

# A PROSPECTIVE STUDY ON PRESCRIPTION PATTERN AND AUDITING OF PRESCRIPTIONS AMONG SCHIZOPHRENIA PATIENTS USING WHO INDICATORS

K.Sampath Reddy<sup>1</sup>, K. Navya sri<sup>1</sup>, B. Jagadeesh Babu<sup>2</sup>, P.Kishore<sup>1\*</sup>

<sup>1</sup>Pharm D Intern, <sup>2</sup>M.B.B.S, DPM (OSM) FIPS.

<sup>1</sup>Department of Pharmacy Practice, Care College of Pharmacy, Oglapur(v), Damera(m), Warangal rural, Telangana-506006, India

<sup>2</sup>Jayakrishna Psychiatric clinic, Hanumakonda, Warangal, Telangana-506006, India

## ABSTRACT

Schizophrenia is a complex, chronic mental health disorder characterized by an array of symptoms and the treatment includes use of antipsychotics. Prescribing pattern has changed with usage of more atypical antipsychotics than typical. Introduction of the core drug use indicators (CDUIs) by the WHO promoted the rational use of drugs. A Prospective observational study was conducted in 100 patients, pertinent information was collected from patients and prescribing pattern was analysed using WHO core indicators. 100 cases of schizophrenia were collected and it was observed that dual therapy (54%) was preferred over mono therapy (43%) and atypical antipsychotics (95%) were used more frequently than typical. Benzodiazepines (38%) and anti cholinergics (33%) were the most preferred choice of drugs in adjunctive therapy. The analysis of prescription pattern by WHO indicators showed deviated results from optimal values which may be due to various factors such as side effect of drugs, socioeconomic reasons and other technical difficulties.

**Keywords:** Schizophrenia, Antipsychotics, prescribing pattern, WHO indicators.

## INTRODUCTION:

Schizophrenia is a complex, chronic mental health disorder characterized by an array of symptoms, including delusions, hallucinations, disorganized speech or behaviour, and impaired cognitive ability. It is a disabling disorder for many patients and their families because of its early onset and chronic course of disease. Disability results from negative and cognitive symptoms and relapse occurs with the array of positive symptoms [1]. Schizophrenia affects more than 23 million people worldwide but is not as common as other mental disorders. It is more common among male (12 million), than female (9 million). Schizophrenia also commonly starts earlier among men. In India the prevalence of schizophrenia is about 3/1000 individuals. People with schizophrenia are 2-3 times more likely to suffer premature mortality [2].

Treatment for schizophrenia includes pharmacotherapy and non-pharmacological psychosocial interventions, antipsychotics are the major part of pharmacological treatment for schizophrenia. They have been categorized as first-generation antipsychotics (FGAs) (otherwise known as typical or conventional) (e.g., loxapine, perphenazine, molindone, haloperidol, trifluoperazine, thiothixine, chlorpromazine) and second-generation antipsychotics (SGAs) (otherwise atypical antipsychotics) (e.g. quetiapine, ziprasidone, aripiprazole, clozapine, risperidone, olanzapine) Patients with schizophrenia take antipsychotic medications for a long duration and for these patients, usage of medications is difficult to maintain adequate symptom control and achieve better health outcomes. Further significant economic burden will be imposed more on the patients and their families. Patients on using antipsychotics usually experience complex side effects such as extra pyramidal symptoms, depression, and sexual dysfunction [3].

In mono therapy, Second-generation antipsychotics (SGAs) are considered first-line. There was lack of consensus regarding use of first-generation antipsychotics (FGAs) as first choice. First-episode patients usually require lower antipsychotic dosing and should be closely monitored due to greater sensitivity to medication side effects. Drugs commonly used are aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone. Dual therapy includes SGA and FGA, combination of SGAs, (FGA or SGA) + ECT, (FGA or SGA) + other agent (e.g anti cholinergics, benzodiazepines and SSRI's) [15]

