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REAL-WORLD EVIDENCE FOR ENDOXIFEN IN THE TREATMENT OF PATIENTS WITH BIPOLAR I DISORDER: A 12-WEEK OPEN-LABEL STUDY

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ABSTRACT

Objective: To understand the profile of bipolar I disorder (BD-I) patients prescribed Endoxifen in real world and evaluate effectiveness and tolerability of Endoxifen in Indian setting. **Method:** This was a real-world, retrospective, observational study carried out by 'Study Investigator group'. Analysis of data was done for patients having at least 3 months follow up details with Endoxifen therapy. No additional evaluation or investigation was performed for this study. **Results:** Data of 258 BD-I patients (166 males/92 females) with mean age of 33.9±11.68 years from 25 centres across India were evaluated in this study. Psychotic symptoms and suicidal tendency were present in 43.3% and 17.1% patients respectively at baseline. Endoxifen was prescribed as an acute treatment in 80% patients and for maintenance in 20% patients. Endoxifen monotherapy was used in 35% patients while commonly co-prescribed medications included valproate, olanzapine, risperidone, lithium and quetiapine. 95% patients received dose of 8mg/day of endoxifen. With 3 months of treatment, endoxifen led to significant improvement ($p<0.0001$) in various clinical scores viz. YMRS (34.04±10.5 to 10.07±7.37), MADRS (24.13±15.63 to 8.61±8.38) and BPRS (53.14±18.54 to 25.98±10.72). Clinical response and remission were achieved by 77.5% and 68.6% patients respectively. Endoxifen was well tolerated with most adverse events being mild to moderate in severity. Most patients reported satisfactory to excellent compliance with Endoxifen. **Conclusion:** Endoxifen is found to be effective and safe in real world clinical practice when prescribed in manic or mixed episodes of BD-I patients.

KEYWORDS: real-world, endoxifen, mania, bipolar I disorder.

INTRODUCTION

Bipolar disorder (BD) is a chronic mood disorder characterized by episodes of mania, hypomania, and alternating episodes of depression. Earlier, it was also known as manic depressive illness. It is a lifetime episodic illness with a variable course which often results in cognitive and functional impairment. It also impairs the quality of life of the patient. It is further classified as bipolar disorder I (BD-I) and bipolar disorder II based on extent and severity of mood elevation with BD-I being more severe and tortuous.[1]

About forty-six million people have been reported across the world to have BD. According to Global Burden of Disease study, the worldwide prevalence of BD varies from 0.3 to 1.2 % from country to country.[2] Prevalence of BD-I is similar in both men and women with the male-to-female ratio about 0.8 (0.5-1.1).[3,4] In India, limited data is available on the epidemiology of BD. However, the national health survey of India conducted in the year 2015-16 showed prevalence of BD to be 0.3%.[2]

Currently, mood stabilisers and second-generation antipsychotics are the mainstay of the treatment for patients suffering from BD-I.[5-7] While many people with BD-1 find relief from these medications, significant problems with tolerability and efficacy still exist. For many years, there has been no new molecule approved for the treatment of mania.

In the pathogenesis of BD, protein kinase C (PKC) plays an important role[8] which is supported by effectiveness demonstrated by PKC inhibitors[9] in the treatment of manic episodes.[10-11]

Endoxifen is the only direct PKC inhibitor currently available in India and approved by Drug Controller General of India (DCGI) for the treatment of acute treatment of manic episodes with or without mixed features of BD-I.[12] It has been found to be effective in landmark clinical trials of short duration with advantages of early remission, less potential for drug-drug interaction and good tolerability profile.[10,11,13] However, the data on its real world usage pattern and long-term use is currently lacking. This real-world retrospective

observational study was conducted to understand the profile of BD-I who were prescribed endoxifen, and to evaluate effectiveness and tolerability of endoxifen among them.

METHODS

Study design

The real-world, retrospective, cross-sectional, observational study was conducted by study investigators group at 25 centres across India including hospitals, clinics, and health care institutes.

