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METABOLIC AND CARDIOVASCULAR ADVERSE DRUG REACTION MONITORING OF PSYCHOPHARMACOLOGICAL AGENTS TARGETED PHARMACOVIGILANCE STUDY

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ABSTRACT

In this targeted Pharmacovigilance study we found increased in metabolic and cardiovascular parameters such as increased in weight that was statically highly significant ($p<0.02$), random blood sugars significant ($p<0.05$) and cholesterol was significantly not increased ($p<0.11$). The systolic, diastolic blood pressure were significantly increased systolic ($p< 0.01$) diastolic ($p<0.02$) and there is no significant increased in higher density lipoprotein (HDL) ($p<0.06$) but low density lipoprotein (LDL) were statically significant ($p< 0.02$). Hence, psychiatrist's patients to information the concept of identify and report of potential adverse drug reaction. There are is very few reports of Adverse effect profile of anti psychotropic medication reported in Pharmacovigilance program of India (PvPI) is still in infancy and ADR reporting rates is low and requires more data. In this study only Patients men and women attending the psychiatric IPD department suffering from psychotic disorder they were include into the study.

KEYWORD: Adverse drug reaction, psychotropic drug, Pharmacovigilance, metabolic adverse effect.

INTRODUCTION

An adverse drug reaction (ADR) is 'a response to a drug that is noxious and unintended and occurs at doses normally used in humans for the prophylaxis, diagnosis, and treatment of disease, or for modification of pharmacological function.[1] The commonly adverse drug effects associate with psychotropic drugs are weight gain, somnolence, tremors, and tardive dyskinesia. These adverse drug effects tend to deteriorate the mental and physical well-being of the patient and thus lead to patient non-adherence to therapy.[2] Forty to sixty-two percent of people with schizophrenia are overweight or obese. Obesity increases these patients' risk for cardiovascular morbidity and mortality. In addition, excessive weight and obesity can have important effects on an individual's adjustment in the community, adherence to prescribed medication, ability to participate in rehabilitation efforts, and self-image.[3] Pharmacovigilance is, "The Pharmacological Science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines.[4] Pharmacovigilance in psychiatry units can play a major role in detecting adverse effect and alerting physicians to the possibility and circumstances of such events, thereby protecting the user population from avoidable harm. Many psychotropic drugs are present in India and their use is increasing day by day. Commonly used psychotropic drugs in psychiatry O.P.D.[5] the patients suffering from schizophrenia are at increased risk for Type II diabetes,[6] because of poor overall physical health, poor health care, less healthy lifestyles, and side effects of antipsychotic medication. The rates of diagnosed diabetes exceeded general population well before the widespread use of the new antipsychotic drugs.[7,8] An increasing body of evidence indicates that, compared with the general population, people with early-stage or previously untreated schizophrenia and bipolar disorder are at an increased risk of overweight (BMI 25–<30 kg/m2), obesity (BMI "30 kg/m2) and central obesity (waist circum ference >102 cm in men and >88 cm in women; that is, a 2.8–3.5-fold increase in the risk of obesity in patients with schizophrenia and a 1.2–1.5-fold increase in patients with bipolar disorder).[9,10] In addition, weight gain is a well-established adverse effect of acute and maintenance antipsychotic treatment in

patients with schizophrenia, and affects between 15% and 72% of patients.15,16 Accumulating evidence suggests that similar effects occur in patients with bipolar disorder.[11-12] Adverse events associated with the use of atypical antipsychotic medications are thought to be largely, but not singularly, contributory to cardio metabolic and endocrine side effects constituting metabolic syndrome; and children and adolescents receiving atypical antipsychotic medications are particularly vulnerable to these effects.[13] There is an immense need to strengthen these activities and develop ADRs profile of psychotropic drugs.[14] Thus, ADR monitoring helps in developing appropriate interventional strategies to manage, prevent and minimize the risk of developing ADRs and thereby reducing the cost of care.[15]

AIMS AND OBJECTIVES

Aim

Monitoring of adverse metabolic effects of psychopharmacological agents: targeted Pharmacovigilance study.

Objectives

The main purpose of this study was to investigate Metabolic and cardiovascular adverse drug reaction monitoring of psychopharmacological agents.

