Journal of PharmaSciTech
ISSN: 2231 3788 (Print)
2321 4376 (Online)
Research Article

Assessment of Prescribing Patterns, Risk Factors, and Co-Morbidity in Psychiatric Disorders

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Abstract

Antipsychotic prescription patterns are fundamentally different across countries due to variations in factors including health care polices, availability, cost of drugs, and preferred treatment modalities. The burden of illness is enormous although it remains grossly under represented. The objectives of this study were to assess the risk factors and co-morbidities in psychiatric disorders, evaluate the prescribing pattern of antipsychotic drugs and its conformance to treatment guidelines, and study drug related problems. Those patients above 18 years diagnosed with psychiatric disorders for at least 6 months were considered eligible. The adverse effects and prescribing pattern of antipsychotics were evaluated. International guidelines were used to create conformance indicators. 100 patients were enrolled for this study out of which 45% were male and 55% were female. The major population belonged to the age group of 31-40 years and majority of these patients were diagnosed with Bipolar Affective Disorder (BPAD). Diabetes and hypertension were the common co-morbidities. Most patients received a combination of mood stabilizers with antipsychotics. Also, most of the patients on lithium reported tremors and headaches. Among the four selected drugs, order of appropriateness from high to low as per indication was lithium and resperidone followed by olanzapine and sodium valproate. Assessment of risk factors and co-morbidities for psychiatric disorders plays a key role, as a considerable number of subjects posses one or more risk factors. This study emphasizes the need for therapeutic drug monitoring of narrow therapeutic index drugs due to high risk of adverse drug reactions.

Keywords: Psychiatric disorder, co morbidity, treatment pattern, adverse effects

Introduction

Mental disorder might simply be regarded as behavior that is unusual or unacceptable to most people in society during the lifetime of the patient [1]. The psychiatric co-morbidity may be defined as the co-occurrence of two psychiatric disorders simultaneously or sequentially [2]. These individuals form an important and challenging subset of population associated with poorer outcomes in various clinical domains, including increased risk of relapse, re-hospitalization, suicide and violence, medical co-morbidity, family discord, and economic burden [3]. Hence, there is an urgent need for mental health education of the public, improvement of professional training, and the development of mental health services.

Antipsychotic prescription patterns are fundamentally different across countries and even regions due to variations in factors including health care policies, availability and cost of drugs, psychiatric training, and preferred treatment modalities. To improve psychiatric services, a large number of countries throughout the world have developed their own guidelines for treatment [4]. Such guidelines generally acknowledge that there is a lack of evidence to support the routine use of combined antipsychotics. However there is an increasing prevalence of antipsychotic drug combination with an increased risk of adverse drug reactions [5].

The burden of illness resulting from psychiatric and behavioral disorders is enormous, although it remains grossly under represented by conventional health statistics, which focus on mortality rather than morbidity or dysfunction [6]. The areas where regulatory policies can improve the prescribing pattern and outcomes are needed to be identified.

Therefore, this study aims to assess the risk factors and co-morbidities that influence psychiatric disorders, to evaluate the prescribing pattern in conformance to American Psychiatric Association treatment guidelines [7-8] and to study drug related problems in psychiatric patients.

Materials & Methods

This open-labeled prospective observational study was conducted at the Department of Psychiatric Medicine in a 900 bedded multispecialty teaching hospital located in the southern region of Tamil Nadu for a period of 1 year; October 2013-2014. Approval of the Institutional Ethics Committee was obtained prior to initiation of the study. The patients were informed about the study in local language and written consent was obtained from those who were willing to participate.

Those patients above 18 years, diagnosed with psychiatry disorder for at least 6 months, were considered eligible for the study. Patients with pregnancy, lactation, alcohol dependence without psychiatric disorder, and substance abuse were excluded. Patient demographics such as age, social history, family history, BMI, co morbidities, disease duration, treatment regimen and its cost were documented from the case sheets. The adverse effects and prescribing pattern of the antipsychotics were evaluated. International guidelines were used to create conformance indicators.

