Research Article

Prescribing Pattern of Medications that induce Extra Pyramidal Symptoms and Weight Gain in Psychotic Patients

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ABSTRACT

The objective of the study is to assess the prescribing pattern of drugs that induces Extra Pyramidal Symptoms (EPS) and weight gain in psychotic patients under treatment. A descriptive-observational study was carried out in the psychiatry department of MVJ medical college and research hospital for a period of six months. A total of 105 in-patients were enrolled into the study after fulfilling the study criteria and obtaining informed consent. The prescription pattern was analyzed and the various medication related problems were identified. The obtained data were analyzed descriptively and statistically. A total of 105 psychotic patients were enrolled into the study. On analyzing the prescription, most of the patients were prescribed with more than 3 drugs. Majority of the patients were prescribed with 3 psychotropic drug (43.80%) in which antipsychotics were prescribed to all the patient. The most commonly given combination of psychotropic drugs are antipsychotic- anti anxiety (42.85%). 70.48% of the study population was on antipsychotic mono therapy. Majority of the patients were taking only atypical antipsychotics (83.80%). Prescribing error (32.38%) was the commonly seen medication error followed by dispensing error. There were a total of 353 interactions identified, out of which 61 were major interactions. Our study showed that extra pyramidal symptoms and weight gain are still serious side effects of the treatment of various psychotic disorders. This is confounded by various factors like medication error, drug-drug interaction, poly pharmacy. The clinicians can be advised to compare the benefit risk ratio based on the needs of the individual patients and thereby choosing an appropriate drug with optimum therapeutic efficacy and low toxic effect. The patients should be advised to control their diet and to involve in physical activities when under treatment to control unnecessary weight gain.

Keywords: Psychotic disorders, Extra pyramidal symptoms, Weight gain, Antipsychotics.

INTRODUCTION

Psychotic disorders are severe mental disorders that cause abnormal thinking and perceptions. People with psychosis lose touch with reality. They make it hard for someone to think clearly, make good judgments, respond emotionally, communicate effectively, understand reality, and behave appropriately.[1] Two main symptoms are delusions and hallucinations. When symptoms are severe, people with psychotic disorders have trouble staying in touch with reality and often are unable to handle daily life.[2] The two important forms of treatment for patients with psychotic disorders are medication therapy and psychotherapy. The main medications which are used to treat psychotic disorders are antipsychotics.[3]

Extra pyramidal side effects are the type of drug reactions that occurs due to interactions with the extra-pyramidal system in our body. Extra pyramidal symptoms (EPSs), such as akathisia, dystonia, psuedoparkinsonism, slurred speech, anxiety, distress, paranoia, and bradyphrenia and dyskinesia are drug-induced side effects that can be problematic for persons who receive antipsychotic medications (APMs) or other dopamine-blocking agents.[4] The clinical manifestations include a number of atypical involuntary muscle contractions that influence gait, movement, and posture. The EPS are caused by dopamine blockade or depletion in basal ganglia; this lack of dopamine often mimics idiopathic pathologies of EPS. Dopamine-blocking drugs such as the antipsychotics (both typical and atypical) and some anti-emetic drugs are the most recognized causes of secondary extra pyramidal movement disorders. The symptoms can develop acutely, be delayed or overlap making diagnosing a challenge.[5]

In general, the life expectancy of patients with severe mental illness (SMI) is reduced compared with the general population. The body weight gain in psychiatric population is a common clinical challenge. Many patients suffering from mental disorders, when exposed to psychotropic medications gain significant body weight with or without other side effects. Being overweight or obese has been acknowledged as a public health problem due to its correlation with mortality and increased co-morbidity of other physical disorders.[6] This association requires new paradigms of management of psychiatric disorders that take into account co-morbid physical disorders like atherosclerosis, lipid dysfunction. Long term use of antipsychotics (AP) is associated with increased mortality risk in people with SMI. In general, it is concluded that AP add to the increased mortality risk of people with SMI either through direct cardio toxic effects or by impacting on weight gain.7 Additionally, this weight-gain may create added psychological or physiological problems that need to be addressed. Thus it is important that the clinicians treat all the problems

on an individual basis by taking precautions to monitor and control weight gain.