Materials and methods study site

In patients is admitted cases of Departments of Psychiatry in CSS Subharti Hospital and Pharmacology, Subharti Medical College, Meerut. The age of the patients was 18–60 years. All the patients was duly informed about the research work, possible effects, and side effects of Psychotropic drug. They was enrolled in the study with their own interest, and a written informed consent was taken from everyone. The duration of this study will be approx 6 months (24 weeks). Institutional ethics committee approval was obtained before the start of the study.

Institutional ethics Reference Number: The study was approved by the Institutional Ethics Committee of Chhatrapati Shivaji Subharti Hospital and Pharmacology, Subharti Medical College, Meerut. **SMC/IEC/2017/193.**

Patients Population: Patients seeking treatment at C.S.S.Subharti hospital was enrolled. Cooperative patients were allocated by the consultant for the study. Clinical monitoring was done by consultant psychiatrist. The data was recorded by pharmacy clinical research associate along with Pharmacovigilance research associate. An investigation was recorded from patients treatment file.

Parameters: A standardized question to record patient characteristics and disease particulars, treatment allocated, out come, adverse effects, metabolic and cardiovascular parameters and any spontaneously reported adverse effect. WHO tools will be used for assessment of causality, severity, preventability and seriousness of adverse effect.

What is Body Mass Index (BMI)

Body Mass Index (BMI) is a measurement of a patient's weight with respected to this or her height. It is more of an indicator than a direct measurement of a patients total body fat.

BMI, more often than not, correlates with total body fat determine. This means that as the BMI score increases, so does a person total body fat.

BMI calculation

Basal metabolic rate in an individual is calculated by the use of a mathematical formula. It can also be estimated using below tables in which one can match height in inches to weight in pounds to estimate BMI. There are convenient calculators available on internet sites that help calculate BMI as well. The formula is BMI = (Weight in kilograms) divided by (Height in meters squared) A normal BMI score is one that falls between 18.5 and 24.9. This indicates that a person is within the normal weight range for his or her height. A Basal metabolic rate chart is used to categorize patients as underweight, normal, overweight, or obese.

Body Mass Index (BMI)	Weight Status
Below 18.5	Underweight
18.5 - 24.9	Normal
25.0 - 29.9	Overweight
30.0 plus	Obese

For example those with a high BMI are at risk of

- High blood cholesterol or other lipid disorders
- High blood pressure
- Type 2 diabetes
- Certain cancers
- Heart disease
- Osteoarthritis and joint disease
- Gallbladder disease
- Sleep apnea and snoring.[16]

Classification of cholesterol levels

Lipid profile level (mg/dl)	Classification
TC	**Total cholesterol**
<200	Desirable
200-239	Borderline high
≥ 240	High
TG	Tri glycerin
<150	Optimal
150-199	Borderline high
200-499	High
≥ 500	Very high
HDL-C	**HDL-C High density lipoprotein cholesterol**
<40	Low
≥ 60	High
LDL-C	**Low- density lipoprotein cholesterol**
<100	Optimal
100-129	Near or above optimal
130-159	Borderline high
160-189	High
≥ 190	Very high
VLDL-C	**Very –low density lipoprotein**
≤ 30	Normal

TC, Total cholesterol; LDL-C, Low- density lipoprotein cholesterol; VLDL-C, Very -low Density lipoprotein; HDL-C, High -density lipoprotein cholesterol; TG, Triglyceride

Blood glucose

The primarily sugar the body makes from the sustenance in the eating routine. Glucose is brought through the circulatory system to give vitality to all cells in the body. Cells can't utilize glucose without the assistance of insulin. Glucose is a direct sugar (a monosaccharide). The body produces it from protein synthesis, fat and, in greatest part, starch. Ingested glucose is held clearly into the blood from the stomach related framework and results in a quick augmentation in blood glucose. Glucose is generally called dextrose.

