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EVALUATION OF ANTIPSYCHOTIC DRUG PRESCRIPTIONS IN HOSPITALIZED SCHIZOPHRENIC PATIENTS

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Abstract: The aim of the study was to evaluate the antipsychotic drug prescriptions in patients with schizophrenia in the in-patient department of a tertiary care teaching hospital. 200 schizophrenic patients between the age group of 18-60 were enrolled in the study. In this observational study we collected the patient's information including age, sex and drug therapy details from the day of admission to the day of discharge. Data was analyzed for defined daily dose (DDD/100 bed days), prescribed daily dose (PDD) and then PDD to DDD ratio was calculated. The prescriptions are also assessed for completeness and rationality according to World Health Organization (WHO) prescribing indicators. The study report shows the following. Average number of drugs per prescription: 3.59. Percentage of antipsychotic drugs prescribed by generic name: 2.36%. Percentage of encounters for prescribing injections of antipsychotics: 30.50%. Percentage of fixed-dose combinations of antipsychotics: 5.84%. Percentage of antipsychotic drugs prescribed from WHO Essential Medicines List (EML): 30.08%. Percentage of antipsychotic drugs prescribed from National List of Essential Medicines (NLEM): 25.62%. Ratio of PDD to DDD for olanzapine and aripiprazole was ≥ 1 , which reflects the sufficiency of dosing. All the other antipsychotics showed a PDD to DDD ratio <1 , which indicates under dosing.

Keywords: Schizophrenia, psychotropic drugs, Drug utilization evaluations.



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INTRODUCTION

The treatment practice is expected to be chiefly based on evidence provided by pre marketing clinical trials, but corresponding information from post marketing phase are needed to provide an satisfactory foundation for improving drug therapy¹. Appliance of pharmacoepidemiological studies often exposes the huge differences that exist between the clinical trials and actual practice after several years into the market life of a pharmaceutical product². To advance the psychiatric services, several countries and organizations throughout the world have created their own guidelines for the management of schizophrenia³. But in some developing nations, researches made on evaluation of drug usage using the WHO drug use indicators found high incidences of polypharmacy⁴. For some reasons the gap between guidelines and prescribing pattern is well-known for antipsychotic drugs⁵. Prescribing patterns of antipsychotic drugs have also altered worldwide with conventional antipsychotics being put backed by new-generation atypical agents. In this manner, psychiatrists are constantly opened to newly launched drugs that are declared to be safe and more effective. Hence, drug use evaluation studies are essential to recognize possibly unproven or unfavourable extensions of the indications for psychotropic drugs.

On this background, the study was conducted to evaluate the prescribing pattern and to identify the consumption of antipsychotics used in schizophrenic patients at a tertiary care teaching hospital of Dakshina Kannada.

MATERIALS AND METHODS

The prospective observational study was conducted at a 1200-bed private tertiary care hospital located in Dakshina Kannada district. All the in-patients aged above 18 years with schizophrenia admitted to the psychiatry department during the study period were enrolled after getting approval from the Institutional Ethics Committee. The patient's case records were reviewed daily. Information's regarding demography details and antipsychotic drug therapy was documented in the suitably designed data collection form. The prescriptions were analyzed for completeness and rationality according to WHO prescribing indicators, defined daily dose (DDD) of the antipsychotics per hundred bed days, prescribed daily dose (PDD) of the antipsychotics and PDD to DDD ratio of the antipsychotics. We applied anatomical therapeutic chemical (ATC) classification⁶ and defined daily dose (DDD) per hundred bed days and prescribed daily dose (PDD) calculations for estimating antipsychotic use in the study site

Prescriptions from August 2011 to March 2014 were evaluated for calculation of DDD in 100 bed days. DDD/100 bed days was calculated by the below mentioned formula⁷.

$$\text{DDD}/100 \text{ bed days} = \frac{\text{Drug consumption (mg)} \times 100}{\text{DDD (mg)} \times \text{No of days in study period} \times \text{Total No of beds} \times \text{Occupancy index}}$$

$$\text{DDD (mg)} \times \text{No of days in study period} \times \text{Total No of beds} \times \text{Occupancy index}$$

Consumption in hospitals expressed in this way gives a rough estimate of the proportion of patients treated with a given drug during a certain period.

PDD was calculated as follows: For each prescription, dose titrations resulted in multiple doses of the antipsychotics, and so we took the average of the daily doses for the antipsychotic as the PDD. This procedure was continued for all indications of each antipsychotic drugs prescribed. Thus we attained the PDDs of each drugs.

PDD to DDD ratio was then calculated.

The collected data was analyzed using SPSS software version 16.0.

RESULTS AND DISCUSSION

During the study period we have enrolled 200 patients who are diagnosed with schizophrenia. Male patients 125 (62.5%) outnumbered the female patients 75 (37.5%). Age distribution among the patients is shown in Table 1.

