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RESEARCH ARTICLE

Drug utilization study of antipsychotic drugs in the psychiatry outpatient department of a tertiary care hospital

Aashal Shah[1], Richa Verma[2], Preeti Yadav[3], Jayshree Patel[3]

[1]Department of Pharmacology, GMERS Medical College, Valsad, Gujarat, India, [2]Drug Safety Physician, Parexel International Ltd, Chandigarh, India, [3]Department of Pharmacology, Government Medical College, Surat, Gujarat, India

Correspondence to: Preeti Yadav, E-mail: aashal_167@yahoo.co.in

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ABSTRACT

Background: Prescribing pattern of antipsychotics has changed over the decade with availability of newer antipsychotics. **Aims and Objectives:** This study aims to analyze the utilization pattern of antipsychotics at our hospital. **Materials and Methods:** A retrospective study of case files of patients receiving antipsychotics was carried out in the psychiatry outpatient department of new civil hospital, Surat, for a period of 6 months. Pattern of antipsychotic prescription, the World Health Organization (WHO) prescribing indicators, defined daily dose (DDD)/1000 inhabitants/day (DID), prescribed daily dose (PDD), and the PDD-to-DDD ratio were assessed. **Results:** A total of 2115 drugs were prescribed in 631 prescriptions, of which 804 (38.01%) were antipsychotics. Schizophrenia (55.31%) was the most common diagnosis. Sedative-hypnotics (30.23%) were the most common coprescribed drug group. Atypical antipsychotics were more commonly prescribed – olanzapine: 47.39%, risperidone: 27.49%, clozapine: 13.06%, and others: 12.06%. The average number of antipsychotics/prescription: 1.29 ± 0.53; prescribing of antipsychotics by generic name: 95.02%; prescribing from the WHO essential medicines list: 43.66%; prescribing from National List of Essential Medicines: 47.89%; prescribing for injections of antipsychotics: 0.62%; prescriptions of fixed-drug combinations: 0.50%, and DID of antipsychotics: 0.014 mg. PDD-to-DDD ratios for trifluoperazine, ziprasidone, amisulpride, and clozapine were <1, while for risperidone and haloperidol, it was =1 and for olanzapine and aripiprazole, it was >1. **Conclusion:** The second-generation antipsychotic olanzapine was the most commonly prescribed antipsychotic. The prescriptions were complete and followed principles of rational prescribing in majority of cases. Prescribing the drugs available from hospital supply will decrease cost of therapy in chronic psychiatric disorders.

KEY WORDS: Anatomical Therapeutic Chemical Classification System; Defined Daily Dose

INTRODUCTION

Medicines play a huge role in the optimal health care and therapy. They are integral components of any national health system. New medicines are being continually developed. These medicines have a significant effect on morbidity and mortality of various disorders; but, there is risk of inappropriate drug use which may lead to significant adverse events. All these have a negative impact on health-care economy. This clearly demonstrates the need for an efficient drug utilization research for better evaluation and understanding of the process of prescribing, dispensing, and consumption of drugs in a population. Drug utilization research is defined by the World Health Organization (WHO) as "*the study of marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting*

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medical, social, and economic consequences."[1] Drug utilization research has evolved over the years to become a cross-disciplinary science that explores the medical, social, and economic consequences of drug utilization.[2] The principal aim of drug utilization research is to facilitate the rational use of drugs in populations.[3]

Antipsychotics, also known as neuroleptics, are one of the most commonly prescribed drugs in the psychiatry outpatient department (OPD). They are used to control psychotic symptoms in a wide range of disorders such as schizophrenia and bipolar disorder.[4] There has been a considerable change in the prescribing pattern of antipsychotic drugs over the past decade. The drug utilization practices differ from place to place depending on the patient characteristics, disease prevalence, sociodemographic parameters, availability of drugs, and practicing manner of psychiatrists. Antipsychotic drugs can be classified into two categories: The first-generation or typical antipsychotics such as haloperidol and chlorpromazine and the second-generation or atypical antipsychotics such as clozapine and olanzapine.[4] There has been a paradigm shift from utilization of typical antipsychotics toward increasing utilization of atypical antipsychotics in the past few years; as these drugs have lesser incidence of extrapyramidal side effect (EPS) and are also effective against negative symptoms as well as treatment-resistant schizophrenia. All the antipsychotics have considerable adverse effects such as involuntary movement, metabolic syndrome, and gynecomastia and thus, the choice of a particular drug depends on efficacy, safety, and affordability of the drug in a particular patient.

