Drug utilization pattern of patients with bipolar affective disorder in a tertiary care hospital in India

Vadla Vidyasagar *, T. Kavya, P. Divya Jyothi, Aruna Surakasula, Dr. Rajshekhar Bipeta, Sharada Srikanth, Dr. M.S. Reddy, T. Ram Mohan Reddy

Department of Pharm D, CMR College of Pharmacy, Kandlakoya, Hyderabad, India.

ABSTRACT

Aim and Objective: To assess the drug utilization pattern of patients with Bipolar Affective Disorder (BPAD) in the Outpatient department of Psychiatry of a tertiary care hospital.
Methods: It is a Cross sectional observational study (6months) carried out at the Outpatient department of Psychiatry in tertiary care hospital.
Results: A total of 122 prescriptions were analyzed. Most common disease was found to be BPAD. Total drugs prescribed were 291 and majority was in oral dosage form. Average no. of drugs per prescription was 2, it was seen that out of 291 drugs mood stabilizers (26.14%), antipsychotics (29.89%), antidepressants (26.14%), anticonvulsants (1.37%), anti-anxiety (16.49%). Antipsychotics given orally were 87 of which Olanzapine 46 (52.87) found to be more than others. Antipsychotics in combination prescription with mood stabilizers, antidepressants, anti-anxiety which included Lithium, Divalproex sodium, Escitaprolam, Clonazepam respectively.
Conclusion: BPAD is serious public health problems that is frequently under diagnosed and in adequately treated, studying and analyzing the prescription patterns seek to monitor, evaluate, and help the physician in understanding how the available drugs can be best put to use practically.

Keywords: Prescription Pattern, Antipsychotics, Bipolar affective disorder

INTRODUCTION

Bipolar affective disorder (manic-depressive illness) is one of the most common severe chronic psychiatric disorders. The bipolar disorder is of two types, bipolar I and bipolar II. Bipolar I disorder occurs equally in men and women with a prevalence of 0.4-1.6%, bipolar II disorder is more common in women, approximately 0.5%. The national co-morbidity survey reported that the lifetime prevalence rate of a manic episode is 1.6%, 0.3% for men and 1.7%, 0.3% for women in the United States (4 million people). [1][2]

Drug utilization pattern of patients with bipolar affective disorder is a difficult change due to the recurrent, episodic, and heterogeneous nature of the disease. [3] There is increased recognition that even while euthymic, patients experience frequent sub syndrome symptoms and an impaired quality of life. [4] This study explored drug utilization patterns in bipolar affective disorder using 6months of daily self-reported data at Psychiatry department. [3] Polypharmacy is prescribed to about two thirds of patents with bipolar affective disorder. In our studies shows, about 75 % of the patients were prescribed with Mood stabilizers, Antipsychotics, Antidepressants. The purpose of this investigation was to analyze the efficacy, adverse reaction and usage of various other psychotropic medications. [5]

METHODS AND METHODOLOGY

Study site and Duration: The study was conducted in out-patient department of psychiatry in a tertiary care hospital for a period of 6month from September 2015 to February 2016, after taking the ethical consideration from the Institutional ethical committee.

Study Design: It is a cross sectional observational study.
Source of data: The medication records of all the patients.

Corresponding Author Address: Mr. Vadla Vidyasagar, Department of Pharm D, CMR College of Pharmacy, Hyderabad, India:
Email: vidyasagarvadla3@gmail.com

Total number of subjects: 122 subjects who were diagnosed as BPAD

Study disease: Subjects with an ICD-10 diagnosis of BPAD.

Selection of patients:-
  ➢ **Inclusion criteria:**
  • Subjects diagnosed with BPAD aged ≥18 years who are willing to give written inform consent for the participation.
  • Both male and female gender.
  ➢ **Exclusion criteria:**
  • Subjects who are diagnosed with BPAD aged ≤18 years.
  • Subjects who are not willing to participate.

