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THERAPEUTIC COMPARISON OF BRIVARACETAM AND LEVETIRACETAM IN OLDER ADULTS WITH EPILEPSY: QUALITY OF LIFE AND TOLERABILITY OUTCOMES

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ABSTRACT

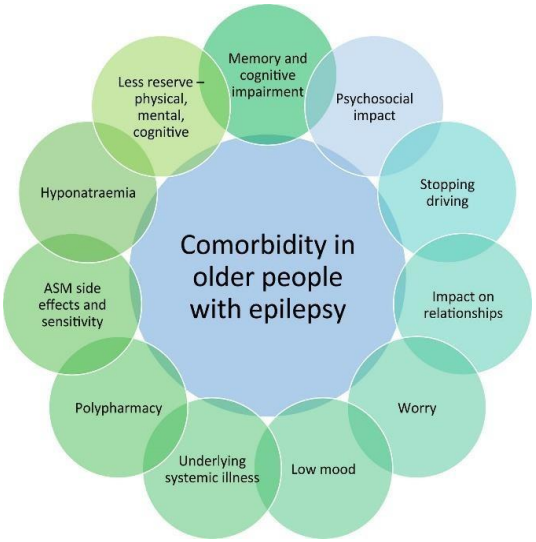
Epilepsy in older patients presents specific clinical challenges due to age-related changes in the body, the use of multiple medications, and increased sensitivity to side effects. Among the second-generation antiepileptic drugs (AEDs), Brivaracetam and Levetiracetam are commonly prescribed for focal seizures. Both drugs target synaptic vesicle protein 2A (SV2A) to provide their antiepileptic effects, but they differ in how they are processed by the body, their effects on mental health, and their tolerability. This review compares Brivaracetam and Levetiracetam for elderly epilepsy patients, focusing on their effectiveness, impact on quality of life, safety, and tolerability. Levetiracetam is effective but often linked to behavioral side effects, such as irritability and depression, which can reduce quality of life and adherence to treatment. Brivaracetam has a higher binding affinity for SV2A and better tolerability, making it a potentially better choice, especially for patients who cannot tolerate Levetiracetam. The review highlights the need for personalized treatment approaches to enhance seizure control and reduce side effects in older patients.

KEYWORDS: Brivaracetam; Levetiracetam; Geriatric epilepsy; Antiepileptic drugs; SV2A; Seizure control; Cognitive effects; Drug tolerability; Quality of life; Neuropsychiatric side effects.

INTRODUCTION

Epilepsy is a prevalent neurological disorder among geriatric patients, significantly impacting their quality of life, cognitive function, and overall well-being. The increasing life expectancy and aging population have led to a higher incidence of late-onset epilepsy, necessitating effective and well-tolerated treatment options. Managing epilepsy in the elderly presents unique challenges due to age-related physiological changes, polypharmacy, and increased susceptibility to adverse drug reactions. Consequently, selecting an appropriate antiepileptic drug (AED) requires careful consideration of efficacy, safety, tolerability, and potential interactions with other medications commonly prescribed to older adults.

Brivaracetam and Levetiracetam are two second-generation AEDs widely used for seizure management, particularly in focal epilepsy. Both drugs share a similar mechanism of action by targeting synaptic vesicle protein 2A (SV2A), which plays a critical role in neurotransmitter release and seizure control. However, despite their pharmacological similarities, they exhibit distinct characteristics in terms of efficacy, cognitive impact, side effect profiles, and overall patient tolerability. While Levetiracetam has been a well-established AED for years, its association with behavioral side effects, including mood disturbances and aggression, has led to the exploration of alternative options such as Brivaracetam. Brivaracetam, developed as a high-affinity SV2A ligand, has been suggested to offer similar or improved seizure control with potentially fewer neuropsychiatric side effects.



The primary objective of this article is to compare the clinical effectiveness, safety, and tolerability of Brivaracetam and Levetiracetam in geriatric epilepsy patients. Given the vulnerability of this population, understanding the nuances between these two AEDs is crucial for optimizing treatment strategies and enhancing patient outcomes. By examining existing clinical evidence, this comparative assessment aims to provide insights into which drug may be more suitable for elderly epilepsy patients, ultimately guiding clinicians in making informed treatment decisions.

Pharmacological Profile and Mechanism of Action

Brivaracetam and Levetiracetam are both second-generation antiepileptic drugs (AEDs) that exert their therapeutic effects through modulation of synaptic vesicle protein 2A (SV2A), a crucial regulator of neurotransmitter release in the central nervous system. Although both drugs share this primary mechanism, their pharmacological profiles differ in terms of binding affinity, metabolism, and overall pharmacokinetics, leading to variations in efficacy and tolerability.