An Indian Psychiatric epidemiological study suggests that about 20% of the adult population in the community is affected with one or the other psychiatric disorder. According to a survey in 2015, overall population have 14.9/1000 prevalence of mental illness. It is higher in rural setting 17.1/1000 than urban 12.7/1000 ($P < 0.001$). There is a strong correlation found with age in rural ($\varrho = 0.910$, $P = 0.001$) and urban ($\varrho = 0.940$, $P = 0.001$).[8] As the numbers of psychiatric disorders is increasing, the prevalence rates of side effects due to psychotropic drugs are also increasing. In addition, poly-pharmacy, which is the prescribing for a single person with more than one drug of the same chemical class (such as antipsychotics), is widely practiced despite little empirical support, and can result in serious adverse reactions and intensified side effects and can lead to early death.

Combination therapy used in psychiatric practice makes drug interactions more likely and increases the risk of adverse outcomes to patients. Even ADRs that are deemed to be "not severe" can have significant impact on the patients with a psychiatric illness, as a growing body of evidence suggests a strong relationship between drug-drug interactions, treatment failures, and higher healthcare costs due to avoidable medical complications.[9] ADRs resulting from drug-drug interactions leading to hospitalization are often preventable. While only a few of the possible drug interactions may be clinically relevant, the practitioner still must consider critical factors associated with drug-drug interactions. Such factors include the potency and concentration of the drugs involved the therapeutic index balance between efficacy and toxicity, the presence of active metabolites, and the extent of the metabolism of the substrate drug.[10]

In Indian scenario, the people with mental illness are seen as outcast and it further causes psychological issues. The side effects EPS and weight gain associated with the treatment of psychotic disorders will cause psychological damage as well as prolong the hospital stay which is troublesome for the patient. Hence, this project titled "Prescribing pattern of medications that induce extra pyramidal symptoms and weight gain in psychotic patients" is important to study the extent to which patients are getting affected by the side effects of drugs used for the treatment of psychotic patients and how they hinder the proper management of diseased condition. The study helps to identify the common medication errors and drug –drug interactions that can lead to increased risk of side effects.

MATERIALS AND METHODS

Ethical approval

The protocol relating to the current study of drug induced extra pyramidal symptoms and weight gain in psychotic patients under treatment was submitted to the ethical committee of MVJ Medical College and Research Hospital, Hoskote for the ethical approval. The study was accepted by the board of members and the ethical clearance certificates were issued on 22.09.16 with certificate number MVJ MC &RH/02/2017.

Study Design

Descriptive observational study.

Study Period

Six months

Study site

Department of Psychiatry, MVJ Medical College & Research Hospital, Bangalore, South India

Study Population

105 In-patients

Sample Technique

Convenient sampling technique

Source of data

Patient Case Records, Laboratory Reports, Doctors, Nurse, Patient's representative, patients

Study Criteria

➢ **Inclusion Criteria**

- All in-patients who were diagnosed as suffering from psychosis, schizophrenia, bipolar disorder and other psycho-affective disorders as per ICD 10 criteria
- All in-patients of either gender and aged from 18 to 65 years

➢ **Exclusion Criteria**

- The patients who were unwilling to participate in the study
- The patients who did not give informed consent
- The patients who were having neuro-psychiatric disorders which can manifest as extra pyramidal symptoms
- The patients who were pregnant
- The patients who are already taking medications other than anti-psychotic medications which were either known to cause or causing weight gain
- The patients with endocrine disorders (Hypothyroidism, Cushing's syndrome)

Study instruments

- Informed Consent Form
- Patient Case Report Form
- Standard Reference for drug-drug interaction (Medscape, Lexicomp And Stockley's Drug

Interaction)

Procedure

All in-patients in the psychiatry department of MVJ MC&RH who meet the study criteria were enrolled into the study after taking informed consent. Clinical, demographic and medication related details were documented in the pre designed special case reporting form for the study. The prescription was analyzed to understand the pattern. The potential drug- drug interactions were assessed using standard references and checked for clinical significance. All prescriptions were audited for medication errors. Data analysis & reporting using descriptive analysis and statistics.