MATERIALS AND METHODS

This was a retrospective, observational study which was carried out in the psychiatry OPD of a tertiary care hospital in Gujarat for a period of 6 months. The study was commenced after getting approval from the Institutional Ethical Committee. In this study, the case files of patients receiving antipsychotics were reviewed and the relevant data were collected in a pre-designed, pre-approved data sheet for evaluation.

Inclusion Criteria

Patients of all ages and both the genders who were diagnosed with psychosis (diagnosed according to ICD-10 criteria) or any condition where at least one antipsychotic was prescribed were included in the study.

Exclusion Criteria

Those patients who did not receive any antipsychotic drugs or who were taking antipsychotic drugs prescribed from somewhere other than our hospital were excluded from the study.

The demographic details of the patients were noted. All the data regarding the diagnosis and treatment of the patients were recorded. The drugs were prescribed in the form of oral tablets to all the patients, except in cases of acutely psychotic patient where intramuscular injections of haloperidol were given. The recorded data were analyzed for psychiatric diagnosis, patterns of antipsychotic prescription, and the rationality of prescriptions according to the WHO prescribing indicators. Furthermore, defined daily dose (DDD) of the antipsychotics per 1000 inhabitants per day, prescribed daily dose (PDD) of the antipsychotics, and the PDD-to-DDD ratio were assessed.

Anatomical therapeutic chemical (ATC) classification and DDD/1000 inhabitants/day (DID) and PDD calculations were used for assessing antipsychotic usage in the community.

As outlined by the WHO,[5] DID was calculated using the population of the Surat, Gujarat, India (because all patients came from here), as per available census data. By adding up the DIDs for individual antipsychotics, the number of DIDs for the antipsychotics as a whole was derived. Furthermore, the average of the daily doses for all indications of each antipsychotic was taken as PDD. The ratio of PDD to DDD was then calculated.

Statistical Analysis

Microsoft Office Excel 2010 was used for the evaluation of data. Representation of results was done using descriptive statistics (percentage, mean ± standard deviation, tables, and graphs).

RESULTS

A total of 631 prescriptions from patients with a diagnosis of psychiatric disorder and who were receiving at least one antipsychotic drug from the psychiatry OPD were evaluated.

The average age of the patients was 38.94 ± 12.57 years. Majority of the patients belonged to 31–40 years of age group (~30%). Majority of the patients were male (63.23%) as compared to female (36.77%). Age distribution of the patients is demonstrated in Table 1.

Table 1: Age distribution of the study participants

Age group (years)	Number of patients	% of patients
<10	0	0
11–20	33	5.23
21–30	158	25.04
31–40	189	29.95
41–50	128	20.29
51–60	87	13.79
61–70	29	4.60
>70	7	1.11

Figure 1 gives the distribution of primary psychiatric diagnosis of the patients receiving antipsychotics. The most common diagnosis among these patients was schizophrenia (55.31%) followed by bipolar disorder (23.45%).

A total of 2115 drugs were prescribed in 631 prescriptions, of which 804 (38.01%) were antipsychotics. In our setting, atypical antipsychotics (94.03%) were more commonly prescribed as compared to typical antipsychotics (5.97%). Among the atypical antipsychotics, olanzapine (47.39%) was the most commonly prescribed antipsychotic followed by risperidone (27.49%). Olanzapine is also the overall most commonly prescribed antipsychotic. Figure 2 gives the prescribing pattern of antipsychotics. Table 2 shows the concomitant medications that were prescribed in these patients. Sedative-hypnotics (30.23%) were the most common coprescribed drug group.

The total number of drugs per prescription among the 631 prescriptions is presented in Table 3. None of the patients in our study were prescribed more than 5 medicines in a single prescription.

