International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1554-1559 www.ijprajournal.com ISSN: 2456-4494

Study Of Role and Efficacy of Anticonvulsants in Bipolar Patients

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Submitted: 10-12-2022 Accepted: 23-12-2022

ABSTRACT

Bipolar disorder is a mental health illness that involves emotional highs (mania) and lows(depression).
Sleep,energy,activity,judgment,conduct,andtheabilityothinkclearlycanallbeaffectedbymoodfluctuations.
Objectives:
Toevaluatetheefficacyofanticonvulsantsamongbipolar patients and tocheckthemedicationadherence.
Methods: A retrospective observational study for a period of 6 months was carried out in the inpatients and outpatient of psychiatry department in 700 bedded multispecialty hospital.Results: All 72 patients were prescribed with anticonvulsants along with other antipsychotics.Theefficacyofthedrugs werestudiedbasedontheobservationsmadebythe physicianinthefollowupsheetsofthecasefiles.Theobservationsincludedpsychomotoractivity,speech,mood,affect,andsleep.Accordingtothese observationsmade,asignificantimprovementinthesymptomswasnoted. Medication adherence was determined by using Medication Possession Ratio (MPR).Theresultsshowedthatallthe 72 patientsshowedhigh medicationadherence. Amongalltheanticonvulsantsprescribed, Valproatewasprescribedthemost.
Ourpresentstudywaseffectivetoprovetheefficacyofanticonvulsantsinthetreatmentofbipolardisorder.Numberofstudiessupportstheuseofanticonvulsants inbipolardisorderforbothmania anddepression.
Conclusion:The case files of the study participants were retreived and were studied from the time ofadmission till the patients were discharged. The efficacy of the drugs were studied based onthe observations made by the physician in the follow up sheets of the case files. Accordingtotheseobservationsmade,a significantimprovementinthesymptomswasnoted

I. INTRODUCTION:

Bipolar disorder, which is listed as a mood disorder, is a common, persistent, and recurrentpsychiatric disordermarkedbyperiods ofmaniaanddepression.[1]Epidemiologicresearchessuggestsatapopulationlevelthatbipolarillnessisofdimensionalcomposition.Bipolarspectrumdisorderconsistawiderangeofbipolarconditions[2]. Andresen, USA was found to have higher rates of bipolar disorder whereasTaiwan wasfound to havelower rates of bipolaraffective disorder. Based on the twosexes, females are found to have greater prevalence of bipolar disorder than male[3]. In spiteofbipolar disorder, women are found to have higher rates of depression than men whereasmen are found to have higher rates of mania than women.[4] In India, higher rates of manicepisodesareseenduetohighersubstanceuseinmen.Co-morbidconditionslikehypothyroidism,migraine andobesitywasfoundhigherinwomenofIndia.[5]

TREATMENT: Comprehensive treatment aims to relieve symptoms, improve one's ability to function, resolve issues that rise as a result of illness at home and at work, and, as a result, minimize the risk of recurrence.[6] In most cases, treatment is divided into two stages. The focus of acute-phase therapy is on managing acute mood episodes (manic, hypomanic, or depressive). The aim of maintenance care is to avoid recurrences of acute episodes.[7]
Bipolar disorder in most of the patients show lithium to be the affective drug both in initial and maintenance phases. Combination therapy has been found efficacious but increases the side effects in patients. The main class of drugs provided for bipolar disorder are:
1.First and Second-Generation Antipsychotics
2. Anticonvulsants [8]
Bipolar mood states of a patient vary with depressed state and mania state while a common trigger is anxiety. Hence, due to the variation, a wide variety of class of drugs are provided as first line namely
1. Antidepressants
2. Mood stabilizers
3. Monoamine oxidase inhibitors
4. Benzodiazepines [9]
Acute management of manic episodes in a bipolar patient involves:
• First line- Lithium, Valproate, Carbamazepine and second generation antipsychotics.