Analysis of data

The data obtained from the patients were analyzed using basic descriptive analysis using Microsoft Word Excel 2010.

RESULTS AND DISCUSSION

The study was conducted among in-patients who were suffering from psychotic disorder for a period of 6 months. A total of 105 patients were enrolled into the study and the prescribing pattern was analyzed.

Distribution based on the number of drugs prescribed

Poly-pharmacy is a commonly seen practice in psychiatric department. The concurrent administration of many drugs increases the risk of its side effects. In our study the trend of poly-pharmacy is followed. Majority of the participants were prescribed with 3 drugs (29.50%) followed by 4 drugs (25.70%), 2 drugs (20%) etc.

Distribution based on the number of psychotropic drugs prescribed

Psychotropic drugs are used for the treatment of any of the psychiatric disorders. There are various categories of psychotropic drugs. Usually a combination of various psychotropic drugs is used for the treatment of various symptoms of a psychiatric disorder. In our study, majority of the participants were prescribed with 3 psychotropic drugs (46 participants, 43.8%) concurrently, followed by 2 psychotropic drugs (30.47%), more than 3 psychotropic drugs (18.09%) and very few were prescribed with just a single psychotropic drug (7.60%).

Distribution based on various psychotropic drugs prescribed

The commonly used psychotropic drugs in psychiatric department are antipsychotics, antidepressants, anti-anxiety, stimulants and mood stabilizers. In our study on psychotic patients, all the participants were prescribed with antipsychotics. Anti-anxiety drugs were used in majority of the participants (74.24%), followed by anti depressants and mood stabilizers (Table 1).

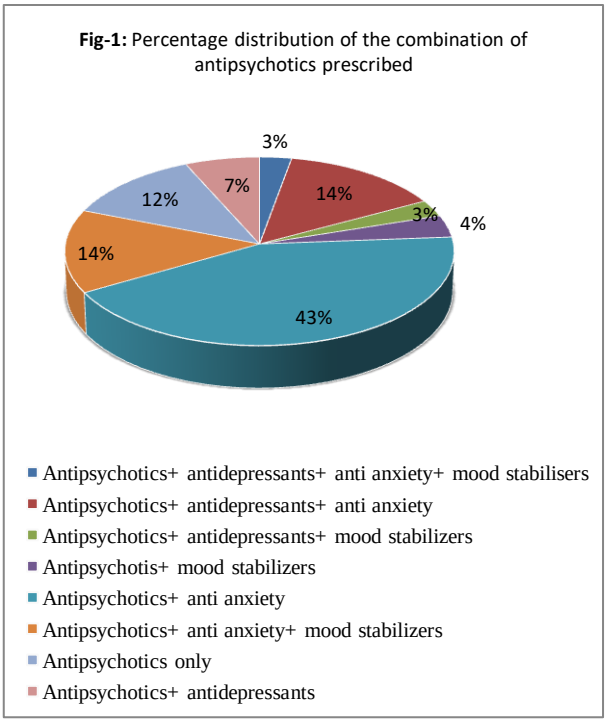
Table 1: Distribution based on the number of various psychotropic drugs prescribed

Psychotropic drug	Number of participants (n=105)
Antipsychotics	105
Antidepressants	28
Anti anxiety	78
Mood stabilizers	25