Study variables

The patients were enrolled, and data was collected between April 2022 and March 2023. Data related to demographic parameters, comorbidities and their management, BD-I variables, management approach before and after initiation of endoxifen therapy were captured. Effectiveness of endoxifen was assessed by using Young Mania Rating Scale (YMRS) score, Clinical Global Impression-Severity of Illness (CGI-S) score, Montogomery Asberg Depression Rating Scale (MADRS) score, and Brief Psychiatric Rating Scale (BPRS) score at baseline and at least 3 months after endoxifen therapy. The improvement in the symptomatology of BD-I was also evaluated by Clinician's Global clinical improvement scale (CGI) at least 3 months after the initiation of treatment with endoxifen. Achievement of clinical response (defined as improvement of YMRS by at least 50% from baseline), remission (YMRS score ≤12 at follow-up visit) and improvement of suicidal tendency with endoxifen therapy were captured. Adverse events reported after initiation of endoxifen and compliance with endoxifen therapy were also collected.

Statistical Analysis

In this study, patients' data was collected retrospectively without any predetermined sample size. The observations from records of patients prescribed endoxifen during stated period were analyzed. The data was collected by study investigators group and statistical analysis was performed at Lambda Therapeutic Research Ltd., Ahmedabad, India. Demographic and baseline characteristics were summarized using descriptive statistics. Categorical variables were summarized with frequency and percentage. Continuous variables were summarized with count, mean, and standard deviation. Wilcoxon Signed-Rank test was applied to know improvement in YMRS, MADRS, and BPRS from baseline to follow-up visit (at least 3 months after baseline visit). Statistical analyses were performed using SAS® version 9.4 (SAS Institute Inc., USA).

Ethics Statement

The study was conducted after the due approval from ACEAS independent ethics committee, Ahmedabad, India. This was a retrospective study without patient identifiers; hence, the informed consent of patients was not mandated. There was no confidentiality breach of the data during its analysis and interpretation.

RESULTS

Data of a total 258 patients diagnosed with BD-I and prescribed endoxifen were collected between April 2022 and March 2023 and analysed. The mean (SD) age of the patients was 33.9 (±11.68) years. Table 1 describes the demographic details of patients enrolled in this study.

Table 1: Demographic Details of Patients Prescribed Endoxifen.

Parameter	**Patients (n=258)**
Age (years mean ± SD)	33.9±11.68
Gender	**N (%)**
Male	166 (64.3)
Female	92(35.7)
Education status	**N (%)**
Illiterate	13 (5.0%)
Primary	24 (9.3%)
Secondary	77 (29.8%)
Graduate	108 (41.9%)
Postgraduate	36 (14.0%)
Employment Status	**N (%)**
Professional (employed)	95 (36.8%)
Unemployed	57 (22.1%)
Housewife	49 (19%)
Student	37 (14.3%)
Temporary/permanent sick leave	11 (4.3%)
Retired	9 (3.5%)
History of Alcohol	**N (%)**
Yes	95 (36.8 %)
No	163 (63.2%)
History of Smoking	**N (%)**
Yes	84 (32.6 %)
No	174 (67.4%)

A total of 70.5% patients had manic episode, 17.8% patients had mixed episode, and rest 11.6% patients had depressive episode. Mean duration of disease among the cohort was 44 ± 56.2 months. At the time of presentation, 44 (17.1%) patients and 112 (43.4%) patients had suicidal tendency and psychotic symptoms respectively. Positive family history of BD-I was found among 36.8% patients.

Comorbid conditions in BD-I patients

In this cohort, 64% patients didn't have any medical comorbidity. Most prevalent comorbidity observed was obesity (15.5%), followed by hypertension (12.0%), thyroid disorder (8.9%) and diabetes (7.0%). Other observed medical comorbidities were coronary artery disease (0.8%), dyslipidemia (0.8%), anemia (0.4%), asthma (0.4%), and varicose Veins (0.4%).

Small number of patients (3.1%) had psychiatric comorbidities like cannabis use (2.7%) and obsessive-compulsive disorder (0.4%).

Treatment with endoxifen

Utilization of drugs before initiation of endoxifen therapy

Out of 258 patients, 61.2% patients were prescribed endoxifen in the treatment of naïve patients while among 38.8% patients, endoxifen was prescribed after treatment with some other medication for management of BD-I. Most commonly prescribed drugs before the initiation of endoxifen therapy were sodium valproate (22.9%), lithium (15.9%), risperidone (8.1%), and olanzapine (4.3%) for the management of BD-I.