The different variables on which the patients were categorized were statistically analyzed by unpaired t-test using graphpad, 4.3 version (San Diego, USA). $P < 0.05$ was considered as the level of significance between the groups.

Results and Discussion

A total of 100 patients were enrolled in the study out of which 2 patients were in the age group of < 20 years, 26 patients were in 21-30 years, 32 patients in 31-40 years, 18 patients in 41-50 years, 15 patients in 51-60 years, and 7 patients were in 61-70 years. Most of the patients enrolled in the study were females (45.0%) compared to males (55.0%).

Mean (BMI) Body mass index was found to be 23.11 $\pm$ 4.76 kg/m2. Out of 100 patients, 10% were under-weight, 66% patients had (BMI) Body mass index in the normal range and 20% patients were found to be overweight. Only 4% patients were found to be obese.

Based on the diagnosis, the patients were categorized into different groups depending on the kind of psychiatric disorder viz., Schizophrenia, Bipolar Affective Disorder (BPAD), and Depression. 18 patients enrolled in the study suffered from Schizophrenia, 71 patients from Bipolar Affective Disorder, and 11 patients from Depression.

The most common co-morbidities were diabetes mellitus, hypertension, and thyroid diseases (Figure 1).

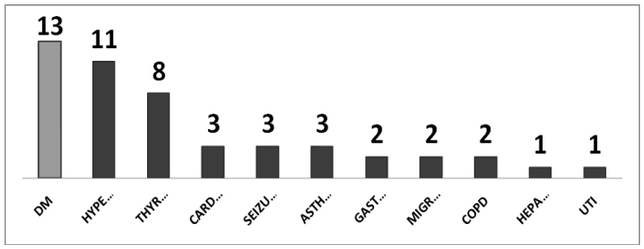

Figure 1: Co-morbidities in psychiatry patients

DM: Diabetes Mellitus; ASTH: Asthma; HYPE: Hypertension; GAST: Gastrology related diseases; THYR: Thyroid; MIGR: Migraine; CARD: Cardiovascular diseases; COPD: Chronic Obstructive Pulmonary disease; SEIZU: Seizures; HEPA: Hepatitis; UTI: Urinary Tract Infection

Monitoring of lithium therapeutic range Out of 100 patients, 46 were on lithium in the dose range of 400-600 mg/day. Of this 46.39 were in normal therapeutic range, 2 were in abnormal range and 5 patients were not monitored.

Monitoring of sodium valproate therapeutic range Out of 100 patients, 38 patients were on sodium valproate in the dose of 200-500mg/day, out of which, 5 were in normal therapeutic range, 2 were in abnormal range, and 31 were not monitored.

Adverse effects Adverse events are the unexpected reactions during one's treatment, where there is need to re-challenge or de-challenge the drug therapy. Most of the patients on lithium reported tremors and headache as the most common side effect (Table 1).

Table 1: Patients reported side effects of lithium during pharmacist interaction

Observed side effects	Number of side effects	Percentage Observed (%)	Theoretical Reported (%)
Sedation	2	4.3	20
Acne	3	6.5	5
EPS	4	8.7	1
Vomiting	4	8.7	10
Weight Gain	5	10.9	20
Nausea	5	10.9	3
Headcahe	21	45.7	2
Tremors	27	58.7	60

During the pharmacist interaction, the commonly reported side effects of olanzapine were dry mouth and increased appetite (Table 2). The major side effects reported by patients on sodium valproate were fatigue, ataxia, and thrombocytopenia (Table 3). Patients on risperidone reported edema and weight gain as the common side effects (Table 4).

Prescribing pattern of drugs The prescribed drugs were categorized into different classes based on pharmacological classification. Results showed that 100 patients were prescribed cumulatively with 129 antipsychotics drugs from one or more classes: 13 antidepressants, 38 anti-convulsants, 46 anti-mania drugs, 23 anti-parkinsonian drugs, and 28 other medications.

