ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 07 | July - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ADVERSE DRUG REACTION MONITORING OF DRUGS USED IN THE TREATMENT OF PSYCHIATRIC ILLNESS IN A TERTIARY CARE INSTITUTION .

Pharmacology

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ABSTRACT

Background: Adverse drug reactions (ADRs) to psychotropic drugs are common. There are very few reports of ADR profile of psychotropic drugs. Pharmacovigilance of psychotropic drugs is essential to improve patient care and create awareness among physicians. **Objective:** To study the pattern of ADRs among patients in the OPD of Psychiatry of Tertiary Care Hospital. **Materials and Methods:** This prospective study was conducted at a Tertiary Care Teaching Hospital and all the patients who developed ADR to atypical antipyschotics and antidepressant drugs formed the study population. Details were documented from OPD prescription slips and filled in ADR reporting form and Causality assessment was done based on WHO Causality scale. Data were subjected to descriptive analysis. **Results:** During the study period, 100 patients developed a total of 180 ADRs. Based on causality assessment in these cases as per WHO Causality scale, most were judged as probable, followed by possible and then certain. The most common ADRs observed were extrapyramidal symptoms. Antipsychotics are the most common group of drugs found responsible for most of the ADRs; olanzapine being the individual drug which caused the maximum number of ADRs. **Conclusion:** Active surveillance from the part of clinicians and pharmacologists will help build a database for ADRs in Indian setting.

KEYWORDS

Adverse drug reactions, causality assessment, atypical antipyschotics, antidepressant drugs, pharmacovigilance

INTRODUCTION

A noxious and unintended response that occurs at drug doses that is usually used in man for treatment, prophylaxis, or diagnosis of a disease or for alteration of physiological function is called an adverse drug reaction (ADR).[1] Adverse events are any unpleasant medical occurrence associated with the use of a drug in humans not considered drug related.[2] A serious adverse event or reaction is any unpleasant medical occurrence at any dose resulting in the death of the patient or one that is life threatening, demands hospitalisation, or the prolongation of existing hospitalisation and which results in persistent or significant disabilities or incapacities.[3]

The science and activities relating to the detection, assessment, understanding, and prevention of adverse effects, or any other medication related problems is defined as pharmacovigilance. Pharmavigilants are the professionals engaged in pharmacovigilance, which is an integral part of drug therapy and it is slowly gaining importance in our country as more numbers of ADR monitoring centres are developing under the Pharmacovigilance Programme of India (PvPI).[4]

The second generation or "atypical" antipsychotic medications are the most widely used antipsychotic drugs in psychiatric practice because the first generation or conventional or "typical" antipsychotics are associated with poor efficacy against negative symptoms and are associated with more unwanted extrapyramidal signs and symptoms (EPS). Particularly at higher doses these typical antipsychotics commonly show bizarre body movements like Parkinsonism, rigidity, and tremors.[5] Currently available atypical antipsychotics are olanzapine, risperidone, clozapine, amisulpride etc. These agents are used in various types of psychiatric manifestations including schizophrenia and bipolar disorder. They have shown to improve quality of life, have better medication compliance, decrease suicidal tendencies, and depression in these patients.[6] In cases of schizophrenia these agents have shown remarkably lower incidence of EPS and significantly reduce both positive and negative symptoms of schizophrenia. The spectrum of ADRs like weight gain, tremor, insomnia, extrapyramidal symptoms, anticholinergic side effects, cardiovascular symptoms, metabolic disturbances, hematological disturbances and gastrointestinal (GI) upset.[7]

In case of antidepressants, SSRIs are preferred over tricyclic antidepressants as they have less anticholinergic side effects, antiadrenergic side effects, antihistaminic side effects. The common side effects seen with SSRIs are gastritis , sedation , oral ulcer , restlessness , erectile dysfunction, tremor , anxiety , insomnia , dizziness , headache , weight gain , vomiting , abdominal discomfort , abdominal distension , diarrhea , postural hypotension , sweating , problem with urination. The commonly prescribed SSRIs are fluoxetine, fluvoxamine, citalopram, paroxetine etc.

