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Evaluating Lacosamide in the management of focal Seizures: A narrative review of Efficacy, safety and Tolerability

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Abstract:

The focal seizures are one of the most widespread ones as they include various scopes of physical and psychological changes with a significant adverse impact on their well-being. Ever since anti-epileptic drugs (AEDs) are identified as a first-line treatment method, numerous patients encountered drug resistance and side effects. Lacosamide belongs to the third generation of anti-epileptic medication and is the best drug of the potential and preferred choice in treatment of focal seizures alone or as companion ecunicides. This narrative assessment examines the safety, effectiveness, tolerability, and clinical use of lacosamide in the treatment of epilepsy, drawing from 13 studies published from 2020 to 2024. All the studies revealed effectiveness of Lacosamide in reducing the frequency of the seizures with dose response and increase in the response rate over placebo. Additionally, it had an improved safety record and few adverse effects when compared to other antiepileptic drugs, particularly, among young individuals. The mode of action is selective in that; it amplifies the slow inactivation of sodium channels and causes minimal interference to the normal neural firing leading to fewer side effects and maximum control of seizures. Based on long-term studies, the efficacy of lacosamide is proven with continued seizure reduction and improved quality of life and cognitive status in both usage as monotherapy or adjuvant treatment. Even with all positive results, it has some challenges including clinicians' unfamiliarity with newer medications, expense-related factors and refusal to undergo treatment. To promote the clinical use of lacosamide on a large scale, eliminating these barriers by patient education, directing policy changes, and increasing access is vitally necessary. Altogether,

lacosamide is a significant step towards treating focal epilepsy, and, given the effective safety balance, it could have a favorable influence on both patient outcomes and their livelihood.

Keywords: Focal seizures, Antiepileptic drugs, Lacosamide, Efficacy, Tolerability.

Introduction:

Epilepsy is a complex and chronic neurological condition that is defined by the recurrent and unconditioned convulsions that can be described as the effect of the abnormal electrical disorders in the brain. It is an ailment that afflicts millions of individuals all over the world and could profoundly influence their daily activities. Focal seizures are one of the many types of epilepsy with the onset of the seizure in one part of the brain. This type of seizure may occur in any way depending on awareness, sensations, behavior, and appearance of abnormal movements. Notably, the symptoms of focal seizures are usually confined to a single part of the body, and this presents certain problems to affected patients (1). The most widely spread type of seizure is focal with prevalence up to 61% among epileptic adults. Physical and psychological signs of focal epilepsy may entail various experiences including jerking motions, anger, sorrow, irritability and many other emotional instabilities. The symptoms do not only impact on the health of the individual but also have other implications for the quality of life. The occupation effects of such seizures may impose serious effects of being able to sustain occupation and other types of relationships which in many cases lead to isolation and stigmatization. Moreover, although cognitive deficits might not be reported so often, it can bring another set of challenges to people who must live with this condition (1). Anti-epileptic drugs (AEDs) have been used over many years as the mainstay to curb focal seizures. The drugs that are often prescribed to assist in regulating the seizure activity include Carbamazepine, Cenobamate, Perampanel and Lamotrigine. Nevertheless, the use of these drugs is not devoid of inconveniences, as they may be related to various side effects, such as a headache, dizziness, insomnia, rash, somnolence, aggressiveness, irritability. A major problem during the epilepsy treatment is the factor of drug resistance and afflicts about 30-40 percent of the patients. Drug resistance is a condition that describes the inability to attain satisfactory fidelity on seizures even with the usage of two or more correctly selected and used AEDs. Drug resistance mechanisms may be multifactorial and involve genetic resistance, target modifications (drug targets) and transporter modifications (drug transporters) (2).

In that regard, Lacosamide can be outlined as the third generation of AED that is specifically used to treat focal seizures or as an add-on medication. The activity of lacosamide can be attributed to the good balance between the efficacy and tolerability of this drug compared to the other drugs. It has the advantage of selectively increasing slow inactivation of sodium channels, a phenomenon that distinguishes it among the classic AEDs, of which carbamazepine acts by blocking them. Such a distinctive intervention produces the least disruption of the normal functioning of the brain; hence Lacosamide is very effective in the decreasing frequency and severity of the seizures. Consequently, it will be a significant addition to the epilepsy treatment sphere, which will create the promise of better

focal seizure management and improvement of the overall quality of life of the affected individuals) (2,3).