Table 2: Patients reported side effects of olanzapine during pharmacist interaction

Observed side effects	Number of side effects	Percentage Observed (%)	Theoretical Reported (%)
Akathesia	4	7.6	20
Appetite	14	26.9	50
Dry mouth	19	36.5	5
Dizziness	4	7.6	50
Tachycardia	9	17.3	30

Table 3: Patients reported side effects of sodium valproate during pharmacist interaction

Observed side effects	Number of side effects	Percentage Observed (%)	Theoretical Reported (%)
Rash	1	2.63	10
Dyspepsia	3	7.8	12
Fatigue	9	23.6	50
Thrombocytopenia	3	7.8	12
Ataxia	3	7.8	20
Diarrhoea	1	2.63	9

Table 4: Patients reported side effects of resperidone during pharmacist interaction

Observed side effects	Number of side effects	Percentage Observed (%)	Theoretical Reported (%)
Weight gain	2	7.6	20
Edema	11	15.3	50
Blurred vision	1	3.8	20

Lithium turned out to be most frequently prescribed mood stabilizer and sodium valproate second in the hierarchy of prescription. Benzodiazapines were the least frequently prescribed drugs.

Olanzapine (38 patients) was the most commonly prescribed drug for patients on single antipsychotic therapy (70 patients). For patients on dual anti psychotic therapy (22 patients), the most commonly prescribed drug was a combination of olanzapine and haloperidol (5 patients). Two patients were on triple antipsychotic therapy, i.e., a combination of olanzapine, haloperidol, and resperidone.

11 patients were on antidepressant therapy out of which 2 patients were on a combination of sertaline and escitalopram. The commonly prescribed antidepressant was venlafaxine (3 patients). The most commonly prescribed benzodiazepine was clonazepam (5 patients).

Psychiatric risk assessment Altered sleep (76%) was found to be the most common risk factor followed by stress (64%) as per the brief psychiatric rating scale (Figure 2) [9].

Usage of drugs The usage of drugs was evaluated based on prescriber indicators. The percentage of appropriateness and inappropriateness of each specification of prescriber and consumer indicators are discussed with respect to indication, dose, adverse effects, contraindication, and drug-drug interaction.

Appropriateness of usage of lithium and sodium valproate is shown in Table 5 and appropriateness of usage of olanzapine and resperdione is given in Table 6.Process of indicators: Drug lithium was given to 46 patients, among them it was indicated for mania in 10 (21%), bipolar affective disorder in 26 (56%), and schizophrenia in 6 (13%) patients, which was found to be 89% appropriate as per the study criteria.

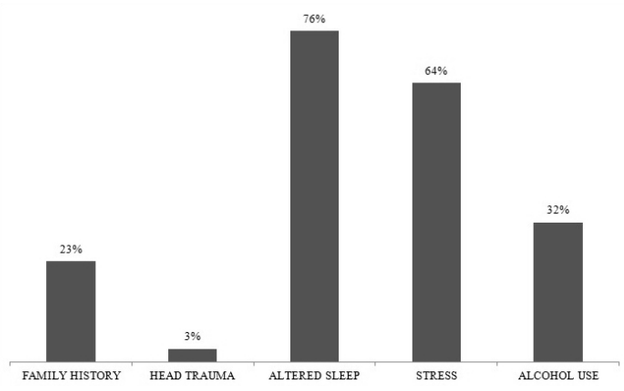

Figure 2: Psychiatric risk assessment in patients

Table 5: Appropriateness of usage of lithium and sodium valproate

Indicators	Tab. Lithium (N = 46)		Tab. Sodium valproate (N = 38)	
	Appropriateness N (%)	Inappropriateness N (%)	Appropriateness N (%)	Inappropriateness N (%)
Indication	41(89)	5(11)	33(87)	5(13)
Dose	46(100)	0	38(100)	0
Contraindication	44(96)	2(4)	30(79)	8(21)
Adverse Effects	16(35)	30(65)	18(47)	20(53)
Drug- drug interaction	42(91)	4(9)	30(79)	8(21)

Table 6: Appropriateness of usage of olanzapine and resperdione

Indicators	Tab. Lithium (N = 52)		Tab. Sodium valproate (N = 19)	
	Appropriateness N (%)	Inappropriateness N (%)	Appropriateness N (%)	Inappropriateness N (%)
Indication	47(90)	5(10)	19(100)	0
Dose	52(100)	0	16(84)	3(16)
Contraindication	44(85)	8(15)	17(89)	2(11)
Adverse Effects	33(63)	19(37)	3(16)	16(84)
Drug- drug interaction	47(90)	5(10)	16(84)	3(16)

Data was analyzed by student t-test, ** representing $P < 0.01$ (level of significance). Among 38 patients, drug sodium valproate was indicated for mania in 26(56%) and bipolar disorder in 10 (26%) patients, which was found to be 87% appropriate as per study criteria.