Tools:
  1. **Socio-demographic preference**: Socio-demographic details such as age, gender, etc, psychiatric and medical history, clinical and treatment details were collected from subject case profiles. The drug utilization pattern was studied by pursuing old prescription; current prescription. The prescription data was analyzed based on details like number of drugs, names of individual drugs (generic/brand), dose, dosage form, dosing schedule and duration of treatment.
  2. **Clinical Global Impression (CGI) Severity:** The Clinical Global Impression Scale (CGI) has become one of the most widely used assessment instruments in psychiatry. The CGI scale is a brief clinician-rated instrument. Severity of illness (CGI-S): To assess overall assessment of the current severity of the patient are symptoms considering your total clinical experience with this particular population, how mentally ill is the patient at this time?

  0 = Not assessed, 1 = Normal ill, 2 = Borderline mentally ill, 3 = mildly ill, 4= moderately ill, 5 = markedly ill, 6 = severely ill, 7 = among the most extremely ill patients

Study procedure:
  ✓ All subjects with a diagnosis of BPAD currently mania, hypomania or depressive episodes presenting to psychiatry OPD fulfilling the inclusion criteria.
  ✓ Data relevant to diagnosis and treatment was documented from the subject's records.
  ✓ Laboratory reports and other relevant documents will be analyzed.
  ✓ Data regarding past medication history, present prescription drugs, and other subject relevant information was obtained.

Materials:

  1. Data collection forms (patient profile form).
  2. Patient medication record.

Statistical analysis: Statistical analysis was performed using Graph pad Prism software, version 5. Data was analyzed using Chi square test. Chi square test was applied to estimate the differences between categorical variables in the study population. P-values <0.05 were considered statistically significant, *p*-values <0.01 were considered very significant and *p*-values <0.001 were considered extremely significant.

Ethical consideration: Approval and permission from the Institutional ethical committee was taken before the study. The identity of the patient and any information that might cause any harm to the patient was not disclosed. All the research activities were carried out under the supervision and guidance of supervisor.

RESULT

In total, 122 patients attended the outpatient psychiatric department during the study period of 6 months (Sept'2015- Feb'2016) and all of them had meaningful data for analysis. Of the total 122 cases analyzed with total of 291drugs were found to be prescribed. The proportion of females (57.37%) and males (42.63%).Maximum subjects with BPAD (31.96%) were observed in the 20-30years age and least (2.45%) seen in >61years.Majority of subjects were housewives (31.96%) and subjects who had degree (32.78%) [Table1].

Among 122 subjects, **Duration of BPAD** in the past history were found to be more in 1-10 years (77.05%), and least >21years(2.45%), where p-value is 0.4287, which is not significant. The diagnosis was made easier by considering the poles of the subjects. The proportion of subjects with depression in the **past pole** (66.39%) and the proportion of subjects with mania in the **current pole** (50%), where the p-value is extremely significant [Table 2].

Total of 122 prescriptions analyzed. The number of drugs prescribed per prescription was a maximum of 2-3drugs and hence **combination of drugs** in BPAD was found with p-value 0.1426 and which is not significant. Of the total 291 prescribed drugs, anti-psychotics (29.89%), constituted the major **class of drugs** being prescribed for BPAD followed by mood stabilizers and anti-depressants (26.11%) each, anticonvulsants (15.12%) and anti-anxiety (2.77%), with extremely significant p-value [Table 3].

Table 4 summarizes findings of the analysis. **Anti-psychotics** were the major group of drugs prescribed for BPAD. Olanzapine (52.87%) constituted the major drug prescribed followed by Risperidone (25.28%), Quetiapine (11.49%), Trifluperazine (5.74%) and Aripiprazole (3.48%). Depots like Zuclopenthixol (1.14%) were less prescribed.

Mood stabilizers and anti-depressants were the second common drug groups being prescribed, of which mood stabilizers like Lithium (61.85%) constituted the major drugs followed by Valproic acid (38.15%). Anti-depressants drugs (26.11%) were commonly prescribed drugs for BPAD, of which Escitaprolam (97.36%) was major drug followed by Fluoxetine (1.32%) and Desvanlafexine (1.32%).**Anti-anxiety drug** (2.77%) was the group of drugs prescribed for depression. Benzodiazepine-Clonazepam was most frequently prescribed drug (83.33%) followed by diazepam constituted 16.66 %. Lamotrigine and Topiramate were the most commonly prescribed anti convulsant drugs.

