



The retention of lacosamide in patients with epilepsy and intellectual disability in three specialised institutions



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ABSTRACT

Purpose: We describe the effectiveness of lacosamide as adjunctive therapy in patients with epilepsy and an intellectual disability. This information is relevant, as few data exist pertaining to this population with a high prevalence of (intractable) epilepsy.

Methods: We performed a retrospective study in three specialised institutions. Inclusion criteria were (1) focal onset or symptomatic generalized (2) therapy-resistant epilepsy, (3) intellectual disability and (4) residence in a care-facility for people with intellectual disabilities (PWID). The primary outcome variables were the retention rates of lacosamide, estimated through Kaplan-Meier survival analysis. Secondary outcomes were reported seizure control, side effects and clinical factors influencing discontinuation.

Results: One hundred and thirty-two patients were included. The median retention time of lacosamide in our cohort was four years. The estimated one-, two- and three-year retention rates of lacosamide were 64%, 57% and 56% respectively. Severity of intellectual disability and seizure type did not influence whether lacosamide was continued. In 48.5% of patients, a reduction of seizure activity was reported. Side effects were at least part of the reason for discontinuing treatment in 26.5% of all patients. Common side effects were tiredness/somnolence (in 30.3%), aggression/agitation (24.2%), and instable gait (15.2%). Five deaths during follow-up were considered unlikely to be related to the use of lacosamide. One patient died unexpectedly within two months of treatment onset, probably this was a case of SUDEP.

Conclusion: These retention rates of lacosamide in PWID are similar to rates of previously registered anti-epileptic drugs in PWID. Behavioural side effects were noted in a high proportion compared to the general literature on lacosamide. Other side effects were in line with this literature. Lacosamide seems effective and safe for PWID and refractory epilepsy.

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1. Introduction

The prevalence of epilepsy in the general population is estimated at 0.5%. Approximately 50% of patients with newly

diagnosed epilepsy become seizure free with initially prescribed anti-epileptic drugs (AED's). Despite the registration of new antiepileptic drugs, 30% of patients will continue to have seizures after treatment with at least two different AED's, successively or concomitant (refractory epilepsy) [1]. In people with intellectual disabilities (IQ less than 70), the prevalence of epilepsy is estimated to be substantially higher than in the general population: 10–30% [2]. With increasing severity of intellectual disability, the prevalence of epilepsy increases as well. Intellectual disability is associated with multiple seizure types within an individual and a poorer prognosis for seizure control – with refractory epilepsy in up to 75% of patients [3,4]. The refractory nature of epilepsy in this population often provides the need for polypharmacy, including new AED's [4].

Abbreviations: PWID, people with an intellectual disability; AED, anti-epileptic drug; RCT, randomised controlled trial; SUDEP, sudden unexplained death in epilepsy.

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Whilst the prevalence of epilepsy is high in people with intellectual disabilities (PWID), they are typically excluded from randomised controlled clinical trials (RCT's) with new AED's, on account of ethical concerns about the capacity to consent, and of foreseen problems with diagnostics, seizure count, assessment of adverse effects and compliance to therapy [5]. As a result, there is little evidence on optimal treatment of epilepsy in PWID. Clinical guidelines for the management of epilepsy in adults with an intellectual disability recommend the same AED's as prescribed in the general population – which include sodium valproate, lamotrigine and potentially carbamazepine or levetiracetam as first options for treatment of focal onset and symptomatic generalized seizures – taking special consideration of potential adverse cognitive and behavioural effects of AED's [6]. A Cochrane review of 14 RCT's on pharmacological interventions for epilepsy in PWID concluded that lamotrigine, topiramate, clobazam, rufinamide and felbamate seem effective and tolerable as adjunctive therapy, and consider this to be evidence supporting the use of similar AED's in PWID as in the general population. The review reports that pharmacological interventions are still under-

investigated in the population of PWID [7]. More recently, retrospective studies have addressed the duration of treatment (retention rate) and – if applicable – the reason for discontinuation of several new anti-epileptic drugs in PWID. The retention rate was used as an indication for efficacy and tolerability of AED's in intellectually disabled patients, where precise registration of seizure frequency is notoriously difficult. The studies present two-year retention rates of 40–75% for lamotrigine, levetiracetam, topiramate and perampanel and of 85% for oxcarbazepine [5,8–10]. Two of these articles concluded gabapentin to seem less effective.

Lacosamide was registered in Europe in 2008, as an adjunctive AED in the treatment of refractory partial-onset seizures with or without secondary generalization. Its mechanism of action is believed to be blockage of sodium channels. Three randomised controlled trials on the efficacy of lacosamide as an adjunctive AED in partial-onset seizures showed a reduction (>50%) in seizure frequency in 30–40% of patients, and a median reduction of seizure frequency of 14 to 45% [11–13]. Three prospective studies and two retrospective studies estimated one-, two- and three-year retention rates of lacosamide to be 62–77%, 45–71% and 35–52.9%

Table 1
Demographic and clinical characteristics of all included patients (n = 132).

Characteristic	Value
Sex, % of all patients	
Male	56.8%
Female	43.2%
Age in years, mean (SD; min – max)	41.7 (15.0; 18.0–78.0)
Weight in kilograms, mean kg (SD)	69.1 (16.5)
Severity of intellectual disability, nr. of patients (% of patients)	
Mild (IQ 50–70)	31 (23.5%)
Moderate (IQ 35–50)	20 (15.2%)
Severe (IQ 20–35)	31 (23.5%)
Profound (IQ <20)	10 (7.6%)
Unknown	40 (30.3%)
Aetiology of epilepsy, nr. of patients (% of patients)	
No known aetiology	54 (40.9%)
Genetic	24 (18.2%)
Perinatal pathology	19 (14.4%)
Post-infectious	16 (12.1%)
Vascular	7 (5.3%)
Posttraumatic	4 (3.0%)
Metabolic	2 (1.5%)
Neoplastic	2 (1.5%)
Post-vaccination	2 (1.5%)
Inflammatory	1 (0.8%)
Intoxication	1 (0.8%)
Seizure type, nr. of patients (% of patients)	
Focal onset	4 (3.0%)
(Multi)focal onset with secondary generalization	77 (58.3%)
Generalized onset	31 (23.5%)
Unknown	20 (15.2%)
Daily dose of lacosamide in milligrams, mean (SD; min – max)	243.7 (104.9; 50.0–450.0)
Number of preceding AED's used, mean (SD; min – max)	7.0 (±3.3; 2–19)
Number of concomitant AED's, mean (SD; min – max)	2.0 (0.9; 1–6)
Sodium Valproate	66 (50.0%)
Carbamazepine	55 (41.7%)
Lamotrigine	43 (32.6%)
Clobazam	38 (28.8%)
Levetiracetam	37 (28.0%)
Topiramate	17 (12.9%)
Oxcarbazepine	16 (12.1%)
Phenytoin	15 (11.4%)
Other concomitant AED's	39 (29.5%)
Concomitant vagal nerve stimulator, nr. of patients (% of patients)	19 (14.4%)
Concomitant behavioural medication, nr. of patients (% of patients)	39 (29.5%)
Antipsychotics	24 (18.2%)
Benzodiazepines	11 (8.3%)
Antidepressants	9 (6.8%)
Follow-up time in years, mean (SD; min – max)	4.6 (2.1; 0.1–7.7)

AED's = antiepileptic drugs.

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