Measurement of Blood glucose level

From Your Fingertip: You prick your finger with a small, sharp needle (called a lancet) and put a drop of blood on a test strip. Then you put the test strip into a meter that shows your blood sugar level. You get results in less than 15 seconds and can store this information for future use A few meters can disclose to you your normal glucose level over some stretch of time and show you diagram and charts of your past test outcomes. You can get glucose meters and strips at your nearbypharmacy.[17]

Procedure: Both admitted and outdoor psychiatric patient was enrolled in the study. This is an exploratory open label study design. Adult patients of either sex were screened by the consultants. The patients to be enrolled in study were selected by consultant psychiatrists. Patient characteristics, diseases particulars, treatment, outcome and adverse effects if any was recorded. Metabolic parameters including major of weight and random blood sugars and cholesterol. Systolic and diastolic blood pressure and higher density lipoprotein (HDL) and low density lipoprotein.

Need for the study: Pharmacotherapy for psychiatric disorders is frequently associated with adverse drug reactions (ADRs). Different drugs may need to be tried in a patient to control the symptoms, which increases the risk of ADR. Almost all the psychiatric diseases have temporary cure and the treatment is lifelong. Hence, psychiatrists need to be informed the concept of identification and reporting of potential ADRs. Pharmacovigilance in India is still in infancy and ADR reporting rates is low and requires more data. There are very few reports of ADR profile of psychotropic drugs. Hence, this targeted Pharmacovigilance study is required to evaluate the pattern of ADRs among hospitalized patients in Psychiatry Department of a Chhatrapati Shivaji Subharti hospital a tertiary care hospital.

Inclusion Criteria

1. Patients men and women attending the psychiatric IPD department suffering from psychotic disorder they was include into the study.[18]

2. All patients (old and new) who were diagnosed with psychiatric disorders as per International Classification of Diseases-ICD10 criteria4 and prescribed antidepressants, antipsychotics or mood stabilizers and benzodiazepine more common prescribe drug.[19]

Exclusion criteria

1. In this study Pregnant Women not considered.
2. HIV Patients
3. Patients with other psychiatric disorder.[20]

RESULT

Table 1: Change in Metabolic Parameters of Adverse effects.

Parameter	Before	After	P –Value
Weight (Kg)	56.6 ± 1.33	60.93 ± 1.31	0.02
RBS (mg/dl)	131.1 ± 2.14	137.7 ± 2.45	0.05
Cholesterol (mg/dl)	170.03 ± 1.3	173.36 ± 1.61	0.11
BP Systolic (mmHg)	129.6 ± 1.60	136 ± 1.83	0.01
BP Diastolic (mmHg)	87.53 ± 0.88	90.36 ± 0.87	0.02
HDL (mg/dl)	46.86 ± 0.96	44.1 ± 1.08	0.06
LDL (mg/dl)	164.2 ± 1.63	170.33 ± 2.18	0.02

Values are expressed as Mean ± SEM, n= 30 in each group. Data was analyzed by unpaired t test

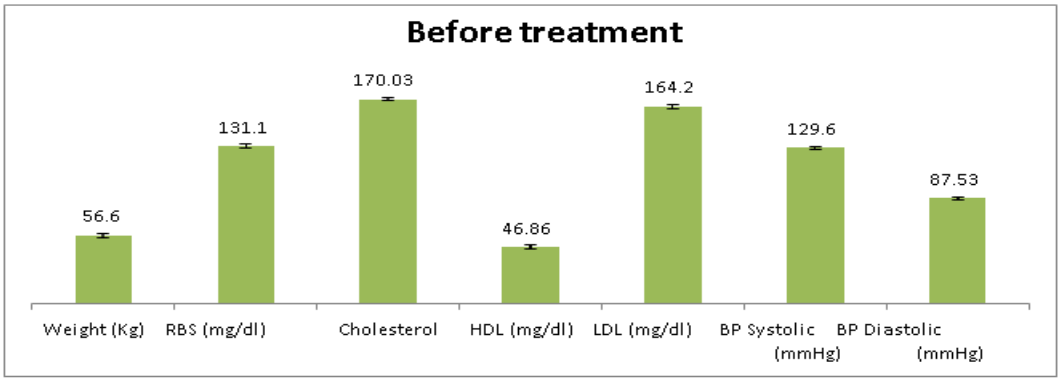

FIGURE: (1)