Prescribing pattern of various psychotropic drug combinations

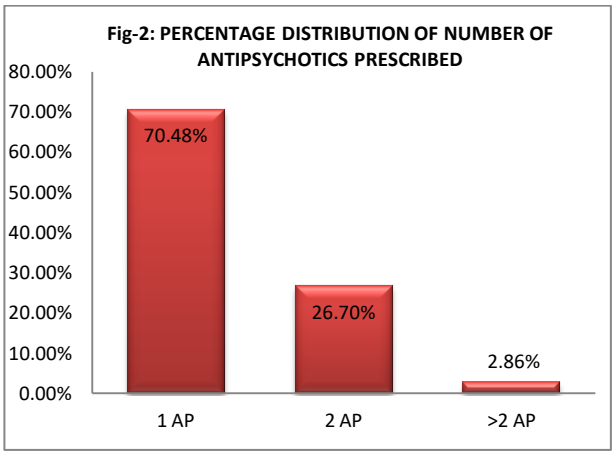
In our study population, the most commonly used combination of psychotropic drugs are antipsychotics+ anti anxiety (45 participants). The least commonly used combination was found to be antipsychotics + antidepressants + anti anxiety + mood stabilizers and antipsychotic + antidepressant + mood stabilizers (figure-1).

Fig-1: Percentage distribution of the combination of antipsychotics prescribed



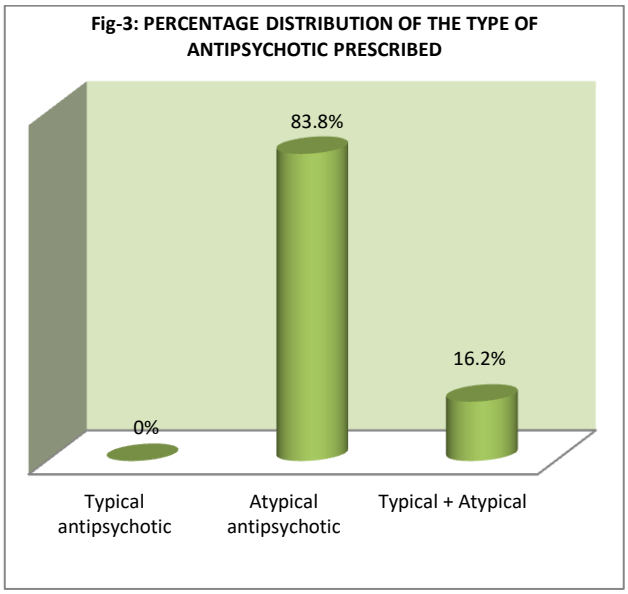
Distribution based on the number of antipsychotics prescribed

It is a common practice to prescribe only one antipsychotic at a time but sometimes more than one antipsychotic is prescribed concomitantly. In our study population, majority of the participants are prescribed with only one antipsychotic drug (74 participants), followed by the use of 2 antipsychotic medication. The use of more than 2 antipsychotic drugs is rarely seen (figure-2).



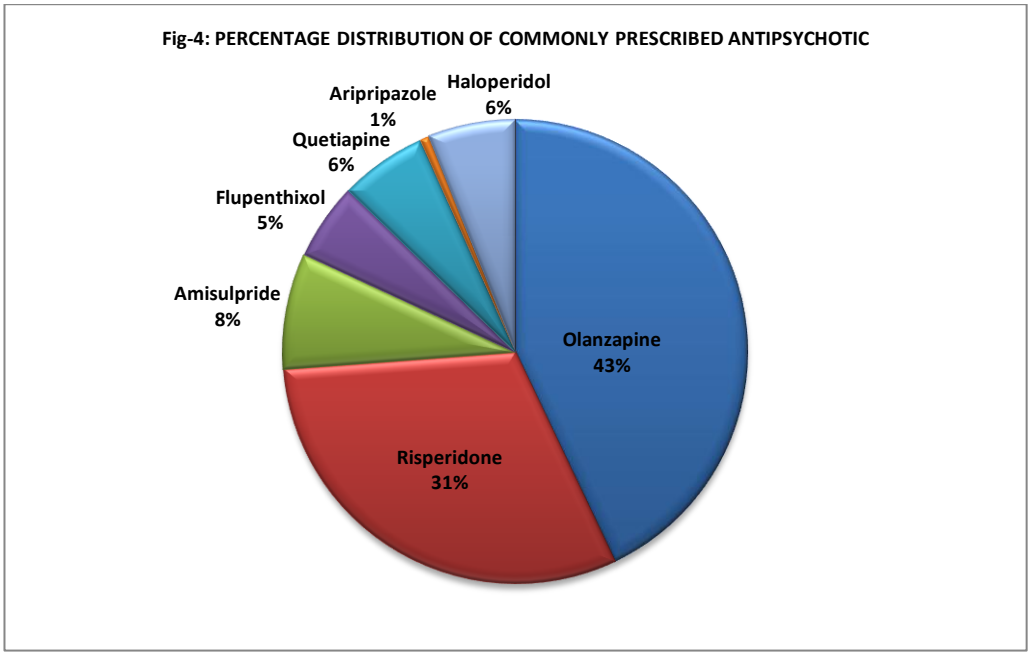
Distribution based on the type of antipsychotic prescribed

