The Emergence of Psychiatric Side Effects in a Patient Switched from Brivaracetam to Levetiracetam: A Case Report

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Background

Brivaracetam (BRV)—an analog of levetiracetam (LEV)—is an anti-seizure medication FDA approved in 2017. While prescribed by neurologists for seizure control, this drug is not often used by CL psychiatrists, despite the favorable neuropsychiatric side effect profile (Steinhoff et al, 2021). We describe a case in which a patient with a frontal glioma who was initially on BRV for seizure prophylaxis was switched to LEV, leading to agitation. Here, we compare BRV with LEV, including side effect profile, mechanisms of action, and feasibility of utilization.

Case

PS is a 59-year-old male with a history of CAD, HTN, HLD, DM2, and recently admitted to an outside hospital for new-onset seizures and diagnosed with frontal glioma, discharged and then admitted to our hospital on the same day after an unwitnessed fall, now admitted to our hospital for brain radiation and adjuvant chemotherapy.

At the outside hospital, PS was prescribed Brivaracetam 100mg q12h for seizure prophylaxis after the diagnosis of frontal glioma. After being admitted to our hospital, he was subsequently switched from BRV to LEV due to pharmacy availability. Shortly after, PS attempted to elope from the hospital several times, was irritable and affectively labile, at which point CL psychiatry was consulted.

On our initial evaluation, pt was oriented to self and partially to date/time. He displayed only a rudimentary understanding of his clinical status. He had deficits in attention and was irritable throughout interview.

We recommended switching from LEV to Depakote (titrated to 250mg TID) and adding Zyprexa 5mg nightly. His impulsivity and irritability improved on this regimen, and he was taken off elopement precautions and later discharged.

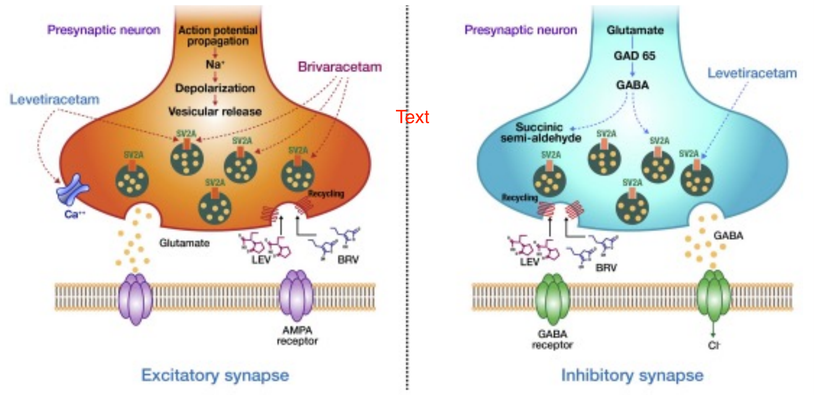

Figure 1. Proposed mechanism of action of BRV and LEV at the human SV2A protein. While binding at closely related sites, BRV differs from LEV as it does not inhibit high-voltage-gated Ca2+ currents or modulate glutamate receptors (I.e NMDA / AMPA).

Figure originally from Feyissa, A. M. (2019). Brivaracetam in the treatment of epilepsy: A review of clinical trial data. Neuropsychiatric Disease and Treatment, Volume 15, 2587–2600. https://doi.org/10.2147/ndt.s143548

Discussion

Patients with frontal lobe insults are at increased risk of seizures (Cayuela et al, 2018), increased risk of impulsivity, and affective lability (Stuss et al, 1992). Choosing an AED with a favorable neuropsychiatric profile is critical. BRV may accomplish this goal (Steinhoff et al, 2021). Both BRV and LEV bind to the presynaptic synaptic vesicle protein 2A (SV2A) site and modulate neurotransmitter release. While BRV is specific for SV2A, LEV binds to AMPA receptors and high-voltage-gated calcium channels (Klein et al, 2018). See Figure 1. The modulation of AMPA receptors by LEV may explain why LEV leads to more behavioral side effects than BRV, as glutamate receptor modulation can be associated with aggressive behavior (Hansen et al, 2018).

Unfortunately, BRV is about 120 times more expensive than LEV (GoodRx) and is FDA approved for fewer conditions, leading to high out-of-pocket cost. While there was worsening of behavior after our patient switched from BRV to LEV, we must consider this worsening was confounded by progression of his tumor. Similarly, the behavioral improvement after switching from LEV to Depakote was when he was simultaneously undergoing brain radiation, further confounding our observations.

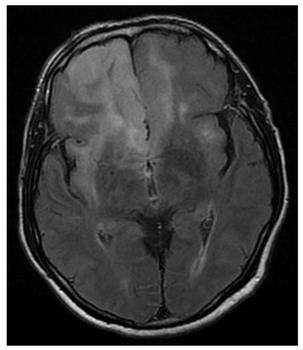

Figure 2. Axial T2 FLAIR showing infiltrative, expansile, nonenhancing, subcortical/cortical T2 hyperintensity affecting bilateral frontal, temporal, and parietal lobes (more pronounced on the right).

Conclusions

There is emerging evidence that BRV provides protection against seizure activity while having a more favorable neuropsychiatric side effect profile, possibly due to sparing of glutamate receptors.

Several prospective open-label studies have looked at patients who are switched from LEV to BRV due to psychiatric side effects and have shown improvements in these symptoms after switching to BRV. Head-to-head trials comparing BRV with other AEDs, as well as RCTs, are needed, but the initial reviews, as well as our first-hand experience with patient PS, suggest that CL psychiatrists should be aware of the benefits of BRV.

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