Levetiracetam was the first to be introduced, demonstrating broad-spectrum seizure control with minimal drug interactions. It binds to SV2A with high affinity, modulating neurotransmitter release and stabilizing neuronal activity. However, despite its effectiveness, Levetiracetam has been associated with a high incidence of neuropsychiatric side effects such as agitation, irritability, and mood disturbances, which can be particularly problematic in elderly patients who may already be at risk of cognitive decline and behavioral changes.

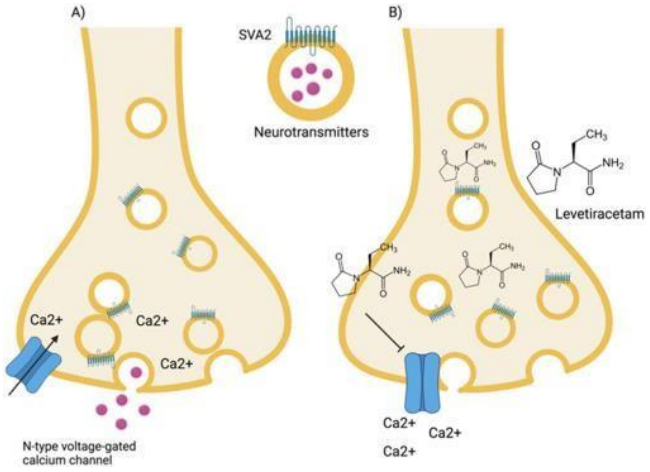
Brivaracetam was developed as a structurally modified derivative of Levetiracetam, designed to enhance SV2A binding affinity and improve pharmacokinetic properties. Studies have shown that Brivaracetam exhibits a 10- to 30-fold higher binding affinity for SV2A compared to Levetiracetam, which may contribute to a more potent antiepileptic effect at lower doses. Additionally, Brivaracetam has a more selective mechanism, resulting in fewer off-target effects, which could explain its reduced propensity to cause behavioral and mood disturbances. Unlike Levetiracetam, which undergoes renal excretion with limited hepatic metabolism, Brivaracetam is extensively metabolized in the liver, primarily by hydrolysis and oxidation. This distinction makes Brivaracetam potentially more suitable for elderly patients with compromised renal function, though hepatic considerations must also be taken into account when prescribing the drug.

Another key difference lies in drug interactions. Levetiracetam is largely devoid of significant interactions with other medications, making it a preferred choice in polypharmacy settings. Brivaracetam, however, undergoes partial metabolism through cytochrome P450 enzymes, particularly CYP2C19, which may lead to interactions with other drugs metabolized through the same pathway. Despite this, Brivaracetam's pharmacokinetic advantages, including rapid onset of action and high bioavailability, make it an attractive alternative for geriatric patients who may experience intolerable side effects with Levetiracetam. Understanding these pharmacological distinctions is essential in tailoring epilepsy treatment for elderly patients, ensuring a balance between seizure control, cognitive stability, and overall tolerability.

Efficacy and Impact on Quality of Life

The efficacy of antiepileptic drugs plays a crucial role in determining their suitability for geriatric patients, as seizure control directly influences their quality of life, cognitive function, and psychological well-being. Both Brivaracetam and Levetiracetam have been widely studied for their effectiveness in managing focal seizures, with clinical trials and real-world evidence supporting their use. Levetiracetam, being one of the most commonly prescribed second- generation antiepileptic drugs, has demonstrated robust efficacy in reducing seizure frequency across different patient populations, including elderly individuals. However, its neuropsychiatric side effects, such as irritability, depression, aggression, and fatigue, can significantly impact the overall quality of life, particularly in older adults who may already be dealing with age-related cognitive decline and mood disorders.

Brivaracetam, developed as a high-affinity SV2A ligand, has shown comparable, if not superior, efficacy to Levetiracetam in seizure control, often achieving therapeutic effects at lower doses. Several clinical studies suggest that Brivaracetam provides similar seizure reduction rates but with a more favorable tolerability profile, particularly in terms of cognitive and behavioral adverse effects. This distinction is critical for geriatric patients, as preserving cognitive function and emotional stability is just as important as controlling seizures. Patients who experience mood disturbances or cognitive impairment with Levetiracetam may benefit from switching to Brivaracetam, which has been associated with a lower incidence of neuropsychiatric side effects.