The findings as per the WHO prescribing indicators were as follows:

- The average number of antipsychotics/prescription: 1.29 ± 0.53
- Prescribing of antipsychotics by generic name: 95.02%
- Prescribing from the WHO essential medicines list (EML): 43.66%
- Prescribing from National List of Essential Medicines (NLEM): 47.89%
- Prescribing for injections of antipsychotics: 0.62%
- Prescriptions of fixed-drug combinations: 0.50%.

The total DID of antipsychotics was 0.014 mg. The ATC coding of the antipsychotics and the values of DID and PDD are given in Table 4. The ratios of PDD/DDD are also presented in Table 4.

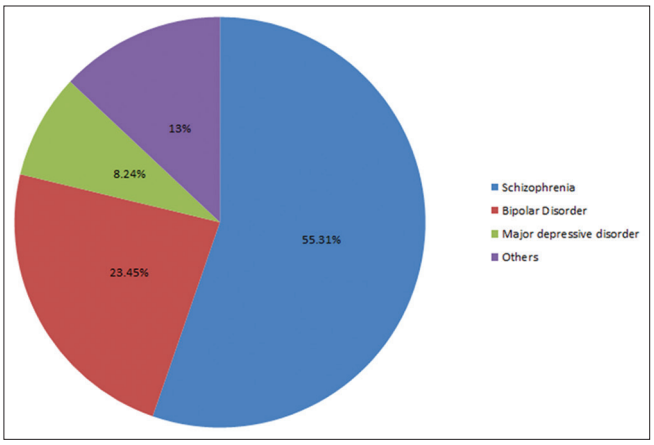

Figure 1: Primary diagnoses of patients receiving antipsychotics

DISCUSSION

Antipsychotics form the backbone of the drugs used in psychiatric illnesses. They are among the most commonly prescribed medications in any psychiatric OPD. Antipsychotics which are categorized into typical and atypical antipsychotics are used in various psychiatric disorders. They are usually prescribed for a long period of time in many of the psychiatric conditions such as schizophrenia and bipolar disorder. Both the groups of drugs are quite efficacious in treating the psychotic symptoms, but the later developed atypical ones are preferred over the typical antipsychotics due to the high risk of extrapyramidal syndrome with the typical ones. All the antipsychotics block the dopamine receptors; moreover, the atypical antipsychotics block the serotonergic receptors as well. The blockade of dopamine receptors in limbic system is responsible for the antipsychotic effect.[6] In our study, we found that schizophrenia was the most common psychiatric diagnosis, for which antipsychotics were being prescribed. Atypical antipsychotics were preferred over typical ones. Among the atypical antipsychotics, olanzapine was most commonly prescribed in our setup. Furthermore, the WHO prescribing indicators for rational prescribing were followed by the doctors. The use of antipsychotics was high in the population as evident by the DIDs calculated for the different antipsychotics in the study.

In our study, we analyzed a total of 631 prescriptions of patients who were being prescribed one or more antipsychotics at the psychiatry OPD. We observed a higher preponderance of male patients as compared to female patients. This was similar to the findings published in the

Table 2: Concomitant drugs prescribed in the study participants

Concomitant drugs	Number of patients	% of patients
Sedative-hypnotics	397	30.23
Antidepressants	326	24.88
Trihexyphenidyl	271	20.68
Mood stabilizers	233	17.77
Antiepileptics	60	4.59
Propranolol	14	1.08
Thyroxine	10	0.77

Table 3: Number of drugs per prescription in the study participants

Total number of drugs per prescription	Number of prescriptions (*n*=631)	% of prescriptions
1	26	4.12
2	108	17.12
3	219	34.71
4	184	29.16
5	94	14.90

