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Research Article

A STUDY ON DRUG-DRUG INTERACTIONS AND ADR'S AMONG PSYCHIATRY OUT-PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL

A.Ramakrishna Prasad [1]*, P. Lakshmi [2], B. Sivakala [1]
[1] Pharm D, Department of Pharmacy Practice, Sri Padmavathi School of Pharmacy, Tiruchanoor, Tirupati, Andhra Pradesh, India
[2] Assistant Professor, Department of Pharmacy Practice, Sri Padmavathi School of Pharmacy, Tiruchanoor, Tirupati, Andhra Pradesh, India
*Corresponding Author Email: ramakrishna24@live.com

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ABSTRACT

The expanding and challenging field of psychopharmacology is constantly seeking new and improved drugs to treat psychiatric disorders. In this way, psychiatrists are continuously exposed to newly introduced drugs that are claimed to be safe and more efficacious. The objective of this study is to assess and evaluate frequency of adverse effects and drug interactions. A prospective observational study conducted in a tertiary care hospital among 216 patients. Patient demographics, past medical history, family and surgical history, diagnosis and present medications prescribed were recorded. The data was obtained by direct patient interview and from patient case profiles. The collected psychotropic drugs were analysed to identify the adverse drug reaction (ADR's) and drug interactions. In a total of 216 patients, mental illness was most commonly observed in females 114 (52.70%). Majority patients were in the range of 21-30 years age group 70 (32.40%). Weight gain was commonly observed ADR with olanzapine. Drug interactions were mostly seen between the carbamazepine and risperidone. Some of the drug interactions and high prevalence ADR'S are therapeutic issues that needs to be addressed to foster evidence-based medicine.

Keywords: olanzapine, Psychotropic drugs, adverse drug reaction, weight gain and drug interactions.

INTRODUCTION

Antipsychotic drugs are the most important medications in treating patients with psychotic disorders. The development of second-generation antipsychotics (SGAs) has improved in the treatment of psychotic disorders. SGAs might have better efficacy in negative or cognitive or affective symptoms, and less extra-pyramidal symptoms (EPS) side effects. But SGAs still have problems, such as somnolence, obesity, hyperglycemia, hyperlipidemia and QTc prolongation, influencing clinicians' prescribing habits and patients' drug adherence[1]. Different SGAs have been suggested with different frequencies to receive metabolic syndrome monitoring. The consensus of the metabolic syndrome monitoring protocol for SGAs has been convened by the American Diabetes Association (ADA), the American Psychiatric Association, the American Association of Clinical Endocrinologists and the North American Association. They focused mostly on the diabetes risk, advised baseline, plasma glucose level in four months and glycosylated haemoglobin test after initiating or changing an antipsychotic medication.

Prescriptions of antipsychotic medications among children and adolescents are increasing greatly in recent years. The safety issues of antipsychotics in children and adolescents are especially a major concern. Previous studies showed that children and adolescents are more sensitive to antipsychotic side effects–extra pyramidal symptoms (EPS), sedation, body weight gain and hyperprolactinemia than adults[2-5]. Furthermore, most of antipsychotic studies are focused on adult population and only few studies on investigating the efficacy and safety of antipsychotics in children and adolescents. Therefore, antipsychotic off-label use is common for children and adolescents with various psychiatric illnesses or symptoms. Only few antipsychotics–haloperidol, thioridazine, pimozide, risperidone, olanzapine and aripiprazole – are approved by the Food and Drug Administration (FDA) of the USA in treating some psychiatric illnesses in children and adolescents.

Extra-pyramidal symptoms (EPS) such as acute dystonia, akathisia and Parkinsonism are among the most common adverse effects of antipsychotics. In clinical practice, anticholinergics are widely used to treat and prevent antipsychotic- induced EPS. Anticholinergics should be prudently prescribed because these drugs in addition to their well-known peripheral side-effects may worsen positive symptoms, appear to partially ameliorate negative symptoms and are associated with impaired cognitive functioning of schizophrenic[6] and cognitive impairment in elderly patients[7]. A recent report[8] has confirmed that there is a wide variation in anticholinergics medication prescribing across various countries; combination of clinical, social, economic and cultural factors are the determinants of the use of these drugs suggesting that there are considerable differences between treatment guidelines and clinical practice.