Prescribing pattern of endoxifen

Majority (79.8%) of the patients were prescribed endoxifen as acute treatment while 20.2% patients were prescribed as maintenance therapy. Most of the patients (95%) were prescribed 8 mg of endoxifen per day but remaining 5% patients were prescribed 16 mg of endoxifen per day. Endoxifen was prescribed as a monotherapy to 35.3% patients and as an adjunctive therapy to 64.7% patients. Most prescribed concomitant medications were sodium valproate (23.3%) followed by olanzapine (11.2%), risperidone (9.7%), lithium (8.5%), quetiapine (6.6%), clonazepam (6.2%), lorazepam (5.04%) and aripiprazole (4.65%).

Data regarding concomitant non-pharmacological therapies was available for 123 patients. Commonly co-prescribed therapies were psychotherapy (33.3%), yoga (5.8%), meditation (4.7%), electroconvulsive therapy (3.5%) and exercise (0.4%).

Effectiveness Outcomes

YMRS score was available for 215 patients for both baseline and follow-up visits. Mean YMRS score was significantly improved from baseline value of 34.04 to 10.07 at follow up visit [$p<0.0001$; calculated using Wilcoxon-Signed-Rank Test for the patients with data of both visits (baseline and follow-up)] (Figure 1).

MADRS score at baseline and follow-up was available for 125 patients. Among them, it significantly decreased from 24.13 ±15.63 to 8.61 ±8.38 [$p<0.0001$; calculated using Wilcoxon-Signed-Rank Test for the patients with data of both visits (baseline and follow-up)] (figure 1).

BPRS score at baseline as well as follow up was available for 135 patients which was significantly decreased from 53.14 ±18.54 to 25.98 ±10.72 [$p<0.0001$; calculated using Wilcoxon-Signed-Rank Test (Figure 1).

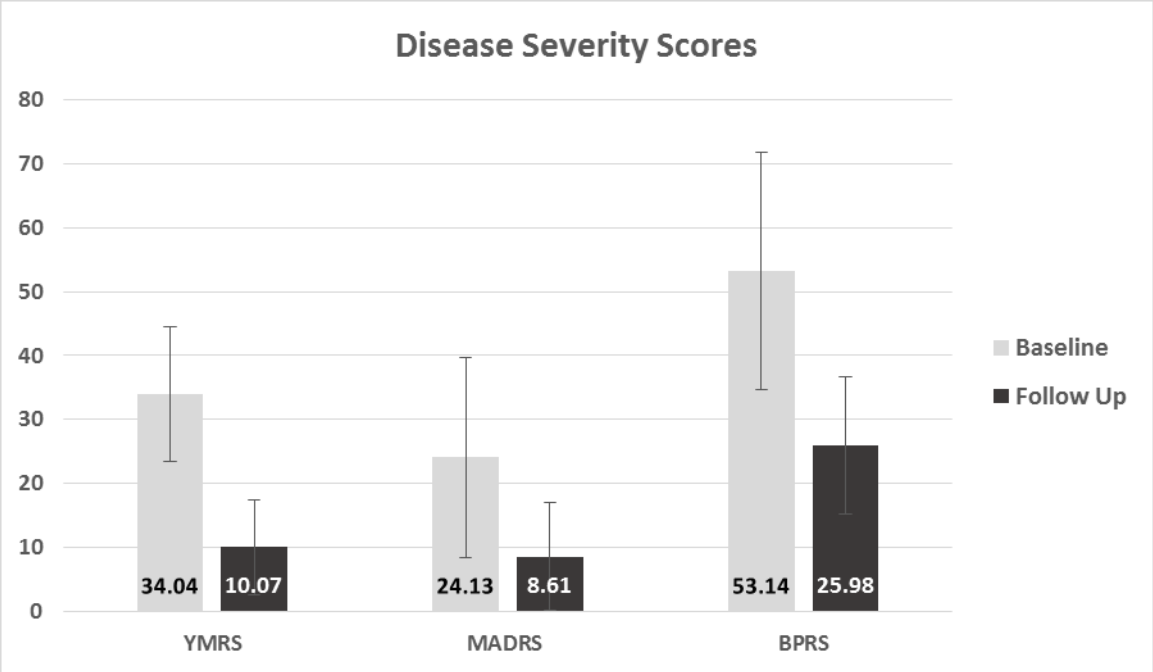

Figure 1: Improvement in Effectiveness Parameters.

