

Adverse Drug Reaction Monitoring in Psychiatry Outpatient Department of a Tertiary Care Teaching Hospital

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Abstract

To study the pattern of adverse drug reactions (ADR) in patients attending psychiatry OPD of a tertiary care teaching hospital. Patients attending psychiatry OPD with ADRs due to drugs prescribed for various psychiatric illnesses over a period of 1 year were included in the study. Adverse event history, medication history and other relevant details were entered in the PvPI format. Causality was assessed by WHO-UMC criteria. A total of 103 ADRs were reported from 85 prescriptions with a female preponderance. Majority of ADRs (45.7%) were seen with antidepressants as they were the commonly prescribed drugs followed by antipsychotics (33.3%) and others by sedative hypnotics and anticonvulsants. ADRs like somnolence topped the list (21.9%) followed by weight gain (18.4%), akathisia (6.8%) and drug induced restless legs syndrome (RLS) (5.8%). The reported ADRs were assessed for causality and maximum (80.6%) belong to the "possible" category. Maximum ADRs were seen with antidepressants followed by antipsychotics. Sedation and weight gain were the most commonly occurring ADRs.

Key Words

Adverse Drug Reactions, Pharmacovigilance, Psychotropic Drugs, Psychiatric Illness

Introduction

Psychotropic drugs are increasingly being prescribed in clinical practice. (1) These drugs are notorious in causing a number of adverse drug reactions (ADRs) which may rarely be fatal. (2) Adverse drug reaction associated with psychotropic drugs causes either non-adherence or at times discontinuation of therapy. (3)

The introduction of new drugs (atypical antipsychotics, SSRIs, SNRIs) has changed psychopharmacological treatment drastically as the issue of drug safety has become increasingly relevant over the last few years. Since ADRs with psychotropic drugs are frequent but

often under reported so, pharmacovigilance in psychiatric unit plays a vital role to ensure therapeutic safety by detecting early alarming signals to estimate risk/ benefit drug profile. (4)

Pharmacovigilance, the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any drug related problem, is highly essential in India, where there is lack of adequate safety related data for drugs in general and psychotropic agents in particular. India seems to rate below 1% in ADR reporting, as against the world rate of 5 %. (5)

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Therefore, there is growing concern among the healthcare personnel to assess adverse drug reactions (ADRs) of psychotropic drugs that has an impact on long term adherence so as to achieve better therapeutic outcome. (6-8) In India, pharmacovigilance activities are still in the nascent stage and data of ADRs particularly related to psychotropic drugs needs to be strengthened. (9)

Materials and Methods

A cross-sectional observational study was undertaken in the psychiatry OPD of a tertiary care teaching hospital (HIHT) for a period of 1 year. It was a part of the ongoing pharmacovigilance activity under Pharmacovigilance Programme of India (PvPI), run by department of Pharmacology having the necessary administrative and institutional ethics committee clearance.

Patients enrolled in the psychiatry OPD were screened for ADRs after taking written informed consent. The screening was carried out by the psychiatrists and the pharmacology residents. Patients were thoroughly reviewed along with the past prescriptions and case notes. Patients with known substance abusers and not accompanied by family care giver were not included in the study. Patient's demographic details, adverse event history, history of medication suspected of having caused the ADR and details of concomitant medication used were recorded in the format of the National Pharmacovigilance Programme of India (PvPI). (10)

Analysis was conducted for the following parameters: total no. of prescriptions with ADRs in 1 year duration ; total no. of ADRs reported; average number of drugs prescribed per person; age and sex distribution of ADRs; common reactions observed as ADRs; common drugs causing ADRs; seriousness of ADRs reported; causality assessment of reports by WHO-UMC guidelines. (11)