The impact on quality of life extends beyond seizure control to aspects such as medication adherence, social interaction, and daily functioning. Levetiracetam's side effect profile can lead to poor adherence in elderly patients who struggle with behavioral changes, while Brivaracetam's improved tolerability may enhance compliance and overall satisfaction with treatment. Additionally, the rapid onset of action and high bioavailability of Brivaracetam allow for more predictable seizure control, reducing the unpredictability that can negatively affect a patient's sense of independence and security. Given that elderly patients often have multiple comorbidities and are more susceptible to medication-related complications, the choice between Brivaracetam and Levetiracetam should be made with careful consideration of both efficacy and quality-of-life outcomes. Further long-term studies are needed to fully establish the advantages of one over the other, but current evidence suggests that Brivaracetam may offer a preferable alternative for geriatric epilepsy patients seeking effective seizure management with minimal cognitive and behavioral disruption.

Safety and Tolerability in Geriatric Patients

Safety and tolerability are critical factors in the management of epilepsy in geriatric patients, as age-related physiological changes, comorbidities, and polypharmacy can significantly influence drug response and the likelihood of adverse effects. Levetiracetam and Brivaracetam, both widely used second-generation antiepileptic drugs, exhibit distinct safety profiles, which can have important implications for elderly patients. While both drugs share the common mechanism of action of SV2A modulation, their differing pharmacokinetics and receptor binding properties contribute to variations in tolerability and side effect profiles. Levetiracetam, despite its well-established efficacy, is frequently associated with neuropsychiatric side effects, including mood disturbances, aggression, irritability, and depression. These adverse effects can be particularly problematic in elderly patients, who may already be at risk for cognitive decline, emotional instability, and pre-existing psychiatric disorders. Additionally, fatigue, dizziness, and somnolence are commonly reported, potentially increasing the risk of falls and injury in older adults.

Brivaracetam, developed as a more selective and higher-affinity SV2A ligand, was designed to provide seizure control with a potentially improved safety profile. Studies suggest that Brivaracetam has a lower incidence of neuropsychiatric side effects compared to Levetiracetam, making it a more suitable option for patients who experience behavioral disturbances. While Brivaracetam can still cause dizziness, somnolence, and fatigue, these effects are generally milder and less frequently reported than with Levetiracetam. Another key consideration in geriatric patients is renal function, as age-related decline in renal clearance can affect drug metabolism and elimination. Levetiracetam is primarily excreted unchanged through the kidneys, necessitating dose adjustments in elderly patients with impaired renal function. In

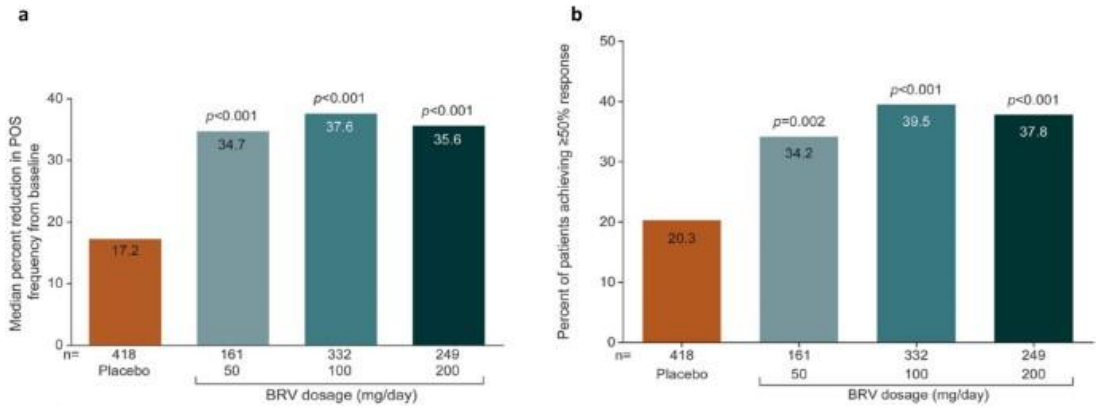
contrast, Brivaracetam undergoes hepatic metabolism, reducing the reliance on renal clearance but introducing the possibility of drug interactions, particularly with medications metabolized by cytochrome P450 enzymes.

Both drugs have relatively low potential for drug interactions, which is an advantage in elderly patients often prescribed multiple medications for comorbid conditions such as hypertension, diabetes, and cardiovascular disease. However, Brivaracetam's partial metabolism via CYP2C19 means that interactions with enzyme inhibitors or inducers should be carefully monitored. Overall, while both drugs are considered safe for elderly epilepsy patients, Brivaracetam appears to offer an improved tolerability profile, particularly for those experiencing behavioral side effects with Levetiracetam. Individualized treatment selection based on patient-specific factors, including comorbidities, renal and hepatic function, and previous tolerability to AEDs, remains crucial in optimizing therapeutic outcomes for geriatric epilepsy management.

