in patients with epilepsy resistant to other AEDs.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2021.108397.

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