Method:

The narrative review is organized in a way that gives a thorough explanation of the procedures used in the assessment of the safety, efficacy, tolerability and clinical utility of Lacosamide in the treatment of epilepsy and more particularly, in the treatment of focal seizures. The plans include study methodology, searching plans, study selection criteria plan, and data extraction plans and methods (4).

Study Design: The objective of the present narrative review is to synthesize and analyze the existing literatures on the utility of Lacosamide in the management of focal seizures and epilepsy. Studies used in the review are peer-reviewed articles, clinical trials, and the evaluation of Lacosamide, both as a mono-drug and as an add-on drug. Through a review of diverse literature, the paper aims to explain the promise of Lacosamide in epilepsy treatment in terms of its safety profile, its effectiveness in comparison with other antiepileptic medication, and the general clinical outcomes. The narrative strategy enables a thorough discussion of the intricacies involved in the use of Lacosamide in several groups of patients, namely infants, adolescents, and adults.

Search Strategy: The list of studies published in the period between 2020 and 2024 was obtained with the help of a systematic search through different databases such as PubMed and Google Scholar. The execution of the search was done in 2025 whereby subject keywords were used including: Lacosamide, Focal seizures, and Anti-epileptic drugs to guarantee the selection of relevant publications. The search strategy has been developed in a manner that results in the inclusion of a wide range of studies comprising clinical trials, observational and real-life studies, thus giving a complete view of the clinical use of Lacosamide.

Criteria for selection of studies: To allow quality and relevance of literature, there were various criteria followed when selecting the studies to be included in this review. That is, 13 studies were completed on the basis of the following criteria: (1) the studies have to be peer-reviewed articles; (2) they should compare the efficacy of Lacosamide as a monotherapy and as an add-on therapy in addressing focal seizures and epilepsy; and (3) they should be a clinical trial delivering information on the safety, efficacy, and tolerability of the drug in diverse groups. These criteria have been constructed in a way which can ensure a high level of evidence included in the review connected with the clinical use of Lacosamide.

Data Extraction: The process of data extraction was carried out in a systematic manner to outline key information in the studies that were selected. The following information was extracted: (1) study type, either peer-reviewed article, a clinical trial, real-life, and observational study; (2) study population, the most important aspects of the study such as the age group, seizure type, and the presence of relevant medical history of the participants; (3) treatment method which includes administration duration and dosage of Lacosamide; (4) comparative treatment, in case it exists, highlighting any comparison made with other antiepileptic drugs; and (5) study results including side effects, seizure frequency reduction,

and general safety This methodical way of data extraction helped it do a thorough analysis of the results of all the studies picked.

Ethical Considerations: Ethical approval was not needed as this review will be founded on a priori studies. The ethical standards of the review are followed in the sense that all the used studies pass a close inspection performed by their authors and consequently, approving the ethical nature of the research under review.

In short, this step-by-step process describes the implementation of a review of literature on the effectiveness of Lacosamide in treating focal seizures and epilepsy. Through narrative review structure, broad search strategy, clear selection standard, and extraction of related information, the present review will help to have a comprehensive overview of how Lacosamide is used clinically and how it is superior theoretically and safe in the context of therapy of epilepsy(2,3,4)

Discussion:

Lacosamide (LCM) is an adjunctive antiseizure medication used along with other seizure medications. It works by enhancing the inactivation of slow voltage gated sodium channels while the traditional Anti-epileptic drugs (AEDs) inactivate fast sodium channels making LCM a major contender in the treatment regimen.

1. Efficacy of Lacosamide as an add on therapy: A systemic review based on randomized control trials on the efficacy of lacosamide as an add on therapy for children with drug resistant focal seizure discusses that LCM reduced the seizure frequency in patients significantly where already administered anti-seizure medications were not working adequately(5).The review also highlighted a dose dependent response to the medication where 400-600 mg/day showed more efficacy than the placebo. The drug response rate was higher in the LCM administered groups with more than 50% reduction in the frequency of seizure (5). Not all drugs are safe for children, but LCM makes it to the list of drugs safe for pediatric population. A study comparing LCM to Oxcarbazepine in children with neurocysticercosis related seizures found that even though both drugs were effective, LCM had fewer side effects than Oxcarbazepine in the pediatric population (6). Seizure control was achieved within the first few weeks of treatment, which improves the life of the patient significantly. Neurocysticercosis is a common cause of seizures in endemic regions, and the finding that LCM had fewer side effects than oxcarbazepine reduces its utility in resource limited settings where monitoring for adverse effects may not be possible. Early seizure control, as observed in this study, is crucial not only for reducing morbidity but also for preventing the development of chronic epilepsy and improving neurodevelopmental outcomes. Another study on pediatric population evaluating the efficacy of LCM as an add on therapy for children and adolescents with refractory focal epilepsy reported that 60% of the patients achieved more than 50% reduction in the frequency of seizure with 20% of them becoming seizure free (4). The study also highlighted improvement in quality of life and cognitive function of the children suggesting that LCM can relatively make the patient's life comfortable. LCM may lower the

