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Pattern of Use of Atypical Anti Psychotics in Psychiatry in Patients Department of a Tertiary Care Teaching Hospital

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ABSTRACT

Psychoses are among the most severe psychiatric disorders. In Schizophrenia there is splitting of perception and interpretation from reality-hallucinations, inability to think coherently. The atypical antipsychotics are widely prescribed based on the perception that they are more effective and produce fewer side effects than the typical antipsychotic. The aim is to study the drug utilization of use of atypical antipsychotics in the inpatient of psychiatry department of a tertiary care teaching hospital. All 131 schizophrenic patients hospitalized during the six month period in 2012 were included in the study. Most commonest antipsychotic prescribed was Olanzapine. In our study antipsychotic polypharmacy 95 (72.5%) was seen in majority of patients. Polypharmacy with atypical antipsychotics is on the rise.

Keywords: Schizophrenia, atypical antipsychotics, Olanzapine, Polypharmacy.

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INTRODUCTION

Psychoses are among the most severe psychiatric disorders, in which there is not only marked impairment of behavior, but also a serious inability to think coherently, to comprehend reality, or to gain insight into the presence of these abnormalities. These common disorders typically include symptoms of false beliefs (delusions) and abnormal sensations (hallucinations). Their etiological basis remains unknown, although genetic, neurodevelopmental, and environmental causative factors have all been proposed[1]. (a) Acute and chronic organic brain syndromes (cognitive disorders): Such as delirium and dementia; some toxic or pathological basis can often be defined; prominent features are confusion, disorientation, defective memory and disorganized behavior. (b) Functional disorders: No underlying cause can be defined; memory and orientation are mostly retained but emotion, thought, reasoning and behavior are seriously altered.

(i) Schizophrenia (split mind): Splitting of perception and interpretation from reality-hallucinations, inability to think coherently.

(ii) Paranoid states: Marked persecutory or other kinds of fixed delusions (false beliefs) and loss of insight into the abnormality.

Since there is no cure for the condition, treatment seeks to decrease the morbidity and mortality associated with the disorder. The general goals of treatment are to decrease the frequency, severity and consequences of episodes and maximize functioning between episodes. Specific goals depend on the specific phases of illness.

Important Considerations in Treatment

Comprehensive and continuous treatment for prolonged periods for most

Integrated, bio-psychosocial approach to care

Active collaboration with the family while planning and delivering treatment

Treatment sensitive to the patient's needs and empirically titrated to the patient's response and progress.

Classification of Antipsychotic agents

Antipsychotic agents may be classified in several ways. (1)

Typical antipsychotics/First generation

1. **Phenothiazines**

Aliphatic side chain: Chlorpromazine, Trifluopromazine

Piperidine side chain: Thioridazine

Piperazine side chain: Trifluoperazine, Fluphenazine

2. Butyrophenones

Haloperidol, Trifluperidol, Penfluridol

3. Thioxanthenes

Flupenthixol

4. Other heterocyclic

Pimozide, Loxapine

Atypical antipsychotic

Clozapine

Risperidone

Olanzapine

Quetiapine

Ziprasidone.

Ziprasidone.

Paliperidone, Iloperidone, Asenapine, and Lurasidone are the newest oral atypical antipsychotic medications to be introduced since the approval of Ziprasidone in 2002.

Atypical antipsychotics

Atypical antipsychotics produce antipsychotic responses with fewer acute extrapyramidal side effects than "conventional" antipsychotic drugs such as akathisia, dystonia, and pseudo Parkinsonism. Atypical antipsychotics may also treat negative symptoms and improve cognitive functioning. The atypicals are widely prescribed based on the perception that they are more effective and produce fewer side effects than the typicals, even though some atypicals are much more expensive. Also these agents present their own spectrum of adverse effects, including hypotension, seizures, weight gain, and increased risk of type II diabetes mellitus and hyperlipidemia.

Distinctive Features of Some of Atypical Antipsychotics [3]

Clozapine

An atypical antipsychotic due to its relative selectivity for D4 receptors, additional 5-HT2 as well as a blockade. Its major limitation is higher incidence of agranulocytosis (0.8%) and other blood dyscrasias, weekly monitoring of leucocyte count is required. Few cases of myocarditis have been reported. Clozapine is used as a reserve drug in resistant schizophrenia.

Risperidone

it is less epileptogenic than clozapine, though frequently causes agitation. Caution has been issued about increased risk of stroke in the elderly.