The initial enthusiasm about the second generation of atypical antipsychotic drugs has changed into criticism and debate culminating in the controversial CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness), CUTLASS (Cost Utility of

the Latest Antipsychotic Drugs in Schizophrenia Study) and EUFEST (European First-Episode Schizophrenia Trial) trials. The debate seems to be driven more by values than by data; some place an emphasis on cost, others focus on extra-pyramidal side effects, weight gain or efficacy[9,10].

MATERIAL AND METHODS

Study site

Sri Venkateswara Ramanarayana Ruia Government General Hospital, Tirupati, Psychiatry department, Psychiatry out-patient pharmacy.

Study design

Prospective observational study

Study population

216 prescriptions

Study period

The present study was carried out for a period of 6 months (november-2018 to april-2019).

Inclusion criteria

Prescriptions of patients of both sex and all ages, suffering from a psychiatric illness and started on at least one psychotropic drug were selected.

Exclusion criteria

- Pregnant and lactating woman.
- In-patients, referred patients
- Patients with epilepsy
- Those cases where diagnosis is not certain.

Method of data collection

Following data was collected from the psychiatric out-patient prescriptions.

- Demographic data of the patient.
- Diagnosis of the patient.
- Drug therapy used in the management of psychiatric disorder.
- Specially designed proforma is used to collect above data.

Data analysis

Data were entered and analyzed using Microsoft Excel 2013. And graph pad prism

Ethical approval

Institutional ethical committee approved project under Proposal No: SPSP/2018-2019/PB01.

RESULT

The sample size of the present study was 216 patients and assessed for drug interaction and adverse drug reactions.

Table 1: Gender wise distribution among patients

Gender	Number of patients (n = 216)	Percentage
Male	102	47.22%
Female	114	52.70%

Out of 216 patients, highest number of patients was under females 114(52.70%), followed by males 102(47.22%).

Table 2: Age wise distribution among patients

Age (years)	Number of patients (n = 216)	Percentage
< 20Y	21	9.70%
21 Y – 30 Y	70	32.40%
31 Y - 40 Y	61	28.24%
41 Y – 50 Y	39	18.05%
51 Y - 60 Y	18	8.33%
61 Y – 70 Y	4	1.80%
> 70Y	3	1.38%

Out of 216 patients, highest number of patients was under the age group of 21 – 30 Y 70 (32.40%) followed by 31-40 Y 61 (28.24%), 41-50 Y 39 (18.5%), < 20Y 21 (9.70%), 51-60 Y 18 (8.33%), 61-70Y 4 (1.80%), > 70Y 3 (1.38%).

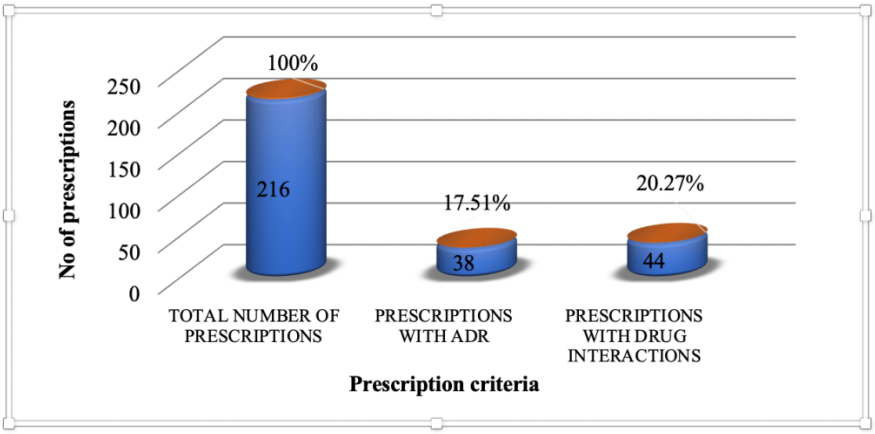

Figure 1: Prescriptions with ADR's and drug interactions

Out of 217 prescriptions 38 prescriptions with ADR'S and 44 prescriptions with drug Interactions