YMRS: Young Mania Rating scale; MADRS: Montogomery Asberg Depression rating scale; BPRS: Brief Psychiatric Rating scale.

At baseline, as per CGI-S, 118 patients were either most extremely ill, severly ill or markedly ill. At follow up visit only 3 patients remained in these categories. Majority (76.5%) of the patients were reported to be normal (not at all ill) or borderline mentally ill during the follow up. (Figure 2)

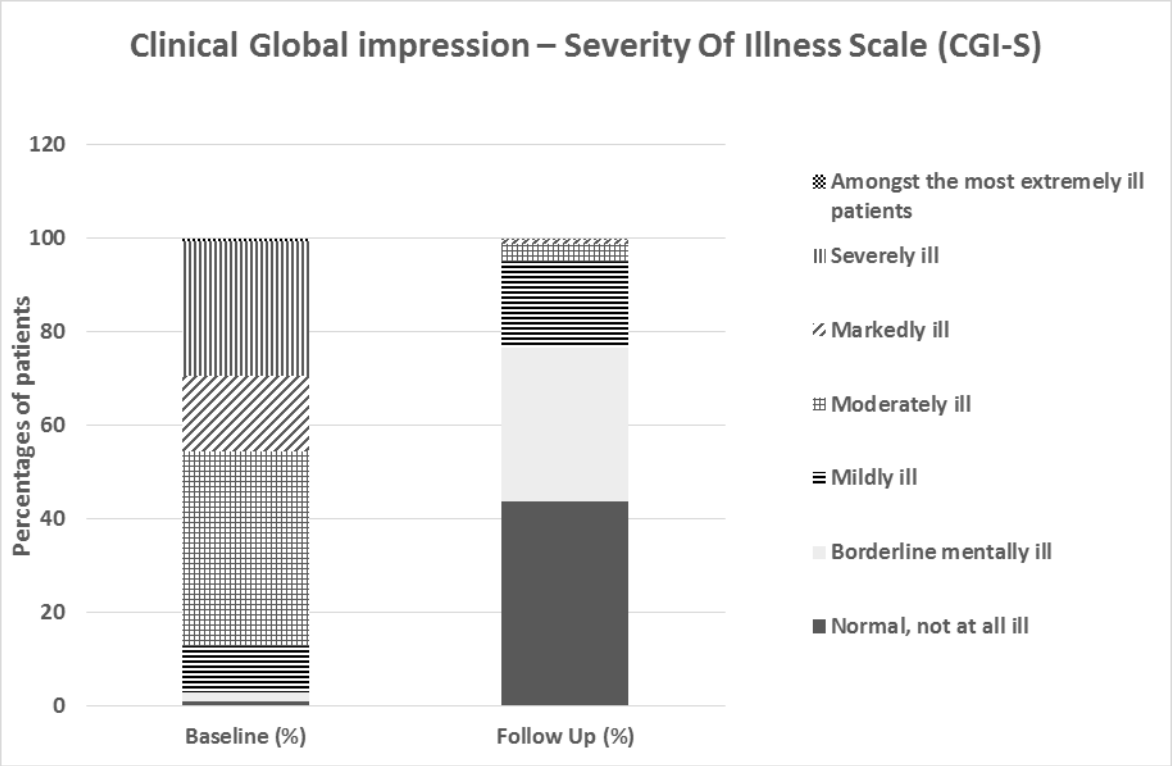

Figure 2: Clinical Global Impression – Severity of Illness Scale (CGI-S).