Table 1 Age wise distribution of patients under study

Sl. No	Age group	N=200	Percentage
1	18-20	10	5
2	21-30	69	34.5
3	31-40	64	32
4	41-50	38	19
5	51-60	19	9.5

Paranoid schizophrenia was the most common psychiatric diagnosis among the study population (n=124), with a prevalence of 62%. The distribution of primary psychiatric diagnosis of patients who received antipsychotics during the study period is given in Table 2

Table 2 Primary ICD-10 psychiatric diagnosis of enrolled patients

Sl. No	Schizophrenia types		
	Type	N= 200	%
1	Paranoid	124	62
2	Unspecified	32	16
3	Undifferentiated	26	13
4	Residual	8	4
5	Hebephrenic	7	3.5
6	Catatonic	3	1.5

On the total of 200 patient's prescriptions, 38 psychotropic drugs were prescribed. The most commonly prescribed atypical antipsychotic drug was olanzapine (45.5%). The second generation antipsychotics olanzapine, risperidone, clozapine, Amisulpride, quetiapine and aripiprazole accounted for the bulk of prescriptions. This report is similar to the findings of other related studies⁸⁻¹¹. Table 5 shows the prescribing frequency of psychotropic drugs.

The DDD is the assumed average maintenance dose per day for a drug used for its major indication in adults¹². The DDD was developed to overcome objections against conventional units of measurement of medicine consumption and to make sure the comparability between different drug utilization studies.

The DDD/100 bed days for olanzapine can be interpreted as 0.65355/100 bed days, i.e, 0.65355 DDDs of olanzapine was used as maintenance dose per 100 bed days of patient care. Similarly, the DDD/100 bed days of risperidone, clozapine, amisulpride, quetiapine, aripiprazole, asenapine, levosulpride, haloperidol, chlorpromazine, trifluoperazine and fluphenazine can be interpreted as consumption of their respective DDD/100 bed days of 0.32677, 1.33180, 0.24785, 0.08092, 0.01550, 0.00318, 0.01996, 0.12629, 0.02328, 0.00777, and 0.00140.

The ATC coding and calculation of DDD/100 bed days and PDD are summarized in Table 3.

The total DDD/100 bed days of the antipsychotics showed low consumption when compared to other studies mentioned here as follows. A 10 year prescription study on antipsychotic utilization in the United States showed comparatively high consumption rates¹³. But a study

conducted in Europe showed declining of antipsychotics consumption. Even though, it was noticed that the consumption was much higher than in our study¹⁴.

The PDD is defined as the average dose prescribed according to a representative sample of prescriptions. It is essential to relate the PDD to the diagnosis on which the dose is based. The PDD represent the average daily amount of a drug that is actually prescribed. PDD is particularly important for drugs where the recommended dosage differs from one indication to another (e.g., psychotropic drugs). When there is a significant discrepancy between the PDD and the DDD, it should be considered when evaluating and interpreting drug utilization data, particularly in terms of morbidity.

Ratio of PDD to DDD is used as an indication of the adequacy of dosing. For olanzapine and aripiprazole the ratio was ≥ 1 , which reflects the adequacy of dosing. All the other antipsychotics showed a PDD to DDD ratio <1 , which indicates under dosing.

Table 3 ATC/DDD classification with calculated DDD/100 bed days, PDD values of prescribed antipsychotics and PDD/DDD ratio.

Sl.No	Drug	ATC code	DDD (mg)	DDD/100 bed days (mg)	PDD (mg)	PDD/DDD
1	Olanzapine	N05AH03	10	0.65355	12.5	1.25
2	Risperidone	N05AX08	5	0.32677	3.0	0.6
3	Clozapine	N05AH02	300	1.33180	93.75	0.3125
4	Amisulpride	N05AL05	400	0.24785	210.0	0.525
5	Quetiapine	N05AH04	400	0.08092	200.0	0.5
6	Aripiprazole	N05AX12	15	0.01550	18.75	1.25
7	Asenapine	N05AH05	20	0.00318	7.5	0.375
8	Levosulpride	N05AL07	400	0.01996	100.0	0.25
9	Haloperidol	N05AD01	8	0.12629	5.0	0.625
10	Chlorpromazine	N05AA01	300	0.02328	75.0	0.25
11	Trifluoperazine	N05AB06	20	0.00777	10.0	0.5

12	Fluphenazine	N05AB02	10	0.00140	25.0	2.5
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ATC: Anatomical Therapeutic Classification, DDD: Defined Daily Dose, PDD: Prescribed Daily Dose

All prescriptions contain the patient’s prime diagnosis, drug(s) prescribed, dosage form, dose, frequency of administration and duration of treatment along with the dates of follow-up. No occasion of inappropriate prescribing of antipsychotic drugs or use of wrong dose, frequency or duration of treatment was noticed. Nevertheless, all patients didn’t have regular follow-up.

Rational prescribing was followed as per the principles of prescription order writing¹⁵. Definitions of polypharmacy that are generally cited are the prescribing of medication not corresponding to the diagnosis and incidence of more than six drugs in a single prescription¹⁶. As per these criteria, there was no polypharmacy as no inappropriate drug was prescribed and no prescription contained more than six drugs. The details are presented in Table 4.