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• Second line- Second generation antipsychotics with lithium or valproate, or lithium and valproate.
• Third line- Electroconvulsive therapy and Clozapine.[10]
Although atypical antipsychotics can be considered for maintenance treatment for manic episodes, there is no definitive proof that their effectiveness in this regard is equivalent to that of lithium or valproate. [11]. Just three prescription therapies for acute bipolar disorder are currently approved:
• Olanzapine/Fluoxetine,
• Quetiapine (immediate or extended release)
• Lurasidone (monotherapy or adjunctive to lithium or valproate).[12]
Anticonvulsant drugs have been used to treat mental conditions for decades. It is believed that the biochemical processes underlying their anti-seizure activity can also contribute to mood and behavior stabilization.[13]

EFFICACY OF ANTI CONVULSANTS:

The efficacy of anticonvulsants are determined when the drug is given in monotherapy or in combination with lithium, a mood stabilizer. Anticonvulsants have a high potency and a long-term prophylactic role in treating bipolar disorder.[14] The antidepressant versus antimanic efficacy in defining mood stabilizers were considered with the introduction of newer anticonvulsants. The efficacy of Valproate for pure and mixed mania, as monotherapy as found very effective globally.[15] Electroconvulsive therapy along with anticonvulsants, mainly carbamazepine and valproate, has a long history for its effective treatment in bipolar disorder.[16]

MEDICATION ADHERENCE:

Medication adherence has a great impact on successful treatment of any illness. Non-adherence often leads to undesirable outcomes. Mainly adherence is measured in three ways:
• Patient self-report
• Pharmacy refill records
• Use of electronic lids [17]

Effective treatment of bipolar disorder depends on medication adherence. Adherence may also increase with age. In bipolar disorder, motivation for adherence is reduced due to hedonic pleasure from manic episodes. Medication adherence plays an important role in psychosocial factors of bipolar disorder.[18] To check medication adherence, the medication possession ratio (MPR) is calculated as the number of days the drugs were prescribed in a period divided by the total number of days during the follow up period.[19]

OBJECTIVES:

Primary objective:
• To evaluate the efficacy of anticonvulsants among bipolar patients.
Secondary objectives:
• To check the medication adherence

II. MATERIALS AND METHODS:

A Retrospective observational study was carried out in the inpatients and outpatients of the psychiatry department for 6 months at Yenepoya Medical College and Hospital, Mangalore, Karnataka. About 72 patients were selected for the study based on inclusion and exclusion criteria. Patient data were collected using patient data collection form.
ETHICAL APPROVAL:
The study was approved by Yenepoya Ethics Committee 2.
Approval date: 16/04/2021
Protocol no:YEC2/761
STUDY CRITERIA:
The study was carried out based on the criteria such as patients who are above 15 years and having bipolar disorder in inpatient or outpatient unit of Psychiatry department.
Study participants below 15 years of age were excluded from the study.
DATA SOURCES:
- Patients case sheets
- Patient data collection form:

Data was collected using a self-designed data collection form, which consist of details like patient demographics, mental status examination, diagnosis, drug therapy and other relevant information.

STATISTICAL ANALYSIS:
For extending the clinical pharmacy service, a retrospective study was conducted to assess the efficacy of anticonvulsants in bipolar patients. The recorded MSE was analysed for the study.The efficacy of the drugs from the anticonvulsant class was easily understood by analysing the improvement in the follow up reports and other examination reports provided by the doctors and the nurses. Data was entered in the excel spreadsheet and analysed.Medication adherence of each patients was also calculated and checked.

III. RESULTS:

Age wise distribution of subjects:

International Journal of Pharmaceutical Research and Applications
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Out of 72 patients, the majority of them i.e 41 (56.9%) patients were found in the age group of 26-50 years followed by 21 (29.2%) patients in the age group of 51-75. 9 (12.5%) patients were found to be less than 25 in age whereas 1 (1.4%) patient was greater than 75 in age. This is represented in Table 1.