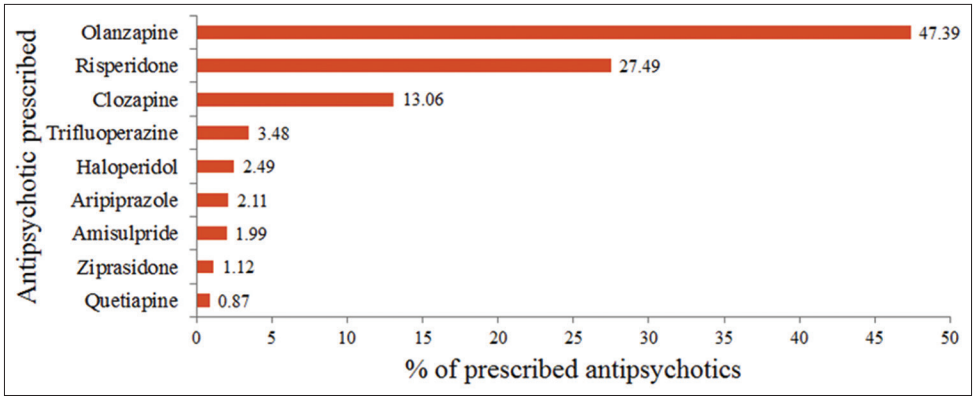

Figure 2: Prescribing frequency of antipsychotic drugs

Table 4: ATC/DDD classification with calculated DID, PDD values of prescribed antipsychotics, and PDD/DDD ratio

Drug	ATC code	DDD (mg)	DID (mg)	PDD (mg)	PDD/DDD
Olanzapine	N05AH03	10	0.0073	12	1.2
Risperidone	N05AX08	5	0.0041	5	1
Trifluoperazine	N05AB06	20	0.00037	10	0.5
Haloperidol	N05AD01	8	0.00031	8	1
Clozapine	N05AH02	300	0.0012	188	0.63
Quetiapine	N05AH04	400	0.000062	200	0.5
Ziprasidone	N05AE04	80	0.000082	60	0.75
Aripiprazole	N05AX12	15	0.00035	15	1
Amisulpride	N05AL05	400	0.000099	135	0.34

DDD: Defined daily dose, PDD: Prescribed daily dose, ATC: Anatomical therapeutic chemical, DID: Defined daily dose/1000 inhabitants/day

study of Paul *et al*. where there was a higher prevalence of antipsychotic prescribing in male patients.[7] Furthermore, in a study done by Chaturvedi and Sharma, there was an overall higher prescribing rate of psychotropics in male patients.[8] The lesser attendance of female patients at the OPD may be due to lack of awareness toward their illness due to various societal and geographical reasons. The majority of patients receiving antipsychotics belonged to the age group of 31–40 years. About 54% of patients were between 21 and 40 years of age. This is similar to findings of an Australian study conducted by Hollingworth *et al*., in which he found higher rates of prescribing for males aged between 25 and 55 years.[9] The most common primary psychiatric diagnosis for which antipsychotics were prescribed was schizophrenia (55.31%). This is similar to various other studies, in which schizophrenia was the most common indication for prescribing antipsychotics.[7,10] Bipolar disorder and major depressive disorder were among the other diagnoses. In our study, atypical antipsychotics (94.03%) were prescribed more often as compared to typical antipsychotics which were prescribed occasionally. This is consistent with the findings of other similar drug utilization studies of antipsychotics.[9,11,12] The increased prescribing of atypical antipsychotics could be due to the fewer side effects and hence better tolerability ultimately giving better patient compliance. Olanzapine (47.39%) was the most commonly prescribed antipsychotic followed by risperidone (27.49%). These findings are similar to the studies published globally.[9,10,12-14] The other antipsychotics prescribed were quetiapine, aripiprazole, trifluoperazine, haloperidol, ziprasidone, clozapine, and amisulpride. This is in accordance with the results of the clinical antipsychotic trials for intervention effectiveness schizophrenia trial, in which olanzapine was found to be the most effective drug for schizophrenia.[15] Olanzapine, being an atypical antipsychotic drug, is effective in controlling both the negative and positive symptoms of schizophrenia. Sedative-hypnotics (30.23%) were the most common concomitantly prescribed drugs. Benzodiazepines have been found to calm the agitated patients of psychosis and provide very short-term sedation.[16] Other concomitant drugs were antidepressants, mood stabilizers, and antiepileptics. Apart from psychotropics, thyroxine (n = 10) and propranolol (n = 14) were also prescribed to some patients. In some cases (n = 271), trihexyphenidyl was prescribed to treat extrapyramidal symptoms of antipsychotics. Trihexyphenidyl is an anticholinergic drug used to treat the EPS due to antipsychotic agents. Polypharmacy, as defined by majority of studies as prescription of five or more medications,[17] was observed in 94 (14.90%) prescriptions in the study. Polypharmacy may be due to concomitant conditions of the patients, for which they were already on treatment. Furthermore, a number of medications were prescribed for treating various adverse effects of psychotropics. The average number of antipsychotics per prescription was <2.

