

Exploring the Efficacy of Novel Antiepileptic Drugs: A Comparative Analysis of Recent Clinical Trials

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Abstract

Epilepsy, a chronic neurological disorder characterized by recurrent seizures, affects approximately 50 million people worldwide. While traditional antiepileptic drugs have made significant strides in managing this condition, there is an ongoing need for novel treatments that offer improved efficacy, fewer side effects and enhanced quality of life for patients. Recent advancements in drug development have led to the emergence of several new AEDs, which have been evaluated in recent clinical trials. Antiepileptic drugs are pivotal in managing epilepsy, a neurological disorder marked by recurrent seizures. Despite the efficacy of established AEDs, the search for new drugs continues due to limitations like insufficient efficacy in refractory cases, adverse side effects and individual variability in drug responses. The advent of novel AEDs reflects advances in our understanding of epilepsy's pathophysiology and pharmacology, aiming to offer improved outcomes.

Keywords: Epilepsy • Chronic neurological disorder • Antiepileptic drugs

Introduction

An analog of levetiracetam, brivaracetam is designed to enhance seizure control with a potentially improved safety profile. Brivaracetam is a derivative of levetiracetam and is thought to act by binding to the synaptic vesicle protein 2A (SV2A), which is involved in neurotransmitter release. Clinical trials have demonstrated that brivaracetam is effective in reducing seizure frequency in patients with drug-resistant partial-onset seizures. Its efficacy is comparable to that of levetiracetam but with potentially fewer side effects. Generally well-tolerated, with common adverse effects including dizziness, somnolence and headache. Compared to levetiracetam, it may have a lower incidence of psychiatric adverse effects. Clinical trials have demonstrated that brivaracetam is effective in reducing seizure frequency in patients with drug-resistant partial-onset seizures. A key trial, the BRIVACT study, reported a significant reduction in seizure frequency compared to placebo. Brivaracetam's efficacy appears comparable to levetiracetam, with the added benefit of a potentially better side effect profile, including fewer psychiatric symptoms.

A selective, non-competitive antagonist of AMPA receptors, perampanel offers a novel mechanism of action. Perampanel is a selective, non-competitive antagonist of AMPA receptors, which are glutamate receptors involved in excitatory neurotransmission. Perampanel has been shown to reduce seizure frequency in patients with focal seizures, both as a monotherapy and adjunctive therapy. It offers a unique approach compared to other AEDs. Common side effects include dizziness, somnolence and irritability [1,2]. There is a notable risk of psychiatric side effects such as aggression and mood changes, necessitating careful patient monitoring. Perampanel has been evaluated in several trials, including the Phase III studies for the adjunctive treatment of focal seizures. Results indicated that perampanel significantly reduced

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Received: 01 June, 2024, Manuscript No. elj-24-143528; Editor Assigned: 03 June, 2024, Pre QC No. P-143528; Reviewed: 17 June, 2024, QC No. Q-143528; Revised: 22 June, 2024, Manuscript No. R-143528; Published: 29 June, 2024, DOI: 10.37421/2472-0895.2024.10.259

seizure frequency in patients who had not achieved adequate seizure control with other AEDs. Its unique AMPA receptor antagonism provides a different approach to seizure management, making it a valuable option for patients with refractory epilepsy.

Literature Review

This AED modulates sodium channels and has shown promise in both partial-onset seizures and generalized seizures. Lacosamide modulates sodium channels and enhances the slow inactivation of these channels, which helps stabilize neuronal membranes and reduce seizure activity. Lacosamide has proven effective in treating partial-onset seizures in both adults and children. It also demonstrates efficacy in generalized seizures. Its effectiveness is similar to that of other AEDs like lamotrigine and levetiracetam. Lacosamide is generally well-tolerated, with side effects such as dizziness, headache and nausea. It has a relatively low incidence of cognitive impairment and is noted for its favorable drug-drug interaction profile. Lacosamide has shown efficacy in treating partial-onset seizures in both adults and children. Trials such as the Study 013 and Study 014 demonstrated that lacosamide significantly reduced seizure frequency and improved seizure control. Its favorable pharmacokinetic profile and lack of significant drug-drug interactions further enhance its utility.

A prodrug of carbamazepine, eslicarbazepine acetate provides a similar mechanism of action with a potentially better side effect profile. Eslicarbazepine acetate is a prodrug that gets converted to eslicarbazepine, which blocks sodium channels similar to carbamazepine but with improved pharmacokinetics. Clinical trials have shown that eslicarbazepine acetate is effective in reducing seizure frequency in patients with partial-onset seizures. It has a similar efficacy profile to carbamazepine but with a potentially lower risk of certain side effects. Common adverse effects include dizziness, somnolence and nausea. Eslicarbazepine acetate may offer a better safety profile compared to carbamazepine, including a lower incidence of hyponatremia [3,4]. In clinical trials like the Study 18 and Study 19, eslicarbazepine acetate demonstrated effectiveness in reducing seizure frequency among patients with partial-onset seizures. Its efficacy is similar to that of carbamazepine, but it may offer a lower incidence of adverse effects, including less frequent hyponatremia.

Discussion

A new addition to the AED armamentarium, cenobamate exhibits dual

mechanisms of action by enhancing GABAergic activity and inhibiting sodium channels. Cenobamate has a dual mechanism of action, enhancing GABAergic neurotransmission and inhibiting sodium channels, which helps stabilize neuronal activity. Cenobamate has been shown to be effective for both focal and generalized seizures. It has demonstrated significant reductions in seizure frequency and has high responder rates in clinical trials. Cenobamate is generally well-tolerated, with common side effects including somnolence, dizziness and headache. It is important to monitor for potential drug interactions due to its impact on various enzyme systems. Cenobamate has been shown to be effective in reducing both focal and generalized seizures. The clinical trials, including the Phase III trials, demonstrated a significant reduction in seizure frequency and a high rate of responder rates. Cenobamate's dual mechanism of action allows it to be effective in various seizure types, making it a versatile option.

The introduction of these novel AEDs represents significant progress in epilepsy management. Each drug offers unique mechanisms and potential advantages, from improved efficacy in refractory cases to better safety profiles and tolerability. As clinical experience with these drugs accumulates, they are expected to play an increasingly vital role in personalized epilepsy treatment, catering to individual patient needs and optimizing seizure control. The emergence of these novel AEDs represents a significant advancement in epilepsy treatment [5,6]. Each drug offers unique benefits, whether through novel mechanisms of action, improved side effect profiles, or enhanced efficacy. However, individualized treatment remains paramount, as the effectiveness and tolerability of AEDs can vary widely among patients.

Conclusion

The landscape of antiepileptic drug therapy continues to evolve with the introduction of novel AEDs. Recent clinical trials have provided valuable insights into the efficacy and safety of these new treatments, highlighting their potential to improve seizure control and quality of life for patients with epilepsy. As research progresses, these advances will hopefully lead to even more effective and personalized approaches to managing this challenging condition. Future research should focus on long-term safety, comparative effectiveness in diverse patient populations and the integration of these new therapies into personalized treatment plans. Additionally, ongoing studies are needed to further understand the mechanisms underlying the efficacy of these drugs and to explore their potential in combination therapies.

Acknowledgement

None.

Conflict of Interest

None.

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How to cite this article: Chandra, Mehar. "Exploring the Efficacy of Novel Antiepileptic Drugs: A Comparative Analysis of Recent Clinical Trials." *Epilepsy J* 10 (2024): 259.