Table 1:Age-wise distribution of study participants

Age (in years)	Frequency	Percentage
</= 25	9	12.5
26-50	41	56.9
51-75	21	29.2
>75	1	1.4

The majority of the study participants were in the age group of 26-50 years.

Gender wise distribution of subjects:

Out of 72 subjects, 45 (62.5%) patients were male and 27 (37.5%) were female which is represented in Table 2.

Table 2: Gender-wise distribution of study participants

	Frequency	Percentage
Male	45	62.5
Female	27	37.5
Total	72	100

Distribution of subjects based on type of bipolar disorder:

Patients were categorized into 3 groups such as mania, depression and mixed. Out of 72 patients, 56 (77.8%) patients had mania, 14 (19.4%) patients had depression and 2 (2.8%) had mixed type of bipolar disorder which is represented in Figure 5.1

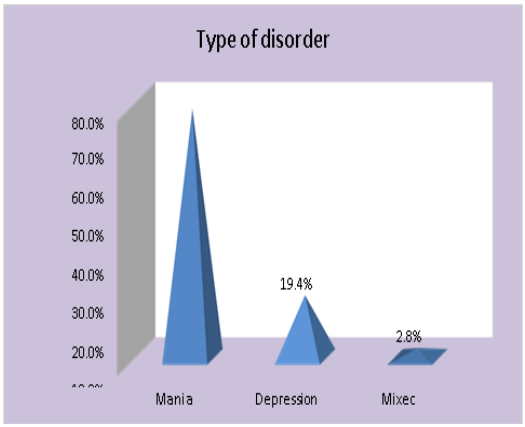

Figure 5.1: Representation of types of Bipolar disorder among the subjects.

Distribution of patients based on Psychotic or Somatic symptoms:

Out of 72 patients, 19 (26.4%) patients presented with Psychotic or Somatic symptoms which is represented in Figure 5.2

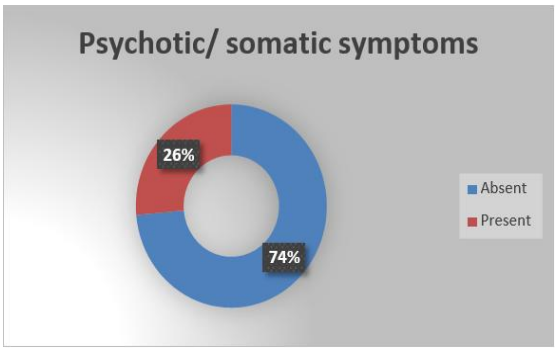

Figure 5.2: Representing patients with Psychotic or Somatic symptoms.

Distribution of patients based on drug received:

The drugs that were given to the patient include Carbamazepine, Valproate, Lamotrigen, Lithium, Risperidone, Olanzapine, Quetiapine, Haloperidol, Clozapine and Lorazepam.

The maximum drug received by the patients is Valproate and the least is Clozapine. It is represented in Table 3.