Olanzapine

This atypical antipsychotic controls both positive and negative symptoms of schizophrenia appear to be benefited. A broader spectrum of efficacy covering schizo-affective disorders has been demonstrated, and it is approved for use in mania. Monotherapy with Olanzapine may be as effective as a combination of Lithium/Valproate + benzodiazepines. It is more epileptogenic than high potency phenothiazines. Incidence of stroke may be increased in the elderly.

Quetiapine

This new short-acting atypical antipsychotic requires twice daily dosing. It blocks 5-HT1A, 5-HT2, D2, a1, a2 and H1 receptors in the brain, but D2 blocking activity is low: extrapyramidal and hyperprolactinaemic side effects are minimal. Weight gain and rise in blood sugar are infrequent. Quetiapine has not been found to benefit negative symptoms of schizophrenia, but can be used in mania /bipolar disorder.

Aripiprazole

It is the latest atypical antipsychotic with combined D2 5+HT2A/2c +α1 blocking property. Antagonistic action 5HT & agonistic activity at 5-HT1A receptor along with moderately potent inhibition of NA reuptake indicates some anxiolytic & antidepressant property as well. More importantly, a dose-related prolongation of QT interval occurs. It has the potential to cause serious cardiac arrhythmias. It is also indicated in mania.

Ziprasidone

Ziprasidone is quite long-acting, dose adjustments should be done after 2 weeks of treatment. It is metabolized by CYP3A4 well as CYP2D6; dose needs to be halved in patients receiving ketoconazole or quinidine and doubled in those taking Carbamazepine. Ziprasidone is indicated in schizophrenia well as mania and bipolar illness.

Adverse drug reaction[3]

Table 1: Adverse drug reactions of antipsychotic drugs

Type	Manifestations	Mechanism
Autonomic nervous system	Loss of accommodation, dry mouth, difficulty urinating, constipation	Muscarinic cholinoceptor blockade
Cardiovascular	Orthostatic hypotension, impotence, failure to ejaculate	Alpha adrenoceptor blockade
Central nervous system	Parkinson's syndrome, akathisia, dystonias	Dopamine receptor blockade
	Tardive dyskinesia	Supersensitivity of dopamine receptors
	Toxic-confusional state	Muscarinic blockade

	Aggravation of seizures in epileptics; even in nonepileptics	
Endocrine system	Amenorrhea-galactorrhea, infertility, impotence	Dopamine receptor blockade resulting in hyperprolactinemia
Other	Weight gain	Possibly combined H_1 and 5-HT_2 blockade

MATERIALS AND METHODS

The aim is to study the drug utilization of use of atypical antipsychotics in the inpatient of psychiatry department of a tertiary care teaching hospital.

Subjects and Methods

The sample consisted of 131 patients from inpatient psychiatry department of a tertiary care teaching hospital. All schizophrenic patients hospitalized during the six month period in 2012 were included in the study. The study was approved by the institutional Ethics Committee. Patients of both sexes, 20- 60 of age, on antipsychotic treatment with an established diagnosis of schizophrenia by the treating psychiatrist were included in the study. The prescription patterns wasanalyzed. The following data was collected for each patient: age, sex, drugs prescribed type and dose of the second generation antipsychotics (SGA), first generation antipsychotics (FGA), anticholinergics, anxiolytics, antimaniac, depression and any other concomitant medication used). Patients then were categorized as either receiving one or more than one antipsychotic combinations of SGA and FGA.

RESULTS AND DISCUSSIONS

Total of 256 patients admitted in psychiatry indoor patient department (I. P. D) of a tertiary care hospital from January 2012-July 2012 were screened. Of these, 131 schizophrenic patients were included in the study after obtaining written informed consent from legally accepted representative. Case record files of the patients included in the study were evaluated. Data was then analysed based on the ICD-10 disease coding. The data collected from case record files was subjected to analysis for evaluation of the indicators of drug use recommended by WHO. This prospective and observational study was done to analyze the prescription pattern of psychotropic drugs in indoor psychiatry patients.

Demographic Profile

In our study demographic profile showed that total number of males were 76 (58.01%) and females 55 (41.98%). In the present study age wise distribution of patients, 30 (22.98%) were in the age group of 18-30 years, 69 (52.61%) were 31-50 years and 32 (24.4%) were above 50 years of age. The age group (30–50 years) accounted for the majority of patients 69 (52.61%) in

majority of the psychiatric disorders as has been seen in many other studies[36]. In this study majority of patients belonged to Paranoid schizophrenia 66 (50.38%) followed by Brief psychotic episode 38 (29.67%).