Table 3: Drug-drug interactions in prescriptions

Drug-drug interaction	Number of drug interactions (n = 44)	Percentage
Carbamazepine-Risperidone	8	18.18%
Lithium carbonate-Olanzapine	6	13.64%
Valproate sodium-Olanzapine	5	11.36%
Lithium carbonate-Risperidone	5	11.36%
Amitriptyline-Escitalopram	5	11.36%
Amitriptyline-Risperidone	3	6.82%
Valproate sodium-Risperidone	3	6.82%
Carbamazepine-Olanzapine	2	4.55%
Carbamazepine-Valproate sodium	2	4.55%
Escitalopram-Olanzapine	2	4.55%
Alprazolam-Carbamazepine	2	4.55%
Trihexyphenidyl (THP)-Valproate sodium	1	2.27%

Out of the total 216 prescriptions 44 drug interactions are seen in which carbamazepine-risperidone 8 (18.18%) are mostly seen followed by the other drugs.

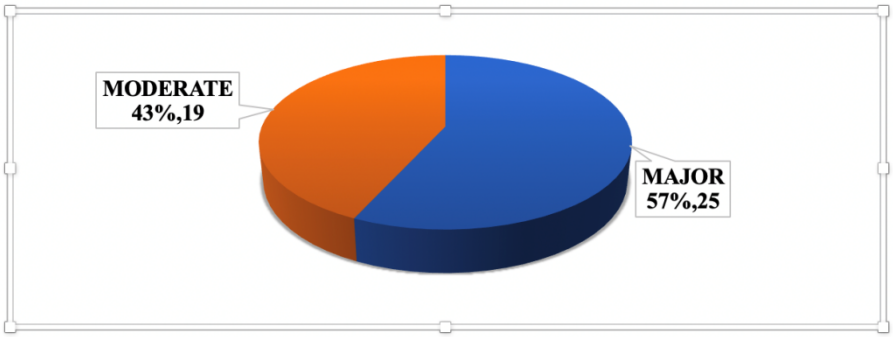

Figure 2: Severity of drug interactions

Out of the total 44 drug interactions 25 drug interactions have major severity and 19 drug interactions have moderate severity.

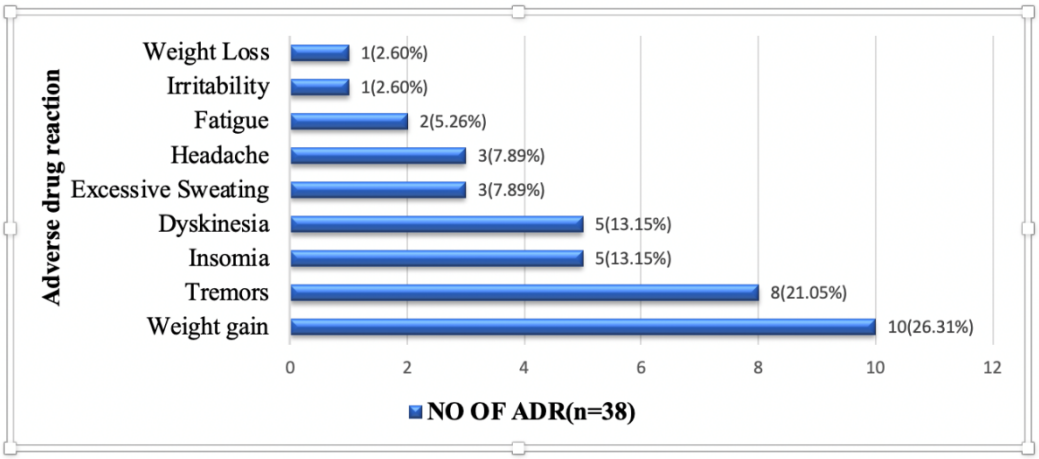

Figure 3: Types of ADRs observed among patients

Out of the total 38 ADRs the most commonly seen ADR is weight gain 10 (26.31%) followed by Tremors 8 (21.50%), Insomnia 5 (13.15%), Dyskinesia 5 (13.15%), Sweating 3 (7.89%), Headache 3 (7.89%), Fatigue 2 (5.26%), Irritability 1 (2.60%) and Weight loss 1 (2.60%)