There are various studies that state that more than half of the drugs are prescribed without reason, in higher doses and in fixed combinations which are irrational. Irrational drug use is likely to reduce the drug effect, waste resources, increased cost, and lead to unnecessary drug interaction and increased drug resistance. The introduction of the core drug use indicators (CDUIs), by the WHO, has been regarded as a critical achievement in promoting the rational use of drugs. Such standardized indicators also provide a simplified tool for effectively assessing the critical aspects of drug use in primary health setting. CDUIs have been categorized into three main types: Prescribing indicators, patient care indicators, and facility indicators. Promoting safe and prudent use of drugs in schizophrenia are essential since the disease itself comes with a package of long-term treatment and side effects associated with it. [5] [6]

**Use of adjunctive medications:** Adjunctive medications are commonly prescribed for co-morbid conditions. Major depression and Obsessive-Compulsive Disorder are common co- morbid conditions in patients with schizophrenia and may respond to antidepressant medications. However, some antidepressants (those that inhibit catecholamine reuptake) can potentially sustain or exacerbate psychotic symptoms in some patients. Benzodiazepines may be helpful for anxiety, although risk of dependence and abuse exists with chronic use of this class of medication. Mood stabilizer and beta blockers can reduce aggression and improve hostility. Many patients with antipsychotic treatment experience extra pyramidal side effects and tardive dyskinesia and to treat

them, anti-cholinergics and other drugs are used. There is some evidence that vitamin E may reduce the risk of development of tardive dyskinesia at a dose of 400–800 IU daily as prophylaxis. [7]

## METHODOLOGY

A prospective observational study was conducted in a psychiatric clinic in Warangal region over a period of 2 months. 100 schizophrenia patients were collected and a pre-designed and pre-tested proforma was used to collect the required information.

Prescriptions were analysed using WHO Core prescribing indicators and compared with optimal value provided by WHO [8] [9]

- Average number of drugs per prescription was calculated by dividing total number of drug products prescribed by number of encounters surveyed.
- Percentage of encounters with an injection prescribed was calculated by dividing number of patient encounters in which an injection was prescribed by total number of encounters surveyed, multiplied by 100.
- Percentage of drugs prescribed from National List of Essential Medicine (NELM) was calculated by dividing number of products prescribed from NELM by total number of drugs prescribed, multiplied by 100.

**Inclusion criteria:** Patients of age 10-80 years were included who were diagnosed with Schizophrenia.

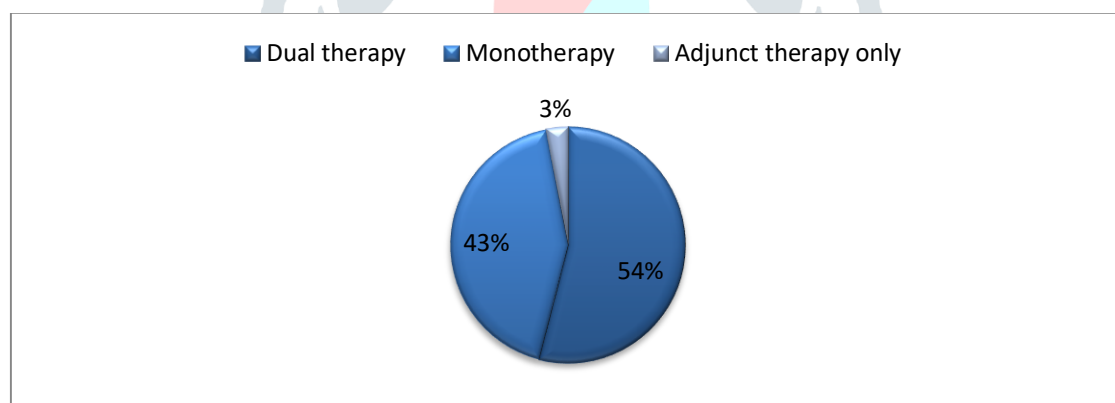
**Exclusion criteria:** In-patients and patients with other psychiatric illness were excluded.