Result

A total of 103 ADRs were reported from 85 prescriptions. Among these prescriptions there was female preponderance (61.2%) as compared to males (38.8%). The median age of the subjects was 30 years. The maximum number of ADRs (32.9%) was reported in the 20 - 29 years age group (*Fig. 1*). Patients were grouped as per the number of drugs prescribed. A total

of 220 drugs were prescribed. On an average approximately 3 drugs were used per prescription. Most of these were psychotropic drugs. A few subjects were taking concomitant medicines for other disorders. The drug history was taken very carefully in such cases before attributing suspected ADRs to the psychotropic medicines concerned. Twenty six different kinds of ADRs were noted (*Table 1*). Somnolence (21.9%) was the commonest; followed by weight gain (18.4%), akathisia (6.8%), and drug induced Restless Legs Syndrome (RLS) (5.8%), decreased appetite (4.9%) and increased appetite (4.9%), constipation (3.9%) and drug induced extrapyramidal symptoms (3.9%), galactorrhoea (2.9%), dryness of mouth (1.9%), nausea and vomiting (1.9%) and others. Causality assessment revealed that 83 Adverse Events (AEs) (80.6%) belong to the "possible" category, whereas 19 (18.4%) were in the "probable" category and only 1 ADR was in the "unlikely" category according to the WHO-UMC scale. No cases could be labeled "certain" as rechallenge was not attempted by the attending psychiatrist, once a drug was withdrawn.

Among the drugs incriminated, anti-depressants were the commonest group of drugs causing ADRs (45.7%), followed by antipsychotics (most commonly atypical antipsychotics) (33.3%), sedative-hypnotics (13.8%) and anti-convulsants (7.2%) (*Fig 2 & 3*). Among anti-depressants, mirtazapine was the commonest drug used (39.7%) followed by paroxetine (11.1%) and esitalopram (11.1%). Among antipsychotics, olanzapine (28.3%) followed by risperidone (17.4%) were the two most commonly used drugs. Among sedative-hypnotics clonazepam (52.6%) followed by lorazepam (21.1%) were commonly used. Among anti-convulsants, sodium valproate (40.0%) and divalproate (40.0%) were the commonly used drugs.

When ADRs were assessed for its onset, it was interesting to note that more than half of the ADRs (51.5%) occurred within 1 day of the medication prescribed. No ADR encountered turned out to be fatal and life threatening, except for two case of extrapyramidal symptoms by haloperidol, which needed hospitalization for management.