Antipsychotics are classified as typical antipsychotics and atypical antipsychotics. The various ways in which these antipsychotics can be prescribed are typical antipsychotics alone, atypical antipsychotics alone or a combination of typical and atypical antipsychotic. On analyzing our study population, majority of the participants were prescribed with atypical antipsychotics alone (83.8%), followed by a combination of typical and atypical antipsychotics (16.2%). None of the participants were prescribed with typical antipsychotics alone (figure-3).



Distribution of commonly used antipsychotics

In our study population, the most commonly prescribed antipsychotic was olanzapine (64 participants), followed by risperidone, amisulpride, quetiapine, haloperidol, flupenthixol and aripiprazole (figure-4).



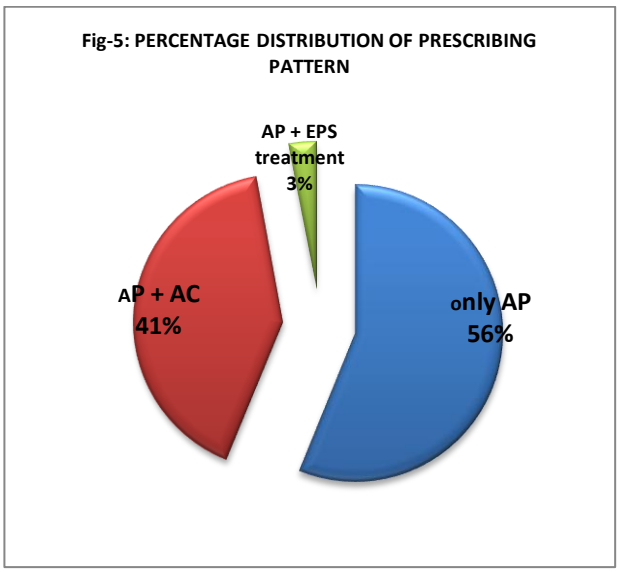
Distribution based on the prescribing pattern of antipsychotics

Antipsychotics, irrespective of the class typical or atypical, have the risk to produce extra pyramidal side effects. Anti cholinergic drugs are sometimes prescribed along with antipsychotics to reduce the incidence of EPS. In our study population 56% of the participants were prescribed only antipsychotics, 41% were prescribed with a combination of antipsychotic and anti cholinergic and 3% were prescribed with antipsychotics+ treatment for EPS (figure-5).

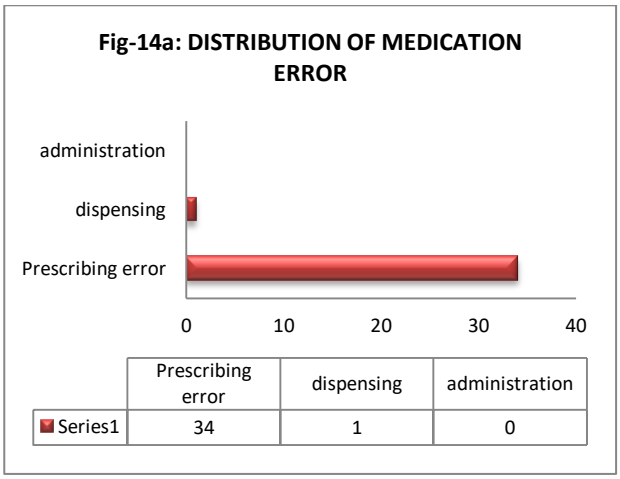
Analysis of medication error

The study prescriptions were analyzed for various medication errors such as prescribing error, dispensing error, administration error, drug duplication, and unintended prescribing. The most commonly seen medication error is prescribing error (32.38%) in which spelling mistake (30 prescriptions) was predominant,

followed by illegibility (8 prescriptions) of the prescription (Figure -6).