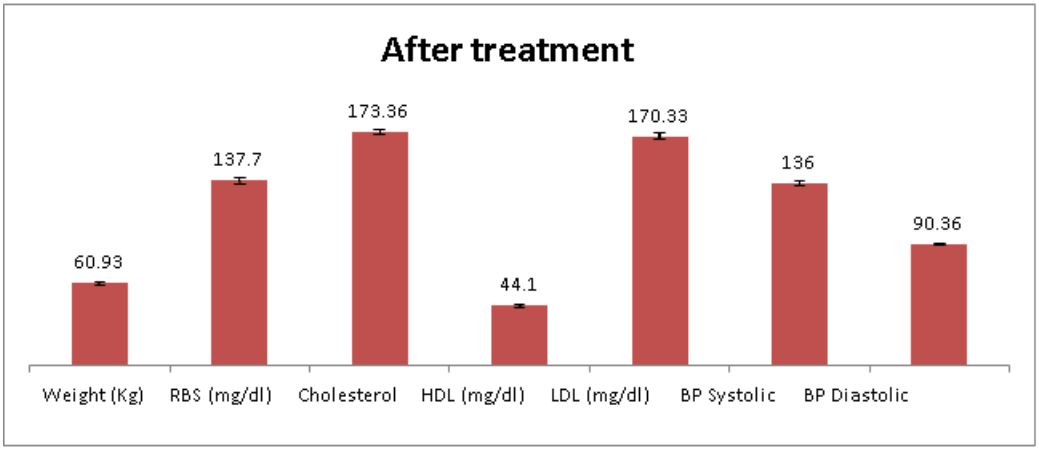

FIGURE: (2)

Graph 1: shows change in metabolic parameters as adverse effects in patients in the study. There was increase in body weight, random blood sugar as well as cholesterol in the 30 of the study patients.

Table: 1 and Graph shows metabolic parameters adverse effects. Weight in these patients was 56.6 kg at the start of treatment and in 4 weeks increased to 58.75 kg. The random blood sugar was 131.10 mg/dL and increased to 137.7 mg/dL after treatment cholesterol was 170.03 mg/dl before and after increase to 173.36 mg /dL after treatment and blood pressure systolic was before treatment 129.6 mmHg and after treatment increase to 136 mmHg. And high density lipoprotein (HDL) was before treatment 46.86mg/dl and after after treatment to 44.10mg/dl and non significant of (HDL). Low density lipoprotein before treatment was 164.20mg/dl and after treatment increase to 170.33mg/dl. There was increase in weight, random blood sugar andcholesterol, and systolic and Diastolic blood pressure and increase in low density lipoprotein (LDL) and decrease was level higher density lipoprotein (HDL) in blood. This increase was significant statistically ($p \leq 0.05$)

DISCUSSION

In Psychiatry Department of a Chhatrapati Shivaji Subharti hospital a tertiary care hospital. Location of hospital near rural area could be cause of more patients (55%) from rural area. Social position of males could be cause of predominance of male (59%) patients. The was reflect side effects of drugs that were predominantly used in these patients. This was more findings about

antipsychotics, antidepressants, sedatives and hypnotics that were most commonly used in the study population. Endocrinal, cardiovascular, central nervous system, autonomic system, gastrointestinal and dermatological systems' side effect were more common. Weight gain, body mass index, cholesterol profile and sugar profile disturbance were the main metabolic parameters affected. The adverse effects are to be seen in context of seriousness of disease condition of the patient. 70(63.6%) had mild adverse effects where as 40(36.4%) had moderate adverse effects and none had severe adverse effects. 38% were definitely preventable, 35% were probably preventable, and 27% were not preventable as per clinical evaluations and application of scale.