## RESULTS

Among the study population, schizophrenia is mostly observed in age group of 21-40 (51 %) years (table 1). Both male and female were affected virtually equal with 51% and 49 % respectively (table 1). In the present study dual therapy (54 %) was preferred over mono therapy (43 %) (figure1). The most preferred antipsychotic drug combination was atypical with atypical (89 %) (table 2), Adjunctive therapy was given in most of the patients like anti-cholinergics (33 %) to reduce or avoid side-effects and benzodiazepines(38%) were given to calm the patient and get better sleep (figure 2).

In mono therapy resperidone was preferred more followed by olanzepine (37 % and 23 % respectively) (table 3). Most preferred combination antipsychotics were olanzepine with clozapine and resperidone with quetiapine (table 4). Atypical antipsychotics are most preferred over typical antipsychotics (95 % and 5 % respectively).

Prescriptions pattern was analyzed according to the WHO Prescribing Indicators and it was observed that average number of drugs per prescription was 4.1 and percentage of drugs prescribed via parental route was 6 %. Drugs prescribed from National list of Essential Medicine 2017 constituted 38 % (table5)



**Figure1: Distribution based on pharmacotherapy**

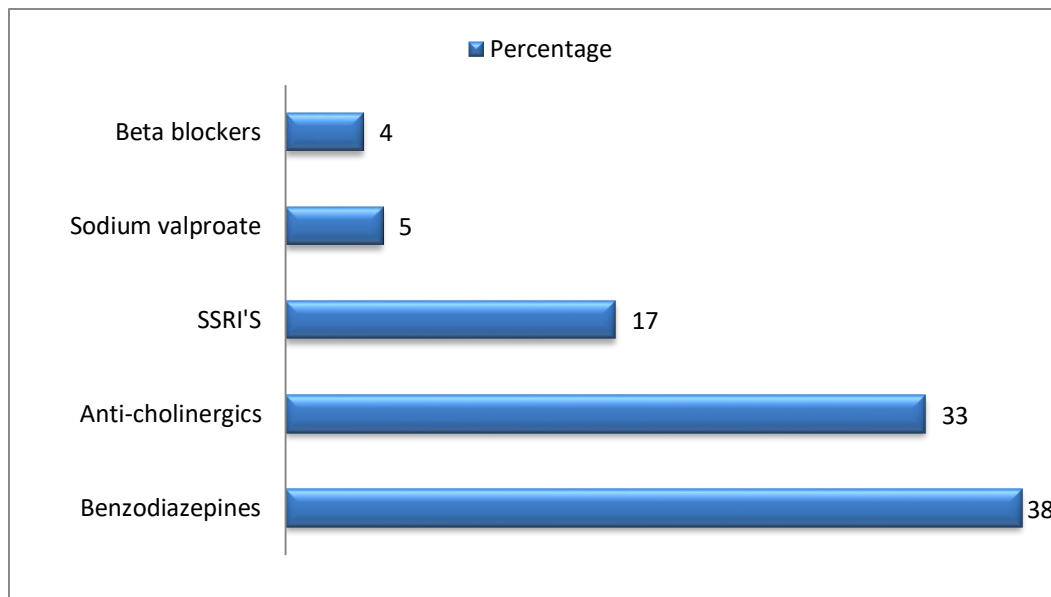
Adjunctive therapy was given only in 3 % of the patients.

**Table 1: Age and gender wise distribution of Patients**

| Age(years)    | %  |
|---------------|----|
| 10-20         | 9  |
| 21-30         | 23 |
| 31-40         | 20 |
| 41-50         | 17 |
| 51-60         | 10 |
| 61-70         | 11 |
| 71-80         | 2  |
| <b>Gender</b> |    |
| Male          | 51 |
| Female        | 49 |

**Table 2: Distribution based on antipsychotic combinations:**

| Antipsychotic drug class | %  |
|--------------------------|----|
| Atypical + Atypical      | 89 |
| Typical + Atypical       | 11 |



**Figure 2: Distribution based on adjunctive therapy**

Beta Blockers are used to control the aggressive affect and sodium valproate is used to control the excessive impulses and also improve positive symptoms. SSRI's are given to improve negative/depressive symptoms of schizophrenia patients.