Table 4 Distribution of number of drugs per prescription

Sl.No	No. of drugs per prescription	No of patients (N=200)	%
1	1	27	13.5
2	2	45	22.5
3	3	48	24.0
4	4	32	16.0
5	5	29	14.5
6	6	19	9.5

As per WHO prescribing indicators, we have observed the following:

Average number of drugs per prescription:

Total number of drugs prescribed/ Total number of prescriptions

$$718/200 = 3.59$$

Percentage of antipsychotic drugs prescribed by generic name:

No of encounters/ Total number of drugs prescribed X 100

$$17/718 \times 100 = 2.36\%$$

Percentage of encounters for prescribing injections of antipsychotics:

No of encounters/ Total number of drugs prescribed

$$219/718 \times 100 = 30.50\%$$

Percentage of fixed-dose combinations of antipsychotics:

No of encounters/ Total number of drugs prescribed X 100

$$42/718 \times 100 = 5.84\%$$

Percentage of antipsychotic drugs prescribed from WHO Essential Medicines List (EML):

No of encounters/ Total number of drugs prescribed X 100

$$216/718 \times 100 = 30.08\%$$

Percentage of antipsychotic drugs prescribed from National List of Essential Medicines (NLEM):

No of encounters/ Total no of drugs prescribed X 100

$$261/718 \times 100 = 36.35\%$$

Most of the drugs were prescribed by trade names. Only 2.36% of the drugs were prescribed by generic name. This is similar to a study done in 2001 on psychotropic drug utilization which shows that 71.3% of the drugs were prescribed by trade names¹⁷. Report on similar studies published has the evidence that by promoting the drugs by trade name will increase the cost of the therapy where other generic alternatives are available¹⁸. We have noticed that percentage of encounters of injections was 30.50% and the percentage of encounters for prescribing fixed-dose combination of antipsychotics was 5.84%. The percentage of drugs prescribed from the WHO EML list was 30.08%. This result was higher than the value (16%) from the studies by Guvon et al¹⁹. Also, the result was lower than the value from studies by Hasra et al²⁰ (45.70%), Otoom et al²¹ (93%), Babalola et al²² (94.16%) and Bosu et al²³ (97%). We observed that only 36.35% of the drugs were prescribed from NLEM 2011. But in another study, the result shows that 89.89% of antipsychotic drugs were prescribed from the NLEM and the authors suggest that the reason may be due to free supply of medicine in government

hospital²⁴. This indicates that there is a need of hospital formulary. The details of the psychotropic drugs prescribed during the study period are mentioned below (Table 5).

Table 5 Prescribing frequency of psychotropic drugs

Sl.No	Drug Name	No of times prescribed	Percentage
1	T.Olanzapine	91	45.5
2	Inj. Haloperidol	81	40.5
3	Inj Lorazepam	79	39.5
4	T.Risperidone	70	35
5	Trihexyphenidyl Hydrochloride	69	34.5
6	T.Lorazepam	57	28.5
7	T. Clozapine	50	25
8	Inj.Zuclopenthixol	41	20.5
9	T.Risperidone+Trihexyphenidyl	38	19
10	T.Amisulpride	21	10.5
11	T.Divalproex Sodium	16	8
12	T.Clonazepam	14	7
13	Inj. Promethazine	13	6.5
14	T. Quetiapine	10	5
15	T.Chlorpromazine	11	5.5
16	T.Aripiprazole	8	4
17	T.Escitalopram	7	3.5
18	T.Fluoxetine	5	2.5
19	T.Trifluoperazine	4	2
20	T.Asenapine	4	2

21	Inj.Fluphenazine	3	1.5
22	T.Lithium	3	1.5
23	T.Levosulpride	2	1
24	T.Sertraline	2	1
25	Inj.Flupenthixol	2	1
26	T.Amitriptyline	2	1
27	T.Oxcarbazepine	2	1
28	T.Trifluoperazine+Trihexyphenidyl	2	1
29	T.Dosulepin	2	1
30	T.Imipramine	1	0.5
31	T.Haloperidol	1	0.5
32	T.Alprazolam+Sertraline	1	0.5
33	T.Diazepam	1	0.5
34	T.Alprazolam	1	0.5
35	T.Carbamazepine	1	0.5
36	T.Chlorpromazine+Trihexyphenidyl+T rifluoperazine	1	0.5
37	T.Procylidine	1	0.5
38	T.Zolpidem	1	0.5
Total		718	

T: Tablet, Inj: Injection

CONCLUSION

The study found that the prescription patterns at the hospital studied were complete and polypharmacy was not seen. Favourable and unfavourable outcomes were seen in the WHO prescribing indicators. Consumption of antipsychotics in the hospital was low. Few

antipsychotics showed a PDD to DDD ratio <1 , which reflects under dosing but, it was noticed that patients responded well to it. The treatment pattern observed associates with the shifting in trends in the treatment of schizophrenia worldwide. The report suggests that there is a need of hospital formulary and incorporating more drugs as per the formulary committee recommendations. Eventually, it will be a model itself on the national and WHO essential medicine list. This may promote the rational use of medicines and ultimately, the quality of patient care.

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