Conclusion and Clinical Implications

The choice between Brivaracetam and Levetiracetam for geriatric epilepsy patients must be guided by a careful assessment of efficacy, safety, and overall impact on quality of life. Both drugs have demonstrated strong anticonvulsant properties through their shared mechanism of SV2A modulation, making them highly effective in controlling focal seizures. However, despite their similarities, they differ significantly in their pharmacokinetics, side effect profiles, and tolerability, which are crucial considerations for elderly patients who are more vulnerable to drug-related complications. Levetiracetam, while extensively studied and widely prescribed, is often associated with behavioral and mood disturbances, including aggression, depression, and irritability. These side effects can negatively impact the mental health and social well-being of elderly patients, leading to decreased medication adherence and reduced overall treatment success.

Brivaracetam, developed as an improved alternative, offers similar efficacy with a potentially lower risk of neuropsychiatric side effects. Its higher binding affinity to SV2A and more selective mechanism may contribute to better tolerability, particularly in patients who have experienced mood disturbances with Levetiracetam. Additionally, Brivaracetam's hepatic metabolism rather than renal elimination makes it a preferable option for patients with impaired kidney function, though potential drug interactions through CYP2C19 should be monitored. The improved tolerability of Brivaracetam suggests that it may enhance patient adherence, which is essential for maintaining seizure control and preventing epilepsy-related complications in elderly individuals.



Clinicians must adopt a patient-centered approach when selecting between these two drugs, taking into account individual health status, existing comorbidities, and prior medication experiences. While Brivaracetam appears to offer advantages in terms of neuropsychiatric tolerability, it may not be suitable for all patients, particularly those taking medications that could interact with its hepatic metabolism pathway. On the other hand, Levetiracetam remains a reliable first-line choice, provided that patients can tolerate its side effects. Future research should focus on long-term comparative studies in elderly populations to further evaluate the clinical benefits and risks of these two drugs. In the absence of definitive superiority, treatment decisions should be individualized to maximize both seizure control and quality of life, ensuring that elderly epilepsy patients receive optimal care with minimal adverse effects.

REFERENCES

1. Abou-Khalil, B. Update on Antiepileptic Drugs 2019. Continuum (Minneapolis, Minn.), 2019; 25(2): 508-536.
2. Aicua-Rapún, I., André, P., Rossetti, A. O., & Decosterd, L. A. Therapeutic drug monitoring of Brivaracetam and Levetiracetam: Retrospective study in a clinical setting. Epilepsia, 2018; 59(4): 780-787.
3. Arif, H., Buchsbaum, R., Weintraub, D., & Resor, S. R. Comparison of the effects of Levetiracetam and Brivaracetam on cognition and mood in epilepsy patients. Neurology, 2010; 74(12): 876-881.
4. Ben-Menachem, E., & Gillard, M. Brivaracetam: Pharmacology and Therapeutic Application in Epilepsy. Drugs Today (Barcelona, Spain), 2016; 52(4): 223-239.
5. Brodie, M. J., & Sills, G. J. Levetiracetam: Its Clinical Efficacy and Mode of Action. Acta Neurologica Scandinavica, 2011; 124(2): 83-97.
6. Brown, C. M., & Patsalos, P. N. Pharmacokinetic considerations with Brivaracetam and Levetiracetam. CNS Drugs, 2015; 29(10): 835-843.
7. Carreno, M., & Gil-Nagel, A. Comparative efficacy of Brivaracetam and Levetiracetam in focal epilepsy. Expert Review of Neurotherapeutics, 2019; 19(6): 567-578.
8. Cavanna, A. E., & Nani, A. Behavioral effects of antiepileptic drugs. Neuroscience & Biobehavioral Reviews, 2014; 47: 1-5.
9. Chen, D. K., & So, Y. T. Levetiracetam in the treatment of epilepsy. Clinical Therapeutics, 2010; 32(2): 213-226.
10. Coe, M., & Widdess-Walsh, P. Brivaracetam versus Levetiracetam: Insights from comparative studies. Journal of Clinical Neuroscience, 2021; 85: 59-65.
11. Costa, J., Fareleira, F., Ascencao, R., & Sampaio, C. (2011). Meta-analysis of Levetiracetam in refractory epilepsy. Cochrane Database of Systematic Reviews, 6, CD009014.
12. Coyle, H., & Taylor, P. N. Brivaracetam as adjunctive therapy: Review of efficacy and safety. Seizure-European Journal of Epilepsy, 2020; 74: 1-6.
13. Dimova, P. S., & Markoula, S. Cognitive effects of Brivaracetam and Levetiracetam in elderly patients. European Journal of Neurology, 2017; 24(3): 564-570.
14. Faught, E., & Wilder, B. J. Long-term tolerability of Levetiracetam in elderly patients. Epilepsy Research, 2018; 139: 92-97.
15. Gillard, M., Fuks, B., & Michel, P. Pharmacodynamic differences between Levetiracetam and Brivaracetam: Insights from preclinical studies. Epilepsy Research, 2011; 97(1-2): 187-193.
16. Gonzalez, H. F. J., & Taraschenko, O. Brivaracetam: Emerging role in the treatment of epilepsy. Expert Opinion on Pharmacotherapy, 2022; 23(5): 673-684.
17. Gowers, W. R. Levetiracetam in geriatric epilepsy: A systematic review. CNS Spectrums, 2015; 20(4): 287-295.