Table 4: Drugs caused ADR's

Drug name	Number of ADR's (n = 38)	Percentage
Olanzapine	8	21%
Risperidone	7	18%
Valproate sodium	7	18%
Diazepam	4	11%
Escitalopram	3	8%
Lithium Carbonate	3	8%
Trihexyphenidyl (THP)	3	8%
Amitriptyline	3	8%

Out of the total 38 ADR'S most ADR'S caused by olanzapine 8 (21%), followed by risperidone 7 (18%), Valproate sodium 7 (18%), Diazepam 4 (11%), Escitalopram 3 (8%), Lithium carbonate 3 (8%), Trihexyphenidyl THP 3 (8%) and Amitriptyline 3 (8%).

DISCUSSION

A total of 216 patients were included in the present study. Among total study population the female patients are found to be more than the male patients. These findings were similar to Venkatesh perumal *et al*.[11] study. These results are contrast to many studies were males are found to be more prone then the females. With poor social support experience mental health problems are more frequent in females than males and those with strong social support. In general, according to literature there is no difference between the genders in the incidence of psychiatry disorder.

In present study population, based on age wise distribution of patients the 21years to 30 years patients are more prone then the other age group patients followed by 31 y – 40 y, 41 y – 50 y, < 20 y, 51 y – 60 y and > 70 y. These findings are similar to the Anjali George *et al*.[12] study. Because increased incidence of mental health, due to failures in the academic and in early career setting this age group are mostly affected to mental health problems, improved mental health literacy in general population.

In the present study population based on ADR's and drug interactions among patients out of total 216 prescriptions 38 prescriptions contain ADR's but most of the ADR causing drugs are not replaced with any other drugs because when assessed with risk vs. benefit ratio it is justifiable and 44 prescriptions contain drug interaction it should be addressed. This study is similar to the Tarun Jain *et al*.[13] study; because most of the psychotropic drugs cause extrapyramidal symptoms.

In the present study severity of drug interactions out of 44 drug interactions 57% of drug interactions have major severity and remaining 43% of drug interactions have moderate severity. This study is similar to the Tarun Jain *et al*.[13] study. The drug interactions among patients need to be addressed.

In the present study types of ADR's among total 38 ADR's weight gain (10) was mostly present followed by tremors (8), Insomnia (5), Dyskinesia (5), Excessive Sweating (3), Headache (3), Fatigue (2), Irritability (1) and Weight loss (1) this study is somewhat similar to the Sathvik Belagodu Sridhar *et al*.[14] study.

In the current study drugs caused ADR's among patients of the total 38 ADR's Olanzapine (8) was mostly seen followed by Risperidone (7), Valproate sodium (7), Diazepam (4), Escitalopram (3), Lithium carbonate (3), Trihexyphenidyl THP (3) and Amitriptyline (3). This study is contrast to the Tarun Sharma *et al*.[15] study. Because prescribing of drugs vary from hospital to hospital so the ADR's caused by drugs changes from study to study.

The present study has certain limitations that we did not evaluate factors such as patient compliance and adherence to treatment while prescribing. The study was conducted in patients attending the out-patient department OPD of government general hospital in south India thus the results cannot be a representative of national data. As the study was performed in government hospital the hospital resources like availability of free medicines etc., govern the issue of poly pharmacy which has not been considered in this study.

CONCLUSION

Some of the dosing strategies, drug interactions and high prevalence of ADR's are therapeutic issues that need to be addressed to foster evidence-based medicine. While some of the patients contain ADR's, the continuation of the drug is justifiable when compared with risk vs. benefit ratio to improve the patient quality of life. Present study will help in further conducting drug utilization studies.

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