Medication errors can lead to unwanted problems such as error in dosing can lead to either over dosing or sub therapeutic dosing of the drug. In our study the commonly seen medication error is prescribing error which was seen in 32.38% of prescriptions followed by dispensing error in 0.95% of prescriptions. Out of the prescribing error 88.23% had spelling mistake and 23.53% had illegible writing which was in account with the study done by Jean Stubbs et al (2006) where prescription writing error (77.4%) was the most common.[11]



Drug – Drug Interaction

The drug- drug interactions in the prescriptions were assessed using standard references such as Stockley's drug interaction, Medscape drug interaction and Lexicomp online drug interaction. They were then categorized as major, moderate and minor depending on its clinical significance. On analyzing the prescription of study participants, 91% of prescriptions had interactions, moderate interactions were found to be common and predominant (284 interactions), followed by major (61 interactions) and minor (8 interactions) drug interactions.

The most commonly seen drug- drug interactions are lorazepam+ olanzapine, lorazepam + risperidone, risperidone+ trihexyphenidyl. These drug interactions can be beneficial as well as can increase the risk of side effects (Table-2).

Table-2: Distribution of commonly observed drug- drug interaction

Drug- drug interaction	Clinical significance	Number of participants(n=105)
Lorazepam + Olanzepine	Moderate	28
Lorazepam + Risperidone	Moderate	22
Risperidone + Trihexyphenidyl	Moderate	17
Lorazepam + Trihexyphenidyl	Moderate	15
Olanzepine + Trihexyphenidyl	Moderate	14
Haloperidol + Lorazepam	Moderate	10
Lorazepam + Valproic acid	Major	7
Haloperidol + Olanzapine	Moderate	7
Clonazepam + Mirtazepine	Moderate	6
Risperidone + Valproic acid	Moderate	6
Lithium + Lorazepam	Moderate	5
Olanzapine + Valproic acid	Moderate	5
Olanzapine + Fluvoxamine	Moderate	4
Amisulpride + Risperidone	Major	3
Amisulpride + Olanzapine	Major	3
Clonazepam + Olanzapine	Major	3

In the current study, a total of 353 drug– drug interactions were identified out of which 61 were major interactions. The most commonly seen interactions are lorazepam-olanzapine, lorazepam- risperidone, risperidone-triheyxphenidyl, lorazepam-valproic acid. Previous study done by Tarun jain et al (2011) had already shown that clinically relevant drug interactions may occur with many couples of psychotropic drugs like olanzapine- haloperidol, risperidone- valproic acid, lithium –antipsychotics .[12] These drug interactions increase the risk of side effects associated with the drugs.

The main limitation of the study is the sample size. A larger sample size is required to analyze the trend of how the EPS development and weight gain due treatment of psychotic patients is distributed.

CONCLUSION

Our study showed that extra pyramidal symptoms and weight gain are serious side effects of the treatment of various psychotic disorders. This is confounded by various factors like medication error, drug- drug interaction, poly pharmacy. It is seen in our study that many of the prescriptions had drug interactions and it can increase the risk of EPS and weight gain Even though the simultaneous use of antipsychotics and anticholinergics are prescribed, the extrapyramidal symptoms are prevalent. The best way to manage is by trying to control and reduce the confounding factors. Poly pharmacy should be avoided where ever possible. The best drug with therapeutic efficacy and low toxic effect should be selected on the basis of the needs of patient.

Second generation antipsychotics are known to cause weight gain and the concomitant use of other psychotropic drug increases the risk of weight gain in such patients. The clinicians can be advised to compare the risk of weight gain to the benefit of treatment before selecting the appropriate drug for the patient. The patients should be advised to control their diet and to involve in physical activities when under treatment to control unnecessary weight gain.

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