Prescribing using generic names were quite high (95.02%). Most commonly oral drugs were preferred and there were very few incidences of using injectables (0.62%) and fixed-dose combinations (FDCs) (0.50%). This is in contrast to the findings published by Yadav *et al*., in which they found overall high incidence of FDC prescriptions in psychiatry patients.[18] This also indicates rational prescribing practices. FDCs of risperidone with trihexyphenidyl were prescribed in four cases. In most cases, the drugs available in the hospital supply were prescribed. The percentage of drugs prescribed from the WHO EML (2015) and NLEM 2015 was <50%. This is similar to the findings published by Oommen *et al*.[14] This can be due to olanzapine being the most commonly prescribed drug in our study, which was not included in the NLEM. This indicates the need for a better synchronization between the clinician's prescribing and the recommendations in NLEM. The ATC classification system classifies the active ingredients of drugs according to the organ or system, on which they act and their therapeutic, pharmacological, and chemical properties.[19,20] DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults.[19] The DDD is a unit of measurement and the data presented in DDD give a rough estimate of drug consumption, but not a representation of actual use. The total DID of antipsychotic use showed high consumption of antipsychotics in the population. This is similar to the findings of a 10-year database-based study conducted in the US[21] and in contrast to the findings of an Indian study conducted by Lahon *et al*. where the antipsychotic consumption was quite low.[10] The DID for olanzapine was calculated as 0.0073, i.e., out of 1000 patients, 0.00073% would have used a dose of 10 mg. Similarly, the DIDs of risperidone, trifluoperazine, haloperidol, clozapine, quetiapine, ziprasidone, aripiprazole, and amisulpride can be interpreted as consumption of their respective DDDs by a population of 0.00004%, 0.00004%, 0.00003%, 0.0001%, 0.000006%, 0.000008%, 0.00003%, and 0.00009%. PDD is defined as the average dose prescribed according to a representative sample of prescriptions. For antipsychotics, the recommended dose varies from one indication to another. In such cases, it is important that diagnosis is linked to the PDD given. For trifluoperazine, clozapine, quetiapine, ziprasidone, and amisulpride, PDDs are lower than DDDs. This may indicate the reluctance of clinicians in prescribing higher range of dosing keeping in mind the safety profile of these drugs. For risperidone, haloperidol, and aripiprazole, the PDD/DDD ratio was equal to 1, and for olanzapine, it was more than one, which indicate adequate dosing with these antipsychotics.

There were several strengths and limitations of our study. Since this was not a prospective study, we could not evaluate patient care indicators and some of the facility indicators like impact of cost on the prescription pattern. Furthermore, it was not possible to monitor the compliance of the patient with the prescribed drugs. However, as the patient records were kept and maintained by the doctors of psychiatry department themselves, the records were complete and up to date.

CONCLUSION

The assessment of drug utilization pattern of antipsychotics in the psychiatry OPD helps in improvising the prescribing pattern and identifying the gaps between the infrastructure and the consumers. The prescriptions were complete and followed principles of rational prescribing in majority of cases, except in some, where polypharmacy was seen. Prescription of drugs from NLEM should be increased. There is a need for prospective drug utilization studies to monitor the consumption and usage of drugs along with its impact on patient health and quality of life. In addition, rational prescribing and continuous medical education in terms of evidence-based medicine should be a part of the hospital guidelines. Furthermore, the patient compliance needs to be monitored frequently. All these will help in improving the quality of patient health care and lower the burden on the health-care system.

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