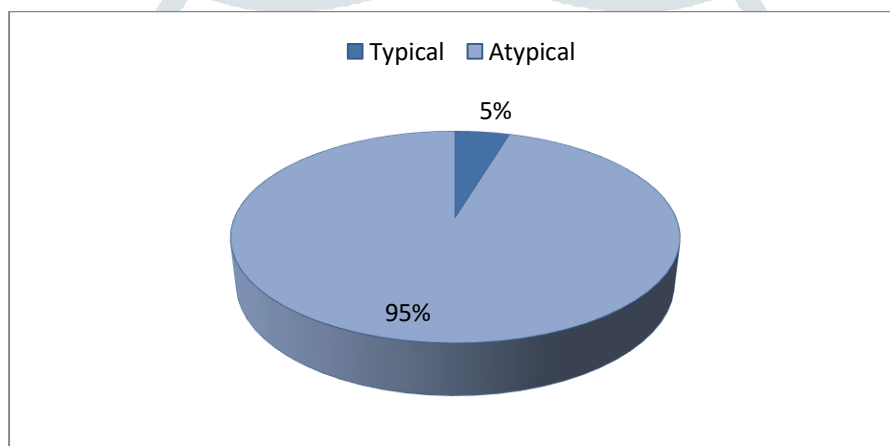
**Table 3: List of drugs used in monotherapy**

| Drug name    | %   |
|--------------|-----|
| Resperidone  | 37  |
| Olanzapine   | 23  |
| Quetiapine   | 14  |
| Amisulpride  | 14  |
| Aripiprazole | 7.5 |
| Flupenthixol | 4.5 |

According to the NLEM, resperidone and clozapine are the essential drugs for schizophrenia. Among them resperidone was most frequently prescribed (37 %) and the least prescribed was flupenthixol (4.5 %).

**Table 4: List of drugs used in combination therapy**

| Combination drugs          | Number of patients |
|----------------------------|--------------------|
| Olanzapine + clozapine     | 13                 |
| Resperidone + quetiapine   | 6                  |
| Olanzapine + amisulpride   | 4                  |
| Amisulpride + quetiapine   | 4                  |
| Resperidone +lurasidone    | 4                  |
| Clozapine + haloperidol    | 4                  |
| Aripiprazole+ lurasidone   | 3                  |
| Olanzapine + lurasidone    | 3                  |
| Quetiapine + olanzepine    | 2                  |
| Aripiprazole + resperidone | 2                  |
| Quetiapine + aripiprazole  | 2                  |
| Others                     | 7                  |



**Figure 3: Typical and atypical antipsychotics used**

**Table 5: Prescription analysis by using WHO core indicators**

| Drug use indicators                           | Outcome | Optimal value |
|---|---------|---------------|
| Average number of drugs prescribed            | 4.1     | 1.6-1.8       |
| Percentage of injectables prescribed          | 6 %     | 13.4-24.1 %   |
| Percentage of drugs prescribed from NLEM 2017 | 38 %    | 100 %         |

**DISCUSSION:**

Age and gender: In the present study, peak incidence of schizophrenia among sample size of 100 patients was observed in the age group of 21-40 years(43%) which is identical to the study conducted by *h.ksushmaet al* 2015 [10] in Bangalore where 69% of schizophrenic patients were in the same age group. The probable reason for the prevalence of schizophrenia in young adults could be environmental and psychosocial stress. In current study,only slight gender difference was observed in schizophrenic population, this is in contrary to the study conducted in Chennai by *shwetaoommen et al*, 2019 [6] where female predominance was observed and in a study conducted in Bangaloreby *h.ksushma et al* , 2015[10] male were most affected.

**Pharmacotherapy:** Dual therapy antipsychotics were prescribed more (54%) than mono therapy (43%) in this study which is similar to the *Nukala et al., 2019*[11] where dual therapy was 81% than monotherapy (19 %). This study is in contrary to the study conducted by *IramShaifali et al 2018* [8] where monotherapy was more (76%) than dual therapy (24%). In our study, use of dual therapy was more than mono therapies, which may be due to partial or minimal response with single drug hence combinations, are used.