Data regarding CGI score was available for 239 patients. After initiation of endoxifen therapy, 88.3% of these patients had improvement, 3.1% of them didn't have any change, while 1.2% patients had worsening in CGI score. Clinical response and remission were achieved among 77.5% and 68% patients respectively. Endoxifen therapy of 3 months duration led to improvement in suicidal tendency among 33% of patients.

Safety Assessment

Total 25 adverse events were reported after initiation of endoxifen during the conduct of the study. Most common adverse events were headache, followed by extrapyramidal syndrome, gastritis, skin rash, and nausea (Table 2). This may be due to co-administered medications with known extrapyramidal effects and not from endoxifen.

Most of the adverse events were found to be mild to moderate. No death or serious adverse event was reported while patients were taking endoxifen therapy in this real-world study. None of the adverse event led to discontinuation of endoxifen therapy.

Table 2: Adverse events reported with endoxifen.

Details of Adverse event (AE)	Count (n)	% of patients
Headache	5	1.9
EPS	3	1.2
Gastritis	3	1.2
Skin rash	3	1.2
Nausea	3	1.2
Loss of Appetite	2	0.8
Light-headedness	1	0.4
Over-sweating	1	0.4
Sleeplessness	1	0.4
Tremors	1	0.4
Vertigo	1	0.4
Giddiness	1	0.4

Compliance to Endoxifen Therapy

More than half of the patients (57.4%) had excellent compliance to endoxifen therapy and satisfactory compliance was observed in 105 (40.7%) patients while poor compliance was observed in 4 (1.6%) of patients.

DISCUSSION

BD remains a serious, chronic psychiatric illness, characterized by mood switch, impulsivity, risk-taking behaviour, and interpersonal conflicts. Endoxifen was introduced in India as a novel therapy for the

management of the BD-I in the year 2021, quickly gaining interest of clinicians[14] due to its unique mechanism of action, comparable efficacy to divalproex (first-line drug) shown in clinical trials, better safety profile with no reported adverse events like weight gain, change in thyroid hormone levels, platelet counts, and noted beneficial effects compared to currently available therapy as less potential for drug-drug interaction.

The quantum of evidence related to use of endoxifen in BD-I[15-19], BD with comorbid substance abuse[17,20-22], BD with impulsivity[23] and various psychiatric disorders[23-24] is growing with publication of new studies as well as case reports. However, high-quality, real-world data is need of the hour to further validate its effectiveness and safety. With this goal, the current study was planned to retrospectively evaluate the available clinical data of BD-I patients who had been prescribed endoxifen in past and for whom the follow up data was available for a minimum duration of 3 months.

In the current study, 64.3% patients were males which is similar to another Indian study showing male preponderance.[25] Further evaluation of the demographic details of study cohort showed that 41.9% patients were graduate and more than one third were employed. Similar socio-demographic profile of BD patients was observed in one of the major recent multicentre studies.[26] Majority of the patients had negative history of alcohol (63.2%) and smoking (67.4%). Only 2.7% of patients had history of cannabis use which is in line with an earlier Indian study reporting small percentage of BD patients having history of substance abuse.[26]

Positive family history of BD-I was observed among 36.8% of patients unlike earlier study conducted by Reddy MS, et al. (2022) reporting only 16% patients of BD having family history of psychiatric illness.[26] This difference may be related to different study design of both study.

Most prevalent comorbidity observed in current study were obesity (15.5%), followed by hypertension (12.0%), thyroid disorder (8.9%) and diabetes (7.0%). The most reported comorbidities by earlier studies were cardiometabolic disorders mainly hypothyroidism (6.8%), followed by hypertension (6.4%) and diabetes mellitus (4.2%).[26]

Various guidelines on the management of BD recommend both monotherapy as well as combination therapies with mood stabilizers and/or second generation antipsychotics.[5-7] Similarly, in the current study, endoxifen was prescribed as monotherapy among 35.3% patients as well as adjunctive therapy to other mood stabilizers/antipsychotic drugs in 64.7% patients. Majority of the patients were prescribed endoxifen in dose of 8 mg daily in this study which is approved and most studied dose of endoxifen for the management of BD-I. Though endoxifen is approved for acute treatment of BD-I in India[12], few patients (20%) were prescribed endoxifen as maintenance therapy as well. The use of endoxifen as maintenance therapy may be ascribed to good safety profile perceived by treating clinicians as well as published case reports on long-term efficacy in recent times.[16,17,19,20,22,24]