Of the 122 cases, regarding the diagnostic type of BPAD, mania (25.40%) type was predominant, followed by unspecified (18.04%), hypomania (13.11 %), depression (9.01%) and psychosis (4.09%). Regarding the diagnostic type of MDD, hypomania (9.83%) was predominant and unspecified (1.66%). Of the 291 drugs prescribed were analyzed. Out of which brand drugs (77.66%), followed by generic (22.34%) [Table5]

Table 1:- Demographic profiles

Subject Demographics	Parameters	Number (%)
Gender	Male	52(42.63%)
	Female	70(57.37%)
Age	20-30	39(31.96%)
	31-40	36(29.55%)
	41-50	32(26.21%)
	51-60	12(9.83%)
	>61	3(2.45%)
Literacy	Uneducated	8(6.55%)
	Tenth standard	30(24.59%)
	Intermediate	19(15.58%)
	Normal degree	40(32.78%)
	Professor degree	19(15.58%)
	PG	6(4.92%)
Occupation	Unemployed	13(10.65%)
	Private employee	34(27.86%)
	Government employee	16(13.12%)
	Pharmacist	4(3.27%)
	Students	16(13.12%)
	House wife's	39(31.96%)

Table 2:- Duration and Poles.

S.No.	Characteristics	Number (%)	Chi-square value	df	p-value

Duration of bipolar disorder (N=122)	<1year 1-10 years 11-20years >21years	19(15.58%) 94(77.05%) 6(4.92%) 3(2.45%)	1.694	2	>0.05 Not significant
Poles (N=122)	**Past poles** Depression Mania Hypomania **Current poles** Depression Mania Hypomania	81(66.39%) 40(32.78%) 1(0.83%) 45(36.88%) 61(50%) 16(13.12%)	21.27	1	<0.0001 Extremely significant.

Table 3:- Pharmacological classification of drugs and Combination of drugs.

S.No	Characteristics	Number (%)	Chi-square value	df	p-value
Combination of drugs(N=122)	**Mania drugs** Two Three **Depression drugs** Two Three	54(44.16%) 34(28.21%) 25(20.42%) 9(7.21%)	2.149	1	>0.05 Not significant
Pharmacological classification of drugs(N=291)	Mood stabilizers Antipsychotics Antidepressants Anticonvulsants Anti-anxiety	76(26.14%) 87(29.89%) 76(26.14%) 4(1.37%) 48(16.49%)	21.41	4	<0.0001 Extremely significant

Table 4:-Individual Drug Classification

Class	Name of drugs Prescribed	Number (%)
Mood stabilizers	Lithium Valproic acid	47(61.85%) 29(38.15%)
Antipsychotics	Olanzapine Risperidone Quetiapine Trifluperazine Aripiprazole Zuclopenthixol	46(52.87%) 22(25.28%) 10(11.49%) 5(5.74%) 3(3.48%) 1(1.14%)
Anticonvulsants	Lamotrigine Topiramate	2(50%) 2(50%)
Antidepressants	Escitaprolam Desvenlafaxine Fluoxetine Hcl	74(97.36%) 1(1.32%) 1(1.32%)
Anti-anxiety	Diazepam Clonazepam	8(16.66%) 40(83.33%)

Table 5:- Diagnosis and Type of drug prescribed

Parameters	Category	Number (%)

Diagnosis(N=122)	BPAD(unspecified)	22(18.04%)
	BPAD with hypomania	16(13.11%)
	BPAD with mania	31(25.40%)
	BPAD with depression	11(9.01%)
	BPAD with Psychosis.	5(4.09%)
	MDD(unspecified)	2(1.66%)
	MDD with Hypomania	12(9.83%)
	MDD with Mania	4(3.27%)
	MDD with Psychosis	19(15.59%)
Type of drug prescribed (N=122)	Brand	226(77.66%)
	Generic	65(22.34%)

