

Endoxifen- A promising molecule for bipolar disorder

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Bipolar I Disorder is a chronic, disabling, and serious mental illness characterized by extreme mood cycles. Protein kinase C (PKC) intracellular signaling is involved in the pathophysiology of Bipolar disorder. PKC plays a crucial role in the regulation of neuronal excitability, neurotransmitter release, regulation of synaptic plasticity and various forms of learning and memory. Tamoxifen is a Protein Kinase C (PKC) inhibitor and it has shown some benefit in Bipolar Disorder with milder adverse events. Endoxifen (4-hydroxy-N-desmethyl Tamoxifen) is a secondary metabolite of Tamoxifen. Compared to Tamoxifen, It has four-fold PKC inhibitory activity and is also independent of CYP2D6 genetic polymorphism. I participated in a Phase II study demonstrating efficacy and safety of Endoxifen in BPD I patients. In this 3-arm study, Endoxifen 8 mg dose showed improvement in total YMRS score compared to baseline and were similar to Divalproex. Endoxifen arm had lower incidence of adverse events versus Divalproex. Here I am presenting a Phase III RCT in a larger patient population evaluating efficacy and safety of 8 mg Endoxifen against active comparator Divalproex Sodium. The primary endpoint of our study was the mean change in total YMRS score at day 21. Results showed Endoxifen (n=116) significantly ($p < 0.0001$) reduced total YMRS score. Early remission of the disease was observed. None of the patients required rescue medication. There was no drug associated withdrawals. Changes in Clinical Global Impressions-Bipolar Disorder and Clinical Global Impression-Severity of Illness scores showed that treatment with Endoxifen were well-tolerated.

Biography

Timirkumar Shah has completed his MD in Psychiatry from Government Medical College Surat, India. He served for 2 decades as Chief Psychiatrist at Kasturba Sevashram- renowned inpatient Psychiatry Hospital established by Mahatma Gandhi. He is the founding director at Divyam Institute of Psychiatry- a premier tertiary level center for comprehensive Psychiatry care. Since 2010, he is Principal Investigator at Divyam Hospital, a leading clinical research site. He has accomplished more than 30 clinical trials as PI. He also serves as the Chairperson at South Gujarat Independent Ethics Committee since 2013.

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