Drug olanzapine was given to 53 patients, among them it was indicated for mania in 7 (12%), bipolar affective disorder in 31(59%), and schizophrenia in 11(19%) patients, which was found to be 90% appropriate as per the study criteria. 10% inappropriate use of olanzapine was for depression in 5(10%) patients.

Among the 13 patients, Drug Resperidone was indicated for schizophrenia in 12 (92%) and depression in 1(7%) patient, which was found to be 100% appropriate.

All the data was analyzed by student t-test.

Dose: Under and over dosing affect the efficacy and safety of drug. The correct dose is required to attain therapeutic effect and to minimize adverse events for a specific drug.

In case of lithium, oral dose range was 900-2400 mg/day in divided dose. The dose range of drug olanzapine was 30-50mg/day, which was indicated for schizophrenia and bipolar as per the study criteria. Both lithium and olanzapine were given in correct dose; hence appropriateness was 100% for these drugs. For Resperidone, the appropriate usage was 84% as per APA Guidelines. Data was analyzed by student t-test.

Contraindications: Contraindication is a condition or factor that might contraindicate or interfere with chosen therapy. Drug lithium and sodium valproate were contraindicated in renal disease, cardiac disease, hepatic disease, and liver disease. Lithium was given to 46 patients out of whom 2 patients were contraindicated. Hence it was taken as inappropriate for 4% patients and appropriate for 96% patients. Sodium valproate was given to 8 (21%) patients with hepatic disease which was inappropriate as per study criteria. Drug olanzapine and Resperidone are contraindicated in seizures, dyslipedemia, epilepsy, and Parkinsonism. Drug olanzapine was given to 8(15%) contraindicated patients and resperidone was given to 2(11%) contraindicated patients. Data was analyzed by student t-test

Drug-Drug interaction: Interacting drugs were prescribed with lithium in 5 patients. Out of that, we found 3 patients who were prescribed with an interacting drug Tab. Chlorpromazine (minor interaction) and 2 patients were prescribed with interacting drug Tab. Haloperidol (moderate interaction).Therefore 42(91%) patients, who were prescribed without interacting drugs, were considered to be in appropriate therapy as per APA Guidelines. Sodium valproate was co administered with interacting drugs in 8(21%) study subjects. Therefore, it was classified as inappropriate as per study criteria. Drug olanzapine had mild interaction with omeprazole in 5(10%) patients. Resperidone, when co administered with Sertraline in 3(16%) study subjects, caused minor interactions. Data was analysed by student t-test.

In this study, a total of 100 patients were enrolled, among which 45% were males and 55% were females. The major population came under the age group of 31 – 40 years. Patients with normal BMI were found to be high, followed by overweight patients. Majority of the patients were diagnosed as BPAD, while depression and schizophrenia was found to be in lesser number of patients. Diabetes and hypertension were the common co-morbidities.

Risk factors for psychiatric disorders such as altered sleep and stress contributed the highest proportion. Familial history of psychiatric illness and alcoholism were also identified as risk factors, which contributed up to 23% and 32% respectively. In our study, major depression was found to be more in females and onset age was more than 30 years. Similar results were observed in the study conducted by Hirschfeld & Myrna, which reported that the risk factors for major depression were female gender followed by familial history, social, and environmental factors. But age of onset was between 25 – 30 years [10]. In the same study, the result showed that the onset age of BPAD is earlier than depression. Similar results were observed in this study which showed the age of onset of BPAD was 21-30 years. Schizophrenia occurs in early adulthood but rarely before adolescence or after 40 years [10].