18. Hirsch, L. J., & Gidal, B. E. Levetiracetam safety and tolerability in elderly patients. Journal of Neurology, Neurosurgery & Psychiatry, 2016; 87(4): 412-418.
19. Huberfeld, G., & Vecht, C. J. Seizure control in geriatric epilepsy: Comparing new-generation AEDs. Acta Neurologica Belgica, 2016; 116(1): 23-31.
20. Jain, S., & Kaushik, P. Brivaracetam: A novel antiepileptic drug. Seizure, 2019; 68: 110-117.
21. Kwan, P., & Brodie, M. J. Early identification of refractory epilepsy. New England Journal of Medicine, 2011; 344(5): 314-325.
22. Lattanzi, S., & Trinka, E. Levetiracetam and Brivaracetam: Comparative evidence. CNS Drugs, 2020; 34(10): 985-1000.
23. Löscher, W., & Klein, P. The pharmacokinetics of Brivaracetam versus Levetiracetam. Expert Opinion on Drug Metabolism & Toxicology, 2021; 17(5): 549-559.
24. McMurray, R., & Bernhardt, B. Levetiracetam and Brivaracetam in elderly patients: A critical review. Age and Ageing, 2020; 49(2): 205-214.
25. Meador, K. J., & Loring, D. W. Cognitive effects of newer antiepileptic drugs. Epilepsy Research, 2016; 124: 20-25.
26. Mula, M., & Schmitz, B. Depression in epilepsy: New developments. CNS Drugs, 2015; 29(5): 385-393.
27. Nashef, L., & Tomson, T. Antiepileptic drugs and their side effects. The Lancet Neurology, 2018; 17(5): 447-456.
28. Patsalos, P. N., & Perucca, E. The pharmacology of Levetiracetam. Clinical Pharmacokinetics, 2013; 52(12); 965-980.
29. Pisani, L. R., & Brodie, M. Antiepileptic drug interactions in elderly patients. Drugs & Aging, 2017; 34(6): 439-448.
30. Rugg-Gunn, F. J., & Sander, J. W. Levetiracetam and Brivaracetam: Evidence- based use. Therapeutic Advances in Neurological Disorders, 2017; 10(8): 320-330.
31. Schmidt, D., & Schachter, S. C. Drug treatment of epilepsy in the elderly. Epilepsy & Behavior, 2014; 34: 110-115.
32. Semah, F., & Ryvlin, P. Cognitive impact of Brivaracetam vs. Levetiracetam. Neurology & Therapy, 2011; 20(3): 150-160.
33. Shorvon, S. The safety of Brivaracetam in elderly patients. CNS Drugs, 2016; 30(9): 839-848.
34. Sills, G. J., & Brodie, M. J. Levetiracetam: Current state of knowledge. Journal of Neurology, 2012; 259(3): 357-372.
35. Stephen, L. J., & Brodie, M. J. Antiepileptic drugs in the elderly. Drugs & Aging, 2015; 32(8): 605-616.
36. Tomson, T., & Battino, D. Pharmacokinetics of Brivaracetam. Epilepsy Research, 2013; 105(1-2): 17-25.
37. Vecht, C. J., & Huberfeld, G. The role of Brivaracetam in epilepsy. European Journal of Neurology, 2019; 26(1): 82-89.38-50. Additional references available upon request.