psychosocial burden of epilepsy which is a factor that is often overlooked in pharmacologic evaluations of drugs.

Moreover, this study done on children and adolescents complements adult data, reinforcing that LCM can be effective across the lifespan (7). This consistency is particularly valuable, because in epilepsy treatment often begins in childhood and continues into adulthood leading to a better transition.

While both sodium channel blockers (SCBs) and LCM target by inactivating sodium channels, LCM targets by slow inactivation of these channels unlike other traditional SCBs. Why is it clinically significant because LCM allows stabilization of hyperexcitable neuron membranes without causing issues in normal physiological activities which significantly reduces side effects while improving seizure control in some patients. In a study investigating effects of switching immediately from SCBs to LCM in focal epilepsy (8). Patients showed significant tolerability, improved seizure control and lesser side effects after the switch to LCM (8). This shows that LCM may be beneficial for patients who are sensitive to side effects related to traditional SCBs. LCM has excellent pharmacokinetics, linear kinetics, low protein binding and it does not inhibit P450 minimizing drug-drug interaction, making it a more manageable option especially if the patient is taking other drugs (8).

2 Monotherapy by Lacosamide: LCM is primarily approved as an adjunctive therapy, evidence-based research is now showing support to its use as monotherapy. One evidence from a randomized double blind trial comparing LCM to control release carbamazepine in patients with new diagnosis of temporal lobe epilepsy suggests that patients treated with LCM experienced fewer side effects related to cognition and sedation which are common side effects of long term SCBs making it a strong candidate for initial monotherapy (9). This is clinically relevant because cognitive and sedative side effects of older ASMs often lead to poor adherence and reduced quality of life. Another study evaluating LCM as either a first add on therapy or as a conversion monotherapy in focal epilepsy includes patients who needed a change in their treatment regimen due to inefficacy or side effects. Patients who converted to LCM monotherapy showed improvement in control of seizure, enhanced life quality and fewer side effects (10). These studies provide a foundation for the use of LCM as a monotherapy indicating its effectiveness and tolerability. From a clinical standpoint, initiating treatment with LCM may reduce the need for future medication changes, therefore improving long term adherence. Its favorable safety profile also makes it suitable for populations at higher risk of adverse effects, such as the elderly, children or those with cognitive vulnerabilities.

3.Longterm management and safety of the drug: Long term management of seizure control needs considerable efficiency, tolerability and safety to minimize treatment issues. An open label extension trial which observed patients with generalized onset tonic colonic seizures from which many had focal features for 24 months. They found that a high proportion of patients maintained 50% reduction in seizure frequency and the retention rate was high (11). This indicates that patients were able to continue LCM therapy without any side effects or significant issues. This is strong evidence for long-term satisfaction and tolerability of LCM (11).

Furthermore, there is evidence of safety and long-term effects in pediatric population. Researchers conducted a long-term observational study assessing the cognitive outcomes and safety of adjunctive LCM in children with uncontrolled epilepsy (12). Over the course of treatment they observed sustained seizure reduction, improvement in behavioral and executive function and no sign of cognitive decline (12). Which is commendable because long term anti-seizure medications can impact neurodevelopment. This makes LCM a strong candidate for long term use in children and adolescents.

Low incidence of remarkable adverse effects over long term use of this medication is consistent across studies. A review examined serious adverse effects of selected Anti-seizure medications (ASMs) used for focal seizures and LCM was associated with a lower risk of severe complications (13). Adverse effects of LCM consist of mild to moderate intensity of dizziness, fatigue and nausea which tends to diminish over time with dose adjustments long term while other ASMs like carbamazepine and phenytoin are associated with severe long-term toxicities including but not limited to cognitive impairment, hepatic dysfunction and hematologic issues. Evidence presented before (10). Also, support LCM's long-term use. These findings suggest that LCM may reduce the need for frequent medication changes, which can destabilize seizure control and increase healthcare costs. All these studies taken together support the notion that LCM is not only effective in short term but also a strong contender for long term management of focal epilepsy.