Table 3: Distribution of drugs received by the patient

Drugs	Frequency	Percentage
Valproate	55	76.4
Carbamazepine	10	13.9

International Journal of Pharmaceutical Research and Applications
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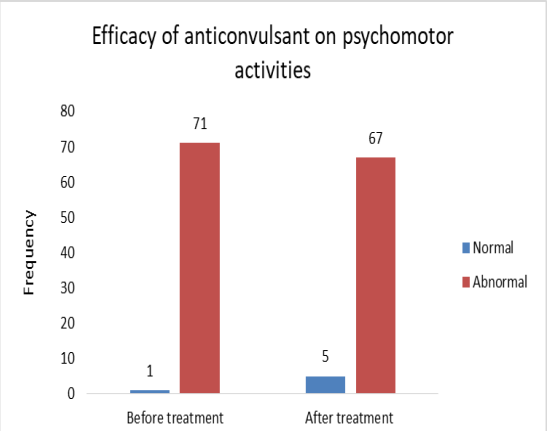
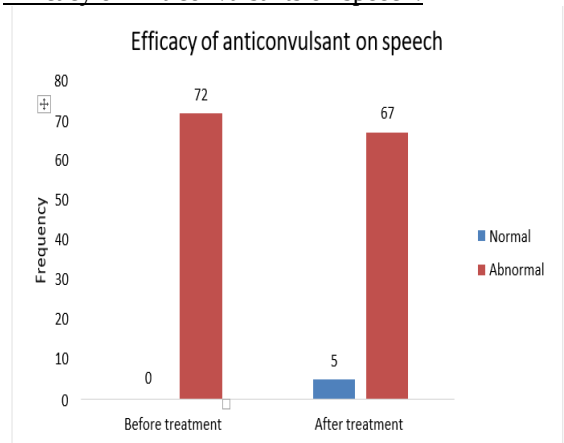
Lamotrigene	9	12.5
Lithium	21	29.2
Risperidone	15	20.8
Olanzapine	31	43.1
Quetiapine	21	29.2
Haloperidol	42	58.3
Clozapine	5	6.9
Lorazepam	6	8.3

EFFECT OF ANTICONVULSANTS ON MENTAL STATUS EXAMINATION:

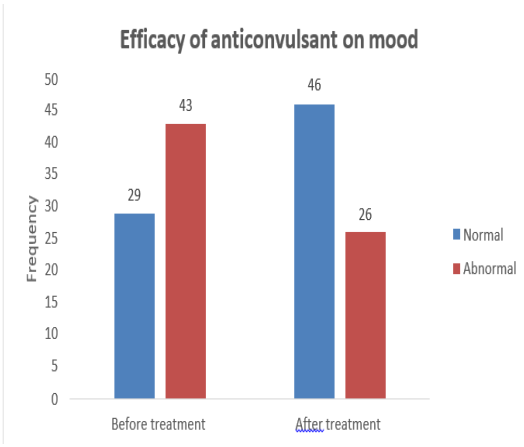
Efficacy of anticonvulsants on psychomotor activities among bipolar patients:



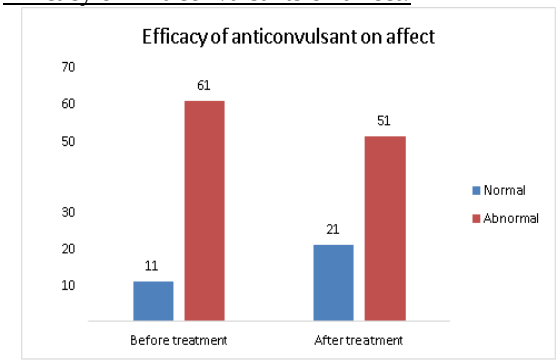
Efficacy of Anticonvulsants on speech:



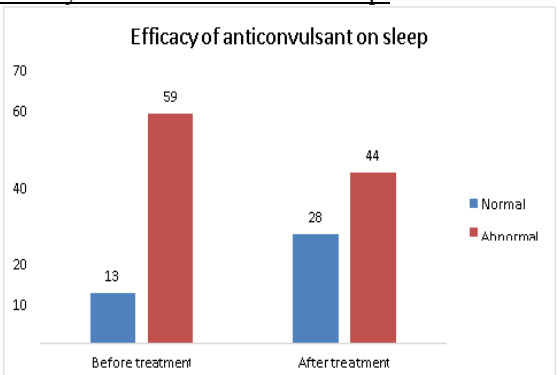
Efficacy of Anticonvulsants on mood among bipolar patients:



Efficacy of Anticonvulsants on affect:



Efficacy of Anticonvulsants on sleep:



DISTRIBUTION OF PATIENTS BASED ON MEDICATION ADHERENCE:

The medication adherence was analysed. The results showed that 69.4% patients were adherent and 12.5% patients were least adherent.

