

How Much Psychiatrists Hate Levetiracetam [Keppra], Is it all bad? A case review of a bipolar disorder patient

Introduction:

Levetiracetam [Keppra] is a unique anticonvulsant approved by the Food and Drug Administration [FDA] for the treatment of seizures as adjunct and used off label for chronic pain and mania [4]. It works by opposing the negative regulators of GABA and glycine gated currents. Also affects synaptic vesicle exocytosis by binding to the Synaptic Vesicle Protein [SV2A] and a partial inhibitor of neuronal N-type calcium current. It is also well known for its anticonvulsant, antiexcitatory and neuroprotective properties which apparently contributes to its efficacy in bipolar [11]. Side effects include anger, agitation, suicidality, apathy, depression, hostility, irritability, anxiety, hostility, aggression, paradoxical mania and psychosis that have made its use in psychiatry limited [1,12]. Neuropsychiatry side effects is reportedly more common in patients with a history of psychiatry disorder [2]. To the best of our knowledge only very few reports are out there on the use of Keppra in the treatment of bipolar disorder. We present a patient with bipolar who responded favorably to Keppra and no other conventional mood stabilizers.

Case presentation:

A.A. is a 60-year-old Caucasian male been treated for Post-Traumatic Stress Disorder[PTSD] from military experience, Opiate Use Disorder and Bipolar II disorder. He reported core symptoms meeting the DSM diagnostic criteria for all three diagnoses. PTSD and Opiate Use Disorder are well controlled on Venlafaxine and Buprenorphine/Naloxone [Suboxone] respectively. He reported having tried several psychotropic medications for mood stability in the past including but not limited to Lithium, Zyprexa, Risperidone, Sertraline, Paroxetine, Lurasidone, Fluoxetine, Citalopram, Escitalopram, Aripiprazole, Valproate, Carbamazepine, Oxcarbazepine, Lamotrigine either as monotherapy or in various combinations. He was commenced on 500 mg of Keppra at bedtime by our team and continued on his previous medications, Venlafaxine at 150 mg daily/Suboxone 8 mg daily. He was followed up for over 6 years and continued to do well on this regimen. He reported "mild" symptoms of hypomania only once throughout the period of observation in which he endorsed discontinuing his medication on his own for about 3-4 months prior to the reoccurring symptoms. He is currently doing well on this regimen and declined any attempt at trial of discontinuation of Keppra. All irrelevant findings are left out in this report [physical and laboratory] and substance induced mood disorder was ruled out.

Discussion:

It is not understood how Keppra stabilizes mood, but its profile appears to combine that of multiple antiepileptic medications [though chemically unrelated], including a unique structure and binding site [SV2A] which might explain its efficacy in bipolar patients poorly responsive to other antiepileptic mood stabilizers [2,3,5]. It is also reported to be neuroprotective with anticonvulsant and inhibitory qualities that is associated with some novel mechanisms of action that ranges from its reductive effect on calcium currents to its ability to reverse the negative allosteric cadence by zinc and beta carbolines on GABA and glycine receptors, these could explain its effect in bipolar illness [3]. There have been reports of adequate mood stabilization in elderly bipolar patient on Keppra monotherapy [2,10]. Its use has been reported in manic and depressed phase of bipolar disorder, some efficacy has also been reported in rapid cyclers, both in the elderly and adolescents [3,12]. Appears to show some efficacy in the treatment of bipolar including bipolar depression as a result of its effect in areas of the brain that is responsible for described pathophysiology of bipolar especially the hippocampus and amygdala [6]. The relevance of this has however been questioned [6,9] as its efficacy in bipolar depression as reported in a double blind, placebo controlled clinical trial and appears to be the reason for lack of interest in trials and full evaluation [7,8]. Its effect doesn't appear to have anything to do with GABA like it is widely believed [11]. It is no news that bipolar patients, especially when there is a comorbid substance use issues or mixed and rapid cycling are very difficult to treat even with polypharmacy, hence the need to consider off label medications. Our patient had tried several psychotropic without significant response until he was stated on Keppra. Our patient has had at least 12 psychotropic medications either as monotherapy or in combination but showed a significant reduction of symptoms within a couple of months and relapse every time he is not compliant. Symptoms again abates when he resumes the medication. Previous reported cases were characterized by a shorter patient follow up period and in another, Keppra was used as an adjunct except one case, for this reasons, our case report has a unique status. Mood stabilizing and antiepileptic properties of mood stabilizers and antiepileptic medications

like Keppra is also linked with its effect on calcium signaling leading to normalization of elevated intracellular calcium, this theory is related to the finding of hyperactive intracellular calcium ion [N type calcium channels] signaling in the peripheral cells of bipolar patients [13].

The use of Keppra either as monotherapy or as adjunct treatment in bipolar patients is rarely reported and there are mixed reports of its efficacy. It has however been used successfully in both case, how it works continues to be looked into. There is a need for further research into its efficacy especially as it has a novel mechanism of action.

Conflict of interest: None to report

Sponsorship: None

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