ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 05 | May - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ADVERSE DRUG REACTION MONITORING IN PSYCHIATRIC OUTPATIENT DEPARTMENT OF A TERTIARY CARE HOSPITAL

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 hospitalized patients in the Department 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 psychotropic drugs formed the study population. Details were documented on an ADR reporting form of Central Drugs Standard Control Organization and Causality assessment was done based on Naranjo algorithm. Data were subjected to descriptive analysis. **Results:** A total of 5746 patients were screened, out of which 288 patients were diagnosed of having ADRs due to PPAs. The overall incidence rate was found to be 7.01%. Maximum percentage of ADRs was observed with olanzapine (25.75%), followed by amitriptyline (20.02%) and clozapine (19.5%). Based on causality assessment in these cases as per Naranjo algorithm, all were judged as probable, except one as possible. 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, psychotropic drugs

INTRODUCTION

Modern lifestyle and unfulfilled desires leads to very common diseases of today like anxiety, depression and schizophrenia. Therefore, last one and half decade there has been an exponential rise in the use of psychotropic medication. Antipsychotic polypharmacy is being practiced with increasing frequency.[1] Polypharmacy is one of the leading cause of adverse drug reactions (ADRs) in psychiatric patients.[2] In India, pharmacovigilance activity is still in initial stages and there are only few reports available on incidence of ADRs due to psychopharmacological agents (PPAs). Also, India rates below 1% in terms of ADR reporting against the world's rate of 5%.[3] Very few studies have described patient characteristics and treatment patterns associated with long-term use of the drugs. This prompted us to do evaluation of adverse drug reactions of PPAs in tertiary referral centre for a longer duration.[4] This study was designed to prospectively monitor and analyze the pattern of occurrence of ADRs to PPAs in OPD of our tertiary care hospital.

MATERIALS AND METHODS:

A prospective study was conducted in the psychiatry out-patient department (OPD) of NMCH, Patna from January 2019 to December 2020. The study was approved by the Institutional Ethics Committee. Thirty five consecutive patients per day were screened during the OPD hours., irrespective of their psychiatric diagnosis for suspected ADRs on 3 rotatory days in a week excluding public holidays. The screening was carried out by two pharmacology residents trained in the psychiatry department under guidance of senior psychiatrist for interviewing the mentally ill patients. Only patients came with their accompanying family members were included in the study after taking verbal consent from patient's attendant. They were interviewed and case notes as well as related past prescriptions if available were reviewed. The suspected adverse drug reaction reporting form, under the Pharmacovigilance Programme of India(PVPI) conducted by CDSCO(Central Drugs Standard Control Organization) was filled with following details—age, sex and body weight of patient, adverse event history, history of suspected medication causing ADR, history of concomitant medication use [5].

Causality was assessed by WHO causality assessment scale 6 and Naranjo's scale 7. Suspected ADRs with causality status more than "possible" were included for further analysis. Severity was assessed using Hartwig and Siegel scale 8 and preventability was assessed by Schumock and Thornton scale 9.

RESULTS:

A total of 5746 patients were screened, out of which 288 patients were diagnosed of having ADRs due to PPAs. The overall incidence rate was found to be 7.01%. Maximum percentage of ADRs was observed with olanzapine (25.75%), followed by amitriptyline (20.02%) and clozapine (19.5%).[Table 1] Result of our study are following. Twenty one different kinds of treatment emergent ADRs were encountered in the patients . [Table 2].

Table 1 : Psychiatry disorders associated with adverse drug reaction

Clinical diagnosis	No. (% of all ADRs , n=288)
Schizophrenic spectrum disorder (including schizophrenia(m.c), brief psychotic disorder, schizophreniform disorder)	123(42.51%)
Mood disorder	77(27%)
Depression	46(16%)
Mania	25(8.11%)
Epilepsy	11(5.16%)
Mental Retardation	6(1%)

Table 2: Spectrum of suspected ADRs noted among 288 patients

Type of Adverse Drug Reaction	No. (% of all ADRs, n=288)
Tremor	81(28.76)
Weight gain	47(16.48)
Hypersalivation	32(11.56)
Extrapyramidal	27(9.35)
reactions Constipation	21(7.63)
Sedation	18(6.65)
Increase appetite	18(6.16)
Dry mouth	12(4.69)
Anorexia	12(4.19)
Headache	9(3.95)
Impaired liver function (liver enzymes over	4(2.72)
twice normal)	
Insomia, vertigo	4(2.47) each
Amenorrhoea,	2(1.98) each
galactorrhoea, impaired glucose tolerance	
Polyuria, polydypsia, increased prolactine level	2(1.74) each
Postural hypotension	2(1.49)
Sexual dysfunction	2(1.25)