Among the 100 patients, 46 patients received lithium therapy in a dosage of 400 – 600 mg/day, out of which monitoring was not done for 5 patients. Due to its narrow therapeutic index and wide range of side effects, lithium therapy should be monitored frequently through plasma lithium concentrations. A 30% reduction in the side effects has been reported in patients treated with average lithium levels of 0.68 mEq/L in comparison to those with levels of 0.85 mEq/L as reported by Peet & Pratt [11]. This study also shows that patients with high plasma lithium levels presented more side effects.Similarly, in our study, patients with high plasma concentration of lithium have shown more side effects and therefore lithium therapy was discontinued. Hence, elevated plasma lithium levels were also a cause of side effects. In this study, tremors and headaches were the common side effects of lithium while nausea,

weight gain, vomiting, EPS (Extra Pyrimidal symptom),acne, and sedation were found to be less common. According to APA guidelines, in theory, tremors were the most common side effect, followed by sedation, weight gain, and vomiting [7-8]. But sedation and weight gain were found to be less frequent in our study. This difference should be confirmed on a larger population. Peet and Pratt stated that these side effects are dose dependent and can be managed by dose adjustment [11]. Another common side effect was hypothyroidism, though not observed in this study usually appear after 6 – 16 months of lithium intake as stated by Johnston & Eagles [12].

Out of 100 patients, sodium valproate was taken by 38 patients in the dose range of 200 – 500 mg/day and most of the patients were not monitored for plasma valproate level. Fatigue was the most common side effect observed, followed by dyspepsia and ataxia in the equal proportion. Rash and diarrhea were the less commonly observed side effects. Similar fashion was found theoretically as per APA guidelines [7-8]. Lithium and valproate were the first line drugs being used for BPAD in this study.

Among the drugs prescribed, antipsychotics were of higher proportion, whereas, benzodiazepines and antidepressants were least prescribed. We also observed that, lithium & valproate were mainly prescribed for BPAD; olanzapine, haloperidol, & resperidone were commonly used for schizophrenia and sertraline, venlafaxine, & escitalopram were commonly used for depression. Similar results were reported by Neela et al who observed that antipsychotics were mostly prescribed alone and benzodiazepines were usually prescribed in combination with antipsychotics [13].

Monotherapy with single antipsychotic agents was prescribed for 70 study subjects, among which olanzapine and quetiapine were prescribed in majority of study subjects. Dual antipsychotic therapy with two antipsychotic medications was observed in 22 study subjects with olanzapine plus haloperidol being the most common combination prescribed. Schorr S C et al observed similar results where patients were mostly prescribed with anti psychotics [14]. But it was followed by benzodiazepines (38%) and anticholinergics. In our study, benzodiazepines were given to least proportion of patients.

It was found that highest number of patients received a combination of mood stabilizers with antipsychotics, which highlights the need for initial symptomatic management and also complaints of presentation. Among the four selected drugs, the order of appropriateness from high to low as per indication was lithium and resperidone followed by olanzapine and sodium valproate. Only resperidone had inappropriate usage with respect to dose. Lithium was most appropriately used while sodium valproate usage was least appropriate with respect to both contraindications and drug- drug interactions. Differences in prescribing pattern exist due to different educational backgrounds,habits and personal beliefs, and perhaps the physicians experience as well as the type of patient treated as stated by D Sternik et al [15].The small sample size of our study is a limitation. Details of patients' illness, indication for prescribing high dose combination, the response to drugs, and long term side effects were not determined.

Conclusion

Assessment of risk factors and co-morbidities for psychiatric disorders play a key role as it was noted that a considerable number of study subjects posses one or more risk factors. Among the drugs included in this study, lithium related adverse drug reactions were observed to be relatively higher. This study emphasizes the need for therapeutic drug monitoring of narrow therapeutic index drugs, especially mood stabilizers due to their high risk of adverse drug reactions. Also, combination therapy without proper monitoring can lead to polypharmacy. The Clinical pharmacist plays a crucial role in this scenario to prevent and manage undesirable effects of the medicines.

Conflict of interest

The authors do not have any conflict of interest.

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