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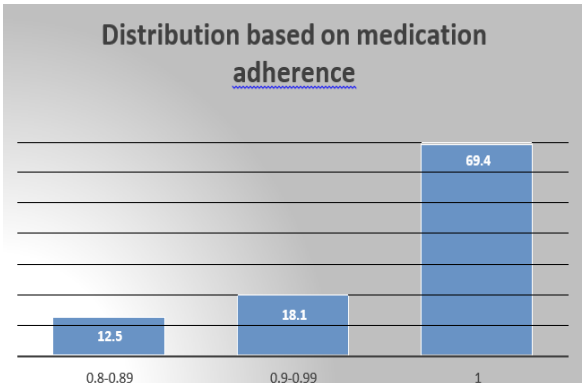

IV. DISCUSSION:

Efficacy is the ability of a medication to produce the desired result under ideal conditions.[20] Efficacy can be assessed accurately only in ideal conditions (ie, when patients are selected by proper criteria and strictly adhere to the dosing schedule). Thus, efficacy is measured under expert supervision in a group of patients most likely to have a response to a drug.

Bipolar disorder is a chronic, episodic illness that causes severe and long-term depression, cognitive disability and morbidity, a loss of quality of life, and is linked to a high mortality risk. The tolerability of treatment is an important consideration when choosing a therapeutic option as patient satisfaction with, and adherence to, treatment can influence health outcomes and quality of life.[21] For studying the efficacy of anticonvulsants, 72 study subjects were selected based on the inclusion and exclusion criteria. All the 72 study subjects were prescribed with anticonvulsants along with other antipsychotics.

Based on the age, patients were divided into 4 age groups such as ≤ 25, 26-50, 51-75 and >75. Based on gender, total there was 72 study participants in that 27 were females and 45 were males. Among the 72 patients, 56 of them were suffering from bipolar mania, 14 were suffering from bipolar depression and 2 were suffering from mixed type of bipolar disorder.

The case files of the study participants were retreived and were studied from the time of admission till the patients were discharged. The efficacy of the drugs were studied based on the observations made by the physician in the follow up sheets of the case files. According to these observations made, a significant improvement in the symptoms was noted.According to the findings of a study done, LAM is effective in treating bipolar depression.[22]

Medication adherence was determined by using Medication Possession Ratio (MPR). MPR is calculated as the number of days the drugs were prescribed in a period divided by the total number of days during the follow up period. The results showed that all the 72 patients showed high medication adherence. This is because all the 72 study subjects were inpatients.

Among all the anticonvulsants prescribed, Valproate was prescribed the most. Numerous scientific literature supports the use of anticonvulsants in manic and non manic subtypes of bipolar illness. As a result, physicians can definitely suggest anticonvulsants to their bipolar disorder patients.

V. CONCLUSION:

Bipolar disorder is a common and important disorder that includes episodes of depression, mixed states or mania. Anticonvulsants have been approved by FDA to apply in the treatment of bipolar disorder. But it is important to note that only valproate, carbamazepine and lamotrigine were proven to be effective. In the long-term treatment of bipolar disorder, other anticonvulsants have insufficient proof of efficacy as monotherapy.

ACKNOWLEDGEMENT:
The authors of the study are heartily thankful for the guidance and support received from all the members who contributed to this project, it was vital for the success of the project.

CONFLICT OF INTEREST:
The authors declare no conflict of interest.

ABBREVIATIONS:
AED: Antiepileptic Drugs, **BPAD:** Bipolar Affective Disorder, **CBZ:** Carbamazepine, **FDA:** Food and Drug Administration, **LAM:** Lamotrigine, **MPR:** Medication Possession Ratio

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Volume 7, Issue 6 Nov-Dec 2022, pp: 1554-1559 www.ijprajournal.com ISSN: 2456-4494

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