Improvement in YMRS score by 24 points and MADRS score by 15 points after treatment with endoxifen was reported in this study which is higher than the improvements reported in the phase III clinical trial of endoxifen (YMRS, 15 points; MADRS, 2 points).[11] In current study, 77.5% patients suffering from BD met clinical response criteria and 68% met clinical remission criteria with endoxifen therapy for 3 months which is again numerically superior to the response noted in phase III study data published by Ahmad et al. who reported response and remission among 49.1% and 37.1% patients respectively.[11] These difference may be explained by longer duration and real world nature of this study unlike phase III clinical trial of endoxifen.

Statistically significant improvement in BPRS score was observed in this study. Improvement in psychotic symptoms has also been previously observed as reported in a case report published by Gowda et al.[18] Improvement in suicidal tendencies was also observed after initiation of endoxifen therapy in this study. Till date, lithium is the only medication which is known to prevent the suicides as per data from clinical trials[27] and is approved for the management of BD-I.[28] As PKC has been implicated in the pathophysiology of BD[8], as well as schizophrenia, and suicidal behaviour[29], improvement in symptoms of BD-I, psychotic symptoms, and suicidal ideation in the present study may probably be explained by PKC inhibitory activity of endoxifen.

Overall safety data of endoxifen observed in this study was in line with its already known safety profile from the landmark clinical trials. Adverse events reported with endoxifen in this study were mild to moderate and did not warrant its discontinuation. No serious adverse events were reported during the conduct of this study. Important safety advantage which can be deduced from this study is that endoxifen can be safely given in BD-I without inducing depressive episodes.

The outcomes of this study further add to the understanding related to effectiveness and safety of endoxifen in BD-I. Given that endoxifen is approved for acute treatment of manic episode of BD-I with or without mixed features, study results of current study support need for further investigations into the efficacy of endoxifen in depressive episode of BD-I, patients with suicidal tendencies and psychotic symptoms. These benefits, if verified with planned randomized controlled trials and generalized accordingly, may redefine the treatment algorithm of BD-I in future.

Strength for the current study is its real-world nature which has generated evidence on the clinical use of endoxifen in management of BD-I. Limitations of this study also do exist inherent to methodologic concerns related to retrospective data collection and no calculation of sample size to evaluate the significance of outcomes. Additionally, confounds such as differential psychopharmacology and medical comorbidities were not accounted for as covariates in biostatistical considerations, as this was not the primary aim of this report, though, this would certainly be of interest in future, larger-scale validation studies addressing this question.

CONCLUSION

The outcomes of this study validate the effectiveness of endoxifen in the management of BD-I. In addition, endoxifen has also led to improvement in psychotic symptoms and suicidal tendency. The safety and tolerability profile of endoxifen over 3 months is also in-line with the outcomes reported by clinical trials. In future, a large prospective study is required to validate and confirm the findings of this study.

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REFERENCES

1. Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. Lancet, 2016 Apr 9; 387(10027): 1561-72.
2. Dattani S, Rodés-Guirao L, Ritchie H, Roser M. Mental Health. Our World Data [Internet]. Available from: https://ourworldindata.org/mental-health. Accessed on March 4, 2024.
3. 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 Aug; 18(5): 440–50.
4. Harrison P, Cowen P, Burns T, Fazel M, Harrison P, Cowen P, et al. Shorter Oxford Textbook of Psychiatry. 7th Ed. Oxford, New York: Oxford University Press, 2017; P-896.
5. Malhi GS, Bassett D, Boyce P, Bryant R, Fitzgerald PB, Fritz K, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust N Z J Psychiatry, 2015 Dec; 49(12): 1087-206.
6. Shah N, Grover S, Rao GP. Clinical Practice Guidelines for Management of Bipolar Disorder. Indian J Psychiatry, 2017 Jan; 59(Suppl 1): S51-S66.
7. Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord, 2018; 20: 97-170.
8. 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(2): 108–24.
9. Talaei A, Pourgholami M, Khatibi-Moghadam H, Faridhosseini F, Farhoudi F, Askari-Noghani A, et al. Tamoxifen: a protein kinase C inhibitor to treat mania. A systematic review and meta-analysis of randomized, placebo-controlled trials. J Clin Psychopharmacol, 2016; 36: 272–5.