CONCLUSION

We found most of adverse effects were labeled and documented e.g. extra pyramidal symptoms, tremor, akathisia, sedation increased appetite, change in sex ability, mood irritability and dryness of mouth. In this study we were also targeting the effects of psychiatric drug on metabolic parameter. We conclude that psychiatric drugs are causing to increase the metabolic disorder. The most commonly observed adverse reactions in metabolic disorder were weight gain, increases cholesterol level, blood glucose level, blood pressure, low density lipoprotein (LDL). Our study builds up the ADR figures of psychotropic drugs likely to be encountered in IPD and OPD of a tertiary care hospital. The study results strongly suggests the need for healthcare team to focus on assessing and reporting suspected ADRs to enhance the quality of monitoring and managing ADRs. A comprehensive daily ADR program or reporting system in a hospital can help to complement organizational risk management activities, assess the safety of drug therapies, ADR incidence rates over time and educate healthcare professionals of drug effects and increase their level of awareness regarding ADRs of new and old drugs

REFERENCE

1. World Health Organization. Requirements for adverse reaction reporting. Geneva, Switzerland: World Health Organization, 1975.
2. Sarumathy S, Menaka K, Samuel Gideon George P, Ravichandiran V. A study on drug use pattern and adverse drug reactions of anti-psychiatric medications in a psychiatry specialized hospital. International Journal of Pharmacy and Pharmaceutical Sciences, 2014; 6: 332-4.
3. Haupt DW. Differential metabolic effects of antipsychotic treatments. Eur Psychopharmacology, 2006; 16(Suppl. 3): 149-55.
4. Faich GA. US adverse drug reaction surveillance 1984-1994. Pharmacoepidemiol Drug Saf., 1996; 5: 393-8.
5. Arason JK. Risk perception in drug therapy. Br J Clin Pharmacology, 2006; 62: 135-7.
6. Subramanian M, SiowAnn C, Elaine P.Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia. Can J Psychiatry, 2003; 48: 345–7.
7. Meyer, Jonathan, Catherine, et al. Prevalence of the metabolic syndrome in veterans with schizophrenia. Journal of Psychiatric Practice, 2006; 12(1): 5-10.
8. Jonathan M, Henry A, Joseph P.et al. Clinical comparison of subgroups with and without the metabolic syndrome. Schizophrenia Research, 2005; 80(1): 9-18. Doi: 10.1016/ j.schres.2005.07.015.
9. Maina, G., Salvi, V., Vitalucci, A., D'Ambrosio, V. & Bogetto, F. Prevalence and correlates of overweight in drug-naïve patients with bipolar disorder. J. Affect. Disord, 2008; 110: 149–155.
10. De Hert, M. et! al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World Psychiatry, 2011; 10: 52–77.
11. Parsons, B. et!al. Weight effects associated with antipsychotics: a comprehensive database analysis. Schizophr. Res., 2009; 110: 103–110.
12. Van Winkel, R. et!al. Prevalence of diabetes and the metabolic syndrome in a sample of patients with bipolar disorder. Bipolar Disord, 2008; 10: 342–348.
13. De Hert M, Dobbelaere M, Sheridan EM, et al. Metabolic and endocrine adverse Effects of second-generation antipsychotics in children and adolescents: a systematic Review of randomized, placebo controlled trials and guidelines for clinical practice. *Eur Psychiatry*, 2011; 26: 144-158.
14. Sengupta G, Bhowmick S, Hazra A, et al. Adverse drug reaction monitoring in psychiatry out-patient department of an Indian teaching hospital. Indian J Pharmacology, 2011; 43(1): 36–39.
15. Rajakannan T, Mallayasamy S, Guddattu V, et al. Cost of adverse drug reactions in a South Indian tertiary care teaching hospital. *J Clin Pharmacology*, 2012; 52(4): 559–565.
16. Kumar T, Khosla PP, Monitoring adverse drug reaction of psychopharmacological agents: a Pharmacovigilance study in tertiary care centre, Pharmacy & Pharmacology International Journal, 2018; 6(6): 485.
17. https://www.news medical.net/ health/what is body mass index BMI asps, 27/04/2018.
18. https:www.webmd.com/diabetes/guide/how-test blood glucose#1(29/04/2018)
19. Lahon K, Shetty Harsha M, Paramel International Journal of Pharma and Bio Sciences, Vol 3/Issue 1, Jan – Mar 2012; 471.
20. Kuma T, Khosla PP, Monitoring adverse drug reaction of psychopharmacological agents: a Pharmacovigilance study in tertiary care centre, Pharmacy & Pharmacology International Journal, 2018; 6(6): 487.