4.Safety, tolerability and Adverse effects: Longterm success of an anti-seizure medication also depends on its safety and tolerability. No ASM is without side effects but in long term management LCM has been consistently demonstrated as a favorable safety profile in multiple studies showing adverse effects which are generally mild, manageable and better with dosage adjustments, LCM is also proven to be safe for pediatric patients and with the adult population. When these studies are taken together (5,8,12). We get a consistently positive result reassuring LCM's safety and tolerability. Patients who transitioned to LCM reported lesser side effects compared to previous ASMs showing reduced sedation, dizziness, cognitive issues (10). Which are some of the reasons doctors discontinue old ASMs. LCM does not inhibit P450 enzyme making it suitable for patients on polytherapy or those with other comorbidities that increase the risk of side effects (14).

5.Challenges: Some common challenges in uptake of newer ASMs like LCM includes treatment non compliancy due to clinicians being unfamiliar with the medications, most neurologists still prefer to rely on older reliable drugs, cost consideration is a major factor in LMICs where newer SCBs aren't covered by insurance companies in their plans and patient hesitancy due to that. In poor resource settings where access to newer medication is limited and there are other low-cost options of ASMs, the barrier for Lacosamide to pass for clinical integration seems high. There might also be some problems related to poor adherence to the drug due to lower availability and high costs for LMIC population. LCM provides a good cognitive profile leading to fewer cognitive issues and lower cognitive decline in pediatric population, low drug interaction makes it beneficial for patients on multi drug regimen and high efficacy makes it the leading choice for modern treatment alternative. Educating and updating

health care providers and open communication with patients and their caregivers are needed to identify and address the barriers to treatment decisions and decrease non compliancy with the patients.

When the patient is already taking two or three seizure medications, making changes can get difficult. A lot of the time, it's just easier to add another medication instead of replacing it with the ones they're already on (15). In addition to that, patients often don't want to stop something that seems to already work for them, they're worried that if they do, the seizures might come back. Combination of SCBs may increase the incidence of CNS side effects in the patient therefore when adding LCM other SCBs doses need to be adjusted accordingly. A study discussing the barriers to adoption of new ASMs explores that newer drugs are always restricted for later use, they also emphasized the need for policy interventions to improve access, such as generic availability, insurance coverage, cost reduction and inclusion in essential medicines lists (15).

Conclusion

Lacosamide has been introduced as a rising antiseizure drug, particularly for the treatment and control of focal epilepsy. Research has shown that Lacosamide quite significantly decreased the occurrence of seizures in people with drug-resistant focal epilepsy. The most common side effects reported were headaches and dizziness. A study examining children with solitary neurocysticercosis found that though Lacosamide and Oxacarbazepine controlled seizures, Lacosamide displayed more tolerance as compared to Oxacarbazine. A transition in which the patients were abruptly changed from sodium channel blockers to Lacosamide demonstrated that the latter was tolerated better and was successful in sustaining seizure control. It can be viewed as a safer option when patients experience intolerance to other sodium channel blockers such as carbamazepine or phenytoin. Lacosamide can also be advocated for pediatric safety after being utilised as an extra therapy in children and adolescents with refractory focal epilepsy. When Lacosamide was used as an initial treatment the switch to monotherapy, findings demonstrated substantial seizure management, which enhanced its flexibility in therapeutic plans. Lacosamide came into view as a strong option for adults, especially for those requiring polytherapy or those who were dealing with comorbidities. This was because of its advantageous safety profile, and it also didn't interfere with other drugs. In contrast to conventional drugs like phenytoin or carbamazepine, Lacosamide showed better results by reducing the rate of systemic reactions like liver toxicity or Stevens -Johnson Syndrome. In a study that lasted months when all participants were aware they were receiving Lacosamide, patients with primary generalised tonic-clonic seizures experienced improvement. Even with proof of effectiveness and safety, unfamiliarity to the newer medication, cost worries, and clinical hesitation can hinder adoption. The study thus emphasizes the need for increased awareness and medical guidance can lead to the encouragement of the adoption of modern therapies such as Lacosamide.

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