Tremor (28.76%) was the commonest ADR noted followed by weight gain (16.48%) (of ≥7% weight gain from baseline weight) and hyper salivation (11.56%). Antipsychotics (70.77%) (typical and atypical) were the commonest group of agents causing ADRs followed by antidepressants (15.50%) . Olanzapine (32.20%) was the commonest drug incriminated followed by risperidone (27.78%)

DISCUSSION:

Pharmacovigilance is defined by WHO as "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.[6] The purpose of the Pharmacovigilance Program of India is to collect, collate and analyze data to arrive at an inference to recommend regulatory interventions, besides communicating risks to health care professionals and the public and thus create awareness among them [7]. The psychotropic drugs present a great variety of different types of adverse reactions and lead to noncompliance or even discontinuation of therapy. There is paucity of such data in the Indian context. The present study had reported the incidence and attempted to profile suspected ADRs to psychotropic drugs in the psychiatry OPD setting in the Indian context. A study by Sengupta et al based on active surveillance reported bipolar affective disorder was the commonest clinical diagnosis among ADRs noted. Regarding drug class, antipsychotics was the commonest group responsible for ADRs while olanzapine was the commonest among this group. Among ADRs noted, tremor was the commonest ADR[8]. A Brazilian study based on spontaneous reporting analyzed 219 notifications of suspected ADRs of psychoactive medicaments and incriminated antidepressants as the commonest group responsible for ADRs while fluoxetine was the commonest among this group [9]. In our study, which is based on active surveillance rather than spontaneous reporting, found antipsychotics to be most commonly responsible for ADRs while tremor was the commonest among ADR noted similar to the study by Sengupta et al. A knowledge, attitude and practice based study conducted in Norway found that ADRs can be prevented by collecting reliable information about their frequencies and possible risk factors [10]. In our study, among the antipsychotics, olanzapine and risperidone were frequently prescribed in our setting, as it was dispensed, free of cost, from the hospital pharmacy. Several new effective psychotropic drugs (e.g.aripiprazole, quetiapine, amisulpride, paliperidone, escitalopram, venlaflaxine) although relatively expensive and not dispensed from the hospital pharmacy, were prescribed to affordable patients from outside the hospital pharmacy.

Regarding causality assessment, our study had no "certain" cases on WHO causality assessment scale since the suspected ADRs were mostly of mild to moderate severity and hence did not require withdrawal of therapy. In cases where dechallenge was done, rechallenge was not attempted with the offending drug while in the Brazilian study where 24 cases were found to be "definite" after rechallenge was attempted [11]. Regarding severity assessment, our study had 2 cases of life threatening "severe" category while in the Brazilian study 12 cases were found to be life threatening "severe" category [12]. Regarding preventability assessment, our study had 8 cases of "preventable" ADRs while in the Thomas et al study where 12 ADRs were found to be "preventable [13]. Our study had certain limitations. Being an OPD-based study, it is possible that we had missed ADRs that were transient or too mild to have inconvenienced the patient to an extent sufficient to report to the doctor on the next hospital visit. We had not taken diet and other confounding factors into the account which might have influenced weight changes. Apart from routine haematological and clinical chemistry reports (e.g., blood sugar, liver function test), we could not generally order tests like ECG screening of patients for QT interval prolongation, serum prolactin level for galactorrhea. There was no access to therapeutic drug monitoring (TDM) for any drug in our hospital setting. However, though TDM of psychotropic agents has been employed, there is lack of consensus regarding its optimum use in clinical practice [14].

CONCLUSION

In this study we analyzed the drug use pattern and common adverse effects of antipsychotic drugs. 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. The most commonly observed adverse reactions in metabolic disorder were weight gain, increases cholesterol level, blood glucose level, blood pressure, 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. The strengthening of existence Governmental Pharmacovigilance programme of India (PvPI) is essential, in order to collect and disseminate information to the healthcare professionals about the occurrence of adverse reactions, takes precautions to prevent as well as to treat them and thus, improve the quality of patient care by ensuing safer use of drugs.

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