

## Endoxifen: A new hope for Bipolar Disorder

Muneeba Amin, Alviya Shafique, Muhammad Yusuf Hafiz

*Madam*, Bipolar Disorder (BD), originally called manic depressive illness, is one of the most challenging and disabling psychiatric disorders to manage with an estimated life time prevalence of 1.02%.<sup>1</sup> One of the challenges is limitations in our understanding of the pathophysiology of the disorder which ultimately will lead to better treatment options. Despite available treatment options, literature reports breakthrough episodes in treated groups ranging from 40% to 60%.<sup>2</sup> This makes it even more crucial to gain more insight into the pathophysiology. Advances in molecular neuropsychiatry have reported that bipolar disorder is associated with overactive protein C kinase intracellular signalling.<sup>3</sup> Reportedly, lithium and valproate are protein C kinase inhibitors. Research has shown promise in effectiveness of Endoxifen. A multicentre, double-blind, active-controlled study was conducted using Endoxifen compared with Divalproex, the current standard treatment, in patients with BD. This new protein kinase C inhibitor has shown effectiveness in the treatment of acute mania and mixed mania.<sup>4</sup> One of the many advantages include similar efficacy as Divalproax without inducing thrombocytopenia and reportedly no need for drug monitoring due to wide therapeutic index is one of the reasons which results in decreased compliance. Additionally, it crosses the blood-brain barrier independent of CYP-2D6 metabolism.<sup>4</sup> With regards to disadvantages, cost effectiveness is a major hurdle. These new insights into

Department of Psychiatry, Aga Khan University, Karachi, Pakistan.

**Correspondence:** Alviya Shafique. e-mail: alviashafique115@yahoo.com

pathophysiology and treatment options are crucial as till date BD remains one the most disabling mental health disorder affecting every aspect of life; individual, social, economic, global. BD is the fifth leading cause among psychiatric disorders of lost years of work.<sup>5</sup> It is therefore imperative that a new treatment is established and further research is warranted in regards to Endoxifen for better understanding to develop safe treatment, not only for management but possible cure.

**Disclaimer:** None.

**Conflict of Interest:** None.

**Funding Sources:** None.

**DOI:** <https://doi.org/10.47391/JPMA.013426>

### References

1. Moreira AL, Van Meter A, Genzlinger J, Youngstrom EA. Review and meta-analysis of epidemiologic studies of adult bipolar disorder. *J Clin Psychiatry*. 2017; 78:1259-69.
2. Goodwin FK, Jamison KR. *Manic-depressive illness: bipolar disorders and recurrent depression*. Oxford, UK: 2007.
3. Saxena A, Scaini G, Bavaresco DV, Leite C, Valvassoria SS, Carvalho AF, et al. Role of protein kinase C in bipolar disorder: a review of the current literature. *Mol Neuropsychiatry*. 2017; 3:108-24.
4. Ahmad A, Sheikh S, Khan MA, Chaturvedi A, Patel P, Patel R, et al. Endoxifen: A New, Protein Kinase C inhibitor to treat acute and mixed mania associated with bipolar I disorder. *Bipolar Disord*. 2020.
5. Ferrari AJ, Stockings E, Khoo JP, Erskine HE, Degenhardt L, Vos T, et al. The prevalence and burden of bipolar disorder: findings from the Global Burden of Disease Study 2013. *Bipolar Disord*. 2016; 18:440-50.