95% of the patients were prescribed with atypical antipsychotics and 5% of the patients were prescribed with typical antipsychotics in the present study. This is identical to the study conducted by *IramShaifali et al 2018*[8] where atypical were (89%) and typical (11%) and also to the study conducted by *Nukala et al., 2019*[11] with atypical (96%) and typical (4%). The use of atypical antipsychotics is more than typical antipsychotics which may be due the use of typical antipsychotics caused more side effects compared to atypical anti psychotics.

In our study, of atypical antipsychotics in mono therapy, predominantly resperidone was the drug of choice and of combination therapy; two atypical antipsychotics were commonly used. This is identical to the study conducted by *chul-eungkim, et al. 2014* [12] where resperidone is the preferred monotherapy and both two atypical, typical and atypical are virtually equal, also it is equal in a study conducted by *Nukala et al., 2019* [11]. The reason may be as resperidone is listed among the essential drugs list NLEM [13] it is more preferred than other drugs.

Mostly used category of combination anti-psychotic drugs in our study are olanzepine with clozapine and resperidone with quetiapine. In the study conducted by *chuleungkim, et al. 2014*[12] risperidone with haloperidol, risperidone with quetiapine, and risperidone with chlorpromazine combination were majorly used. The reason for use of olanzepine and clozapine in dual therapy may be due to superior therapeutic effect of these drugs compared to other drugs [2].

Anticholinergics (33 %) and benzodiazepines (38%) were the frequently used adjunctive class of drugs in present study which is similar to the study conducted by *Nukala et al., 2019* [11] and *chul-eungkim, et al. 2014*[12] in which anticholinergics were (64.42 %) and (28.8 %) respectively and benzodiazepines were (20.19 %) and (30.3 %) respectively. The use may be due to anti cholinergic were given to reduce or avoid side-effects and benzodiazepines were given to calm the patient and to get better sleep. In our study, we conducted prescription auditing of schizophrenia patients in psychiatry OPD and compared the quality of prescriptions against the World Health Organization (WHO) recommended core prescribing indicators to investigate rational use of drugs[9]. In our study the auditing results showed that a total of 410 drugs were observed in 100 prescriptions. The average drugs per prescription were 4.1 which is higher than the WHO indicators optimal value which is 1.6-1.8. Our study results are similar to the study conducted by *Shaifali I et al 2018* [8] and *Nukala et al., 2019* [11], where average drugs per prescription was 3.15 and 2.23 respectively. Average drugs prescribed per person should be in a range of WHO optimal values so that the patient can avoid adverse effects, drug interactions and economic burden.

In our study, antipsychotics were mostly prescribed by oral route and in very few cases parental route (6 %) was preferred to control the severe symptoms. Present study results are similar to the study conducted by *Shaifali I et al., 2018* [8] and *Nukala et al., 2019*[11]; where in percentage of injections prescribed was 5.2% and 1.92% respectively. In present study, 38% of the drugs were prescribed from NLEM 2017[13]. Present study findings are similar with *Shaifali I et al. 2018*[8] and *Nukala et al., 2019* [11] in which percentage of the drugs were prescribed from NLME 2015 [14] was 43 % and 46 % respectively.

## CONCLUSION:

By conducting this study, we observed that mostly male patients suffered with schizophrenia and they were amongst age group of 21-40 years. The most commonly preferred class of antipsychotics were atypical and the therapy mostly included dual therapy followed by mono therapy. Anti cholinergics were prescribed along with antipsychotics to prevent extra pyramidal side effects due to anti psychotics and benzodiazepines were prescribed to provide better sleep and calm the patients. The average number of drugs prescribed was slightly higher than the optimal value which may be due to co morbid conditions and other factors. The choice of drugs from NLEM 2017 is also less which may be due to socioeconomic and other factors. This study over all provides the choice of antipsychotics used and outline of treatment pattern used in schizophrenia patients. Further studies are needed to improve the standard treatment in schizophrenia with rational use of antipsychotics for better patient care.

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