Observed drug use pattern in schizophrenia

Total number of drugs prescribed was 319. In our study population of patients suffering from schizophrenia, different drug classes prescribed were antipsychotics 220 (68.98%), anti-cholinergics60 (18.83%), anxiolytics 30 (9.4%), anti-depressants 7 (2.17%), mood stabilizers 2 (0.6%). Most commonly prescribed antipsychotics in descending order were Olanzapine-91 (41.36%), Haloperidol- 37 (16.6%), Aripiprazole37 (16.6%), Ziprasidone 30 (13.36%) Quetiapine12 (5.46%) Risperidone-7 (3.18%) &others. Amongst anticholinergics, Phenargan is commonly prescribed in 56 (93%) followed by Trihexiphenidyl 2 (3.31%) &Benztropine 02 (3.31%)

Table 2: Observed drug use pattern in schizophrenia

Drug	**N (%)**
Olanzapine	91 (41.36%)
Haloperidol	37 (16.6%)
Aripiprazole	37 (16.6%)
Ziprasidone	30 (13.36%)
Clozapine	12 (5.4%)
Risperidone	7 (3.18%)
Anti-cholinergics	60 (27.5%)
Phenargan	40 (17.64%)
Trihexiphenidyl	2 (3.31%)
Benztropine	02 (3.31%)

Number of antipsychotics per patient in schizophrenia

Antipsychotic polypharmacy was prescribed in 95 (72.51%) & monotherapy in 36(27.48%) of cases. Of patients receiving antipsychotic Polypharmacy 83 (63.35%), and 12 (9.16%) were prescribed two & three antipsychotics respectively. Most commonly used combination was Olanzapine+ Aripiprazole (25), followed by Olanzapine + Haloperidol (15).Clozapine is given to most of the patients with more than two antipsychotics -12. The total number of A typical antipsychotics prescribed were 177(80.47%), While typical prescribed were 97(19.54%). Most commonly prescribed antipsychotics was Olanzapine 91 (41.36%) (atypical antipsychotic) followed by Haloperidol- 37(16.81%), Aripiprazole 37 (14.09%). This is in accordance with several other studies[4,5]. Most commonly used atypicalcombination was Olanzapine+ Aripiprazole 25 (19.08%) in patients. Haloperidol is given along with olanzapine in 15 (11.45%). This is the combination of atypical with typical & in accordance with several other

studies[4,5]. The above results suggest changing trend towards atypical antipsychotics. Most of the published guidelines favors the use of atypical ones[4]. This is in accordance with the general findings that the arrival of the newer atypical antipsychotics has achieved rapid acceptance by prescribers because of enhanced safety profiles, relative to those observed with conventional antipsychotics[(48)].Besides their evident antipsychotic efficacy, they have been found to offer a larger pharmacological profile than conventional antipsychotics[4]. The popularity of atypical antipsychotics is mostly due to its lower incidence of extra pyramidal side effects[5]. In our study antipsychotic polypharmacy 95 (72.5%) was seen in majority of patients and 36(27.49%), 83 (63.38%) and 12 (12.23% of patients received one, two and three antipsychotic drugs respectively was similar with those reported in other studies[6,7,8,]. Documented reasons for antipsychotic polypharmacy are residual symptoms on single antipsychotic, adverse effects of existing antipsychotic drug, noncompliance with oral medication &Different mechanism of action required[7,8]. In practice, typical and atypical antipsychotics are commonly co-prescribed despite clear evidence that such prescribing substantially increases the use of anticholinergic medication[8,9] 2000a,b. Clozapine is given to most of the patients who are receiving more than two antipsychotics. National Institute of Clinical Excellence (NICE) guidelines - 2010, suggested that Clozapine may be offered only after primary failure of two antipsychotic drugs[10]. Overall 45% of patients on antipsychotic therapy were prescribed anti-cholinergic drug. However, this represents an excess use of the anti–cholinergic drugs. Many observers have noted that the addition of anticholinergic medication can exacerbate existing Tardive Dyskinesia (TD), and that discontinuing anticholinergic drugs may improve the condition[11,12]. Based on a number of studies, the WHO has recommended that anticholinergic should be used routinely for preventing extra–pyramidal side effects in individuals with psychotic disorders treated with anti–psychotics for short term use in selected cases.

CONCLUSION

Polypharmacy with atypical antipsychotics is on the rise.

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