Therefore, for achieving a successful treatment in patients with different psychiatric manifestations healthcare professionals have to detect and assess ADRs of atypical antipsychotic drugs and antidepressants and report, if any to PvPI which after analysing shall forward the data to Uppsala ADR monitoring in Sweden for signal generation. ADR reports from psychiatric units are very less.[8] To protect the population on antipsychotic and antidepressant drugs from avoidable harm, assessment of ADRs in psychiatric department can play a vital role by detecting ADRs and alerting the physicians to the possibility and circumstances of such events. There is a definite lack of Indian studies on pharmacovigilance activities in mental health sector. Hence, the present study was conducted to evaluate the surveillance of ADRs of atypical antipsychotic drugs and antidepressant drugs in the department of psychiatry in a tertiary care hospital of Amritsar.

OBJECTIVE:

1. To monitor the adverse drug reactions (ADRs) of drugs given for pyschosis, depression, mania, bipolar disorder, obsessive compulsive disorder, in the outpatient department (OPD) of psychiatry in Guru Nanak Dev Hospital, Amritsar attached to government medical college ,Amritsar.
2. To know the safety of two group of drugs used for treatment of psychiatric illness.
3. To know about the most prescribed drug in two groups ie atypical antipsychotics and antidepressants .
4. To evaluate the drug causing maximum number of side effects in two groups.
5. To evaluate the causality assessment and severity of various adverse drug reactions noted.

METHODOLOGY:

It was a prospective observational study carried in OPD of psychiatry in Guru Nanak Dev Hospital, Amritsar attached to government medical college, Amritsar. Total 100 patients were included in this study. Study was conducted for a period of nine months from September 2020 to May 2021.

INCLUSION CRITERIA

Patients with any psychiatric disorder above 18 years of either sex who are prescribed antipsychotic drugs or antidepressant were included.

EXCLUSION CRITERIA

Patients admitted in wards. Patients of any history of drug abuse. Patients with any other medical or surgical disease. Pregnant women were also excluded from the study.

ADRs reported spontaneously by the patients on the prescription slips were recorded . ADRs were documented on ADR reporting form and sent to PVPI .Causality assessment using WHO Causality scale of the ADRs and severity of ADRs were reported . Atypical antipyschotics prescribed are olanzapine, risperidone, clozapine and amisulpride.

Antidepressants given are SSRIs like fluoxetine, fluvoxamine , citalopram, paroxetine. Patients complained of different types of adverse drug reactions after taking the medicines were counted.

Incidence of drugs prescribed in male and female patients were recorded. Total different types of ADRs were detected with the use of these drugs. Weight gain, extrapyramidal symptoms like akathesia, drug induced restless legs syndrome (RLS), acute muscle dystonia ,parkinsonism and tardive dyskinesia incidence, anticholinergic side effects, haematological side effects, metabolic side effects, gastrointestinal side effects and cardiovascular side effects were recorded in case of antipsychotic drugs. Gastritis , sedation , oral ulcer , restlessness , erectile dysfunction, tremor , anxiety , insomnia , dizziness , headache , weight gain , vomiting , abdominal discomfort , abdominal distension , diarrhea , postural hypotension , sweating , problem with urination were recorded in case of SSRIs.

The most common group of drugs found responsible for most of the ADRs were recorded. In two groups the most common drug causing ADRs were noted followed by decreasing frequency of adverse drug reactions.

RESULTS

Table 1 : Number of ADRs according to the prescribed atypical antipsychotic drugs

Name of atypical antipyschotic drug	No. of drugs prescribed (n=57)	No. of ADRs observed (n= 100)	Percentage of ADRs(%)
Olanzapine	20	50	50
Risperidone	15	25	25
Amisulpride	12	15	15
Clozapine	10	10	10

Table 2: Number of ADRs according to the prescribed SSRIs

Name of SSRI	No. of drugs prescribed (n=43)	No. of ADRs observed (n=80)	Percentage of ADRs(%)
Citalopram	20	35	43.75
Fluoxetine	10	20	25
Paroxetine	8	15	18.75
Fluvoxamine	5	10	12.5

Table 3 : Spectrum of suspected ADRs noted among 57 patients prescribed atypical antipsychotic drugs

Type of ADR	No. of ADRs (n=100)	Percentage of ADRs (%)
Weight gain	20	20
Akathesia	15	15
Restless leg syndrome	5	5
Acute muscle dystonia	5	5
Parkinsonism	4	4
Tardive dyskinesia	3	3
Anaemia	5	5
Neutropenia	5	5
Thrombocytopenia	4	4
Agranulocytosis	4	4
Dyslipidaemia	12	12
Constipation	3	3
Nausea/ vomiting	2	2
Dry mouth	2	2
Insomnia	2	2
Blurred vision	2	2
Tachycardia	5	5
QT prolongation	2	2