DISCUSSION

Worldwide prevalence of bipolar disorder is 2%-4%. Therefore a prescription may be taken as a reflection of the physician's attitude towards the disease and the role of the drug in its treatment providing an insight into the nature of the health-care delivery system. Out of 122 prescriptions analyzed, more female (57.73%) subjects visited the psychiatry OPD than men (42.63%), which is consistent with studies by Karan B.Thakkar *et al*., Dutta *et al*., Menon and Patel. [6, 7, 8] Majority of the subjects were in the age group of 20-30 years(31.96%) in both sexes, which is similar to those reported in studies by Dutta *et al*., Menon and Patel, [7, 8] and contradicted to the study of Rode SB *et al*. [9]

It was found that the reproductive group, who are literates (32.78%) and working accounted for the majority of psychiatric disorder. Depression was more common among housewives (31.96%), which is consistent with that reported in a study by Dutta *et al*. [7]

Our study focused on the factors such as duration of illness, poles and severity of symptoms which is important given the fact that the dosage of medication is different in various phases and severity. The diagnosis of BPAD in our study is based on the duration and poles. The duration of illness and poles in our study i.e. 1-10 years (77.05%) which meant the disease were untreated or unrecognized. The diagnosis was differently categorized because most of the subjects were diagnosed with BPAD associated with mania followed by depression. The past pole was found to be extremely significant (P<0.0001) which were mostly depression cases (66.39%).

Majority of the subjects were prescribed psychotropic drugs from 5 different category viz. antipsychotics, antidepressants, anticonvulsants, anxiolytics, mood stabilizers or different compound from same category. Other studies consistently found trend is consistent even after prescription monitoring, similar to that reported in previous studies by Rode SB *et al*., Deshmukh *et al*. [9, 10]

The drug utilization pattern in our study subjects shows that antipsychotics were the most commonly used psychotropic drugs followed by mood stabilizers and anti-depressants, anxiolytic and anticonvulsants. In our study, more than half of the anti-psychotics (29.89%) were prescribed. Atypical anti-psychotics were the most commonly prescribed class of anti-psychotics followed by depots, which is consistent with that reported in previous studies by Dutta *et al,* and Deshmukh *et al*. [7, 10] Olanzapine(52.87%) was most commonly prescribed drug followed by Risperidone(25.28%), this was also found in previous reported study carried out by Dutta et al., Paul *et al*. [7, 11] Atypical anti-psychotics are now rated as first line agents because of their low propensity to cause extra pyramidal side effects, efficacy against refractory cases, better control over negative symptoms, low relapse rate, and safer adverse effect profile, which are similar to those reported in study by Dutta *et al.* Deshmukh *et al.,* [7, 10]

We found that mood stabilizers (26.14%) were mostly prescribed; Lithium and Valproic acid were two of the most commonly prescribed medications for this disorder. In this study, Lithium(61.85%) was the most commonly used mood stabilizer than Valproic acid(38.15%) similar to Pichet Udomratn[12] study and this was contradicted with the studies reported by Karan B. Thakkar *et al.,* Dutta *et al.,* and Rode SB *et al*. [6,7,9]

It was found that antidepressants (26.11%) were prescribed in our study. SSRIs were the most commonly prescribed class of antidepressants followed by SNRIs, which consistent with that reported in previous studies by Dutta *et al.,* Rode SB *et al*. [7,9] Escitalopram(97.36%) and Fluoxetine

(1.32%) were the most commonly prescribed SSRIs which is consistent with previous studies of Dutta *et al*. [7] Desvenlafaxine (1.32%) was belonged to SNRIs were prescribed. SSRIs are generally free of sedative effects and safer at higher doses. Better tolerability, combined with their mild adverse effects accounts for their popularity as the most widely prescribed antidepressants.

Out of total anti-anxiety drugs (16.49%) prescribed, majority were benzodiazepines, which is consistent with that reported in Dutta *et al.,* Rode SB *et al*., [7,9] Clonazepam(83.33%) was the most commonly prescribed followed by Diazepam(16.66%). studies showed that Clonazepam being the most commonly prescribed, like studies reported by Dutta S *et al* [7] **,** the reason for higher rate of prescription of benzodiazepine could be anticipated worsening of anxiety, which is commonly seen with the use of SSRIs.