Fig. 1 Age and Sex Distribution in Patients with ADRs Due to Psychotropic Agents

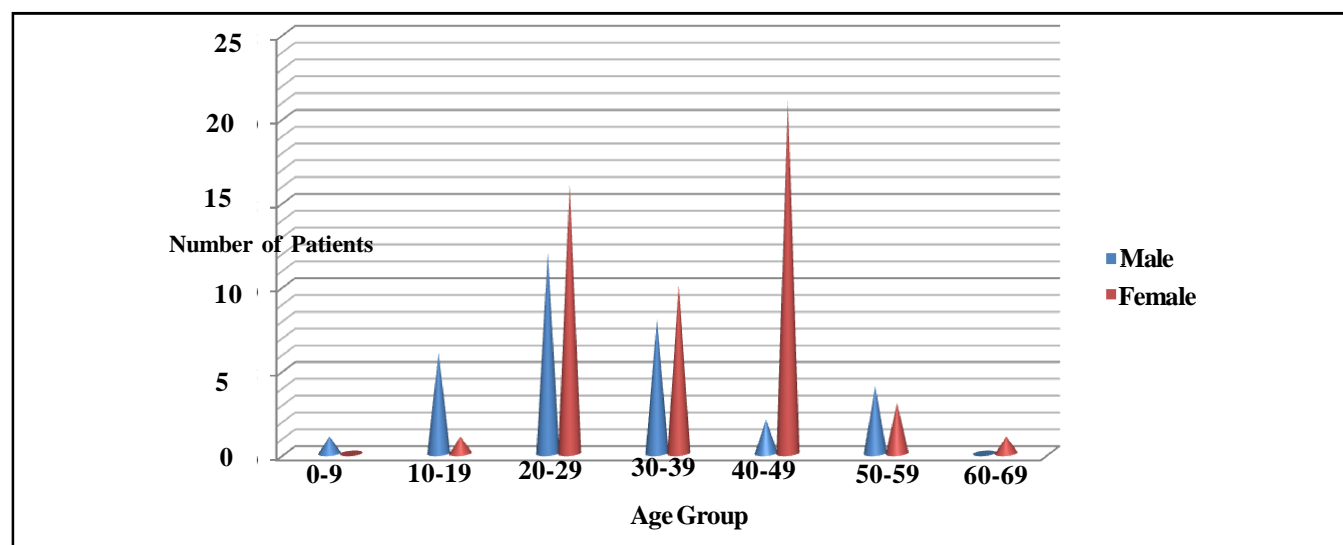
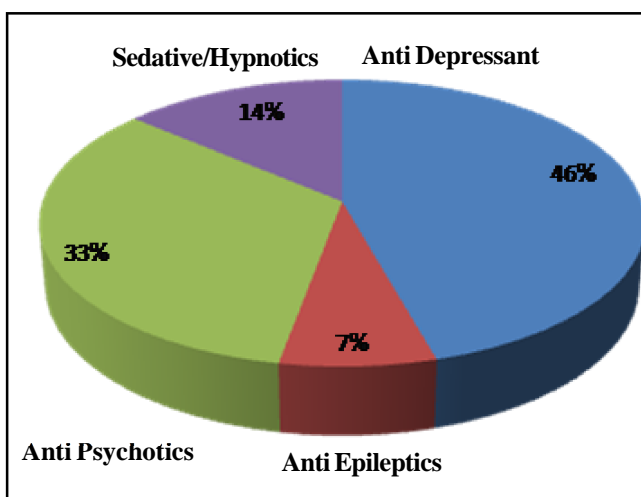


Table 1. Pattern of ADRs

| ADRs | Percentage ADRs |
|----------------------|-----------------|
| Somnolence | 29.1 |
| Weight gain | 18.4 |
| Akathisia | 6.8 |
| RLS | 5.8 |
| Decreased appetite | 4.9 |
| Increased Appetite | 4.9 |
| Constipation | 3.9 |
| EPS | 3.9 |
| Galactorrhoea | 2.9 |
| Anxiety | 1.9 |
| Dryness of mouth | 1.9 |
| Nausea & Vomiting | 1.9 |
| Difficulty Urination | 1.0 |
| Diffuse alopecia | 1.0 |
| Gynacomastia | 1.0 |
| Parkinson's disease | 1.0 |
| Acidity | 1.0 |
| Acne | 1.0 |
| Amenorrhea | 1.0 |
| Delayed Ejaculation | 1.0 |
| Dizziness | 1.0 |
| Dry Eye | 1.0 |
| Gastritis | 1.0 |
| Skin Rash | 1.0 |
| Sleep Talking | 1.0 |
| Weakness | 1.0 |