10. Ahmad A, Sheikh S, Shah T, Reddy MS, Prasad B, Verma KK, et al. Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen. Clin Transl Sci, 2016 Oct; 9(5): 252-9.
11. 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, 2021; 23(6): 595-603.
12. List of new drugs approved in the year 2019 till date. https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadApprovalNewDrugs/newdrugaapproaldec2019.pdf. Accessed on March 4, 2024.
13. ZONALTA (Endoxifen 8 mg tablets) [Package insert]. Intas Pharmaceuticals Ltd., Gujarat, India. https://zonalta.in/wp-content/uploads/2021/03/10-4731-0-6004212-ZONALTA-PIL-1.pdf. Accessed on March 4, 2024.
14. Reddy MS, Malhotra S, Ajit A, Kapoor J, Gauthamadas U, Vincent A, et al. Prescribing Trends in Bipolar I Disorder and Usage of Endoxifen: An Indian Perspective. International Multispecialty Journal of Health (IMJH), 2023; 9(6): 1-12.
15. Dubey V. Long-term effectiveness and safety of endoxifen in the treatment of bipolar mania: a case report. Int J Adv Med, 2022; 9: 169-72.
16. Thanvi V. Real-World Long-Term Experience on Endoxifen in Bipolar Disorder with Psychotic Symptoms. Case Rep Psychiatry, 2022 Jul 2; 2022: 3684181.
17. Gowda M, Dewani K. Cost-effectiveness of endoxifen therapy in severe psychotic bipolar I disorder: A case report. International Journal of Applied Research, 2022; 8(8): 09-13.
18. Chakladar A, Kumar N, Verma R, Brar MK. Long-Term Effectiveness and Safety Of Endoxifen In The Treatment Of Acute Bipolar Mania: A Case Report. Research Square, 2022. DOI: 10.21203/rs.3.rs-2340214/v1.
19. Garg S. First Report of Endoxifen Treatment for 1 Year: A Case Report of Bipolar Disorder. International Multispecialty Journal of Health (IMJH), 2022; 8(5): 1-4.
20. Dave M, Shanmugasundaram N. Endoxifen for the management of bipolar disorder with comorbid substance use disorder: A report of two cases. Arch Biol Psychiatry, 2023; 1: 25-8.
21. Dubey V. Long-term use of endoxifen in the treatment of bipolar mania: case report. Int J Adv Med, 2022; 9: 169-72.
22. Dave D. Tackling Bipolar Disease with Impulsivity: The Role of Endoxifen. International Multispecialty Journal of Health (IMJH), 2023; 9(3): 1-3.
23. Singh H. Endoxifen Response in Schizoaffective Disorder: A Case Series. International Multispecialty Journal of Health (IMJH), 2022; 8(2): 1-5.
24. Elangovan S, Sundaramoorthy J, Dhuruvasan S. Real world experience of Endoxifen augmentation therapy in a case of resistant OCD. Biomedicine, 2023; 43(2): 805-7.
25. Trivedi JK, Sareen H, Yadav VS, Rai SB. Prescription pattern of mood stabilizers for bipolar disorder at a tertiary health care centre in north India. Indian J Psychiatr, 2013; 55: 131-4.
26. Reddy MS, Rao GP, Kumar S, Seshadri V, Prasan P. Clinical characteristics, sociodemographic profile, and treatment pattern of bipolar disorder - A multicenter study from India. Psychiatry Research Communications, 2022; 2(2): 100039.
27. Cipriani A, Hawton K, Stockton S, Geddes JR. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. BMJ, 2013; 346: f3646.
28. Lithium capsules. Prescribing information. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2004/16860slr074,18152slr020_eskalith_lbl.pdf. Accessed on March 4, 2024.
29. Pandey GN. Biological basis of suicide and suicidal behavior. Bipolar Disord, 2013 Aug; 15(5): 524-41.