The drug utilization pattern in our study subjects shows that anti-convulsants (1.37%) constituted a minor portion in BPAD. Drugs like Topiramate and Lamotrigine were prescribed almost equally and they constituted 50%each. Topiramate, which is an anti-epileptic drug, was used exclusively for alcohol dependence.

Mostly number of drugs was prescribed by brand name (77.66%). Prescribers are using brand names for the rational use of drugs. The average number of drugs per prescription is an important index of the scope for review and educational intervention in prescribing practices and was found to be two and at the maximum four.

CONCLUSION

We conclude that BPAD was more prevalent in females between the ages of 20-30 years. Mostly benzodiazepines, Clonazepam, olanzapine and Escitalopram were prescribed in rational terms. Lithium was preferred over valproic acid as a mood stabilizer. Poly pharmacy was limited and rationality of drug use was observed. In our study

the percentage of generic drug prescribed is low, the issue of frequent use of brand names needs to be addressed. More detailed studies are finding to efficacy, adverse reactions and usage of various other psychotropic medication.

BPAD was very much prevalent but limited studies were done in this population. Hence our study conclude that BPAD is a serious public health problem that is frequently under recognised .more studies focussing on the diagnosis, prescription pattern must be performed.

STUDY LIMITATION

- ☑ We did not study the appropriateness of prescription of the psychotropic drugs with regard to the diagnosis and co-morbidities.
- ☑ We did not evaluate factors such as cost, subject compliance, concerns of the subjects about side effects, and adherence to treatment guidelines while prescribing.
- ☑ We did not collect data on the illness factors such as drug compliance, phase of drug treatment.
- ☑ Our study was carried out with a relatively small sample size.

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REFFERENCES

1. Joseph T. Dipiro et al. Pharmacotherapy A Pathophysiologic Approach. Seventh edition MC Graw-Hill. New York 2008: 1158.
2. Mohit P. Chopra et al. The course of bipolar disorder in rural India. Indian Journal of Psychiatry; Oct-Dec 2006; 48(4): 254–257.
3. Michael Bauer et al. Drug treatment patterns in bipolar disorder: analysis of long-term self-reported data. International Journal of bipolar disorder; 2013:1-2.
4. J. k. Trivedi et al. Prescription pattern of mood stabilizers for bipolar disorder at a tertiary health care centre in north India. Indian Journal of Psychiatry 55(2); Apr-Jun 2013: 131-132.
5. Rita Bauer et al. anti depressant dosage taken by patients with bipolar disorder: factors associated with irregularity. International Journal of bipolar disorder; 2013:1-2.
6. Karan B.Thakkar et al. A Drug utilization study of psychotropic drugs prescribing in the psychiatry outpatients department of a tertiary care hospital. Journal of Clinical and Diagnostic Research; Dec 2013; Vol-7(12): 2759-2764.
7. Shaktibala Dutta et al. A psychotropic drug use study among depression patients attending private psychiatric practitioners of Dehradun, Uttarakhand. International Journal of Medical Sciences and Public Health; Vol.4; Issue.5:634.

8. Aksha Memon, Kamlesh Patel. Drug use pattern of antidepreaants agents in psychiatric patients-A prospective study.NHL Journal of medical sciences; july2013; vol.2; issue 2: 33.

9. Sonali B. Rode et al. A Study on drug prescribing pattern in psychiatry out-patient department from a tertiary care teaching hospital. International Journal of basic & clinical pharmacology; May- June2014; Vol.3; Issue3: 517.

10. Dr.Sarang Anantrao Deshmukh, Dr.Teli Saikh Emaran. Evaluation of Psychotropic Drugs Use Pattern among Out Patients Attending Psychiatry Department at Government Medical College and Hospital, Nagpur: A Cross Sectional Study. Int J Pharm Bio Sci; July 2012: 428-436.

11. Pranab Kumar Paul et al. To study the prescribing pattern of antipsychotic drugs in a tertiary care hospital of Assam. Int Pharm Sci; Vol.6; Issue 4; page 435-437.

12. Pichet udomratn. Outpatient drug prescribing pattern for bipolar disorder patient's southern Thailand. ASEAN Journal of Psychiatry; July-Dec 2009; Vol.10:2-3.