Fig 2. Various Classes of Psychotropic Drugs Causing ADRs

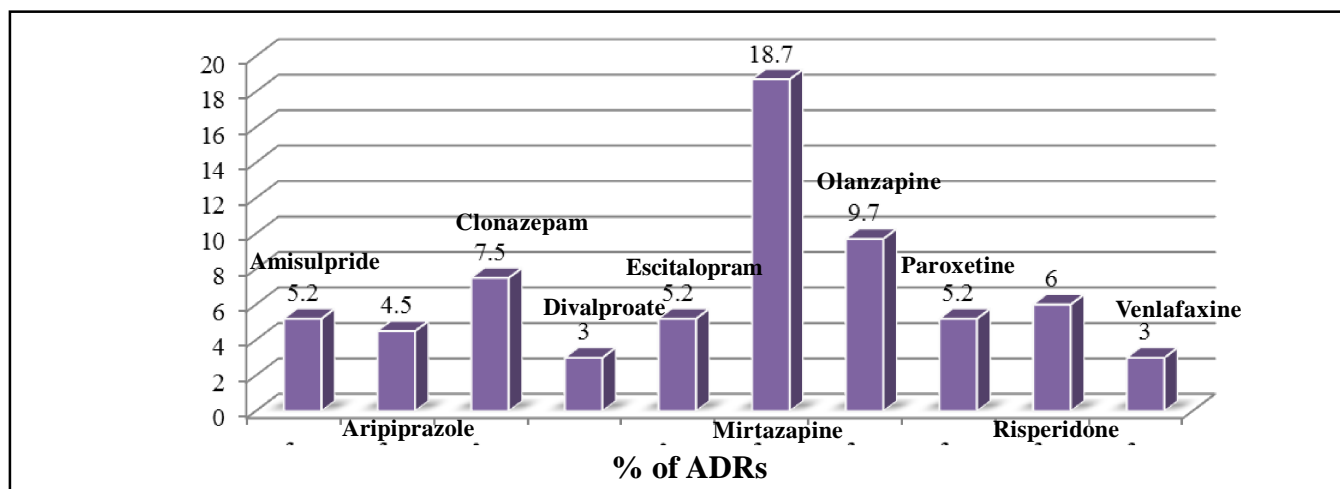


collecting reliable information about their frequencies and possible risk factors. (12) Spontaneous reporting is the best most common method used in pharmacovigilance and the best one to generate signals on new or rare ADRs. Under reporting is a major drawback of this system due to lack of awareness both at the level of healthcare professionals and patients. (13) Present study for the assessment of ADRs of various psychotropic drugs was hard on active surveillance in addition to the ADRs spontaneously reported by patients or clinicians. This suggests that active surveillance is very important in reporting ADRs.

Discussion

A knowledge, practice, attitude based study conducted in Norway found that ADRs can be prevented by

Fig 3. Individual Drugs Causing Maximum ADRs



It is well recognized that females appear to be at higher risk factor for developing ADRs. A number of studies clearly suggest that ADRs are 50% to 75% more likely in women than in men. (14, 15) It has also been suggested that there is a female preponderance in the number of ADRs experienced with psychotropic drugs in accordance with the result of our study. (16)

Among the ADRs in our study, increased sleep occurred in maximum number of patients. Increased sleep can have significant disruption of sleep/wake cycle due to side effects of psychotropic agents. (17) At times this could be serious, e.g. diurnal somnolence associated with risks of road accidents and, in the elderly, the risk of falls. (18)

Second most common ADR observed in our study was weight gain. The most common drug to cause weight gain in our study was mirtazapine as seen in other studies. (19, 20) Weight gain apart from an immediate side-effect, may generate secondary side-effects such as hypertension, diabetes, osteoarthritis, sedentary lifestyle, coronary artery disease, etc. and may complicate comorbid medical conditions such as obesity and heart diseases. (21)

In our study it was observed that drug induced extrapyramidal syndrome at a higher risk with first generation antipsychotics especially with haloperidol than with second generation antipsychotics, which was also seen in other studies. (22 - 25) EPS are important as

they can impair quality of life, stigmatize patients and lead to poor antipsychotic adherence and relapse.

Our study had limitations. Being an OPD based study; it is likely that we have missed ADRs that were transient or too mild that the patient would not be able to report the same.

Although this post marketing surveillance study cannot provide incidence, it offer a pattern of ADRs profile of psychotropic drugs likely to be encountered. Compliance with therapy is a major aim in psychiatric patients. Constant vigil in detecting ADRs and subsequent dose adjustments can make therapy with psychotropic drugs safer and more effective.

Psychotropic drug data base built up on the basis of such studies conducted across multiple centers, through active collaboration of psychiatrists, pharmacologists, can be a worthy long term goal. Such a database can provide early warning signals of drug reaction if kept under active scrutiny.

Acknowledgement

We are thankful to Dr. Mohan Dhyani, Department of Psychiatry for informing about the cases of ADR reported in the psychiatry OPD and Miss Upasana Sharma, Technical Associate, Department of Pharmacology for her co-operation and adding up data and information to our study.

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