Table 4 : Spectrum of suspected ADRs noted among 43 patients prescribed SSRIs

Type of ADR	No. of ADRs (n=80)	Percentage of ADRs(%)
Gastritis	20	27
Sedation	3	4
Oral ulcer	3	4
Restlessness	8	10
Erectile dysfunction	8	10
Tremor	8	10
Anxiety	8	10
Insomnia	2	2
Dizziness	2	2
Headache	1	1
Abdominal discomfort	2	2
Abdominal distension	2	2
Postural hypotension	8	10
Sweating	3	4
Problem with urination	2	2

Table 5: Causality assessment of observed ADRs

Type of Causality assessment	No. of ADRs (n=180)	Percentage of ADRs(%)
Probable	80	44.44
Possible	60	33.33
Certain	40	22.22

Table 6 : Severity of observed ADRs

Degree of severity	No. of ADRs (n=180)	Percentage of ADRs(%)
Mild	140	77.77
Moderate	38	21.11
Severe	2	1.11

DISCUSSION

The study was conducted to evaluate pattern of ADRs to atypical antipsychotics and antidepressant drugs in the Psychiatry Department of a Tertiary Care Hospital. Incidence of ADR was found to be more in males (55)when compared to females(45). Among all the ADRs reported, maximum number of ADRs was seen in patients who were on antipsychotic drugs which were comparable to the study by Sengupta et al.,[8] Rothschild et al. [9] and Jayanthi et al. [10] Atypical antipsychotic drugs formed the main class of drugs as they were most frequently prescribed in the hospital. Over the last few years, atypical antipsychotics(e.g., clozapine, olanzapine) have been increasingly prescribed in the treatment of schizophrenia and other related psychotic disorders because they significantly reduce both positive and negative symptoms of schizophrenia. Even though EPS is observed less frequently with atypical antipsychotics, metabolic complications such as dyslipidemia are more observed.[11,12] In the present study, olanzapine was the most common drug causing ADR and this finding was similar to the studies of Sengupta et al.,[8] Jayanthi et al.,[10] and Farhat et al. [13] Risperidone and clozapine were the next common drugs causing ADRs. [3] In a retrospective study by Iuppa et al.,[14] mood stabilizers formed the major medications causing ADRs. Shah and MD[15] reported antidepressants as a major group of drugs causing ADRs. Common adverse effects observed with antipsychotics drugs were Parkinsonism, tachycardia, weight gain and akathisia. Tremor and extrapyramidal reactions were also reported as common ADRs by Jayanthi et al. [10] In the present study, weight gain was reported with olanzapine. Based on causality assessment, using Naranjo algorithm, all ADRs are probable which is similar to the study by Prajapati et al. [16].

Antidotes can be combined with drugs with established ADR such as anticholinergics to treat extrapyramidal side effects caused by antipsychotics. Nonpharmacological management such as electroconvulsive therapy (ECT), behavioral therapy, and supportive psychotherapy to patients and bystanders can be combined with drug therapy. ECT and repeated transcranial magnetic stimulation is also useful in managing extrapyramidal side effects. Sudden stoppage of a drug or restarting a drug in high dosage is not recommended. Close monitoring of blood count when clozapine is prescribed and monitoring of serum levels for optimizing the dosage when lithium is used is needed to reduce ADR. Specific investigations to look for metabolic and other ADR should be done according to the drugs prescribed. Probiotics such as fish liver oil and thyroxine have been found to increase the efficacy of clozapine. Fish liver oil helps reduce dose of clozapine and also improve physical health and reduce ADR.[17]

CONCLUSION

Information regarding ADR can be obtained from preclinical evaluation and different phases of clinical trials, but the real life situation can be observed only in clinical practice. Hence, this study was intended to create awareness among psychiatrists to identify and report ADRs and actively participate in pharmacovigilance. The data received can be conveyed to drug regulatory authorities who can assess the drug information for safe and judicious use. All health professionals and other trained personnel along with patients should be

educated on the importance and benefit of ADR reporting and encouraged to report any suspected ADR and respect the confidentiality of the patient.

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