Adverse Drug Reaction Monitoring In Psychiatric Outpatient Department Of A Tertiary Care Hospital

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Abstracts Background:Pharmacovigilance in psychiatry units can play vital role in detecting adverse drug reactions (ADRs) and alerting physician to such events, thereby protecting the user population from avoidable harm. Objective: To assess the suspected ADRs profile of psychotropic drugs in psychiatry OPD of a tertiary care hospital and its comparison with available literature data as well as to create awareness among the consultant psychiatrists to these ADRs profile. Materials and Methods: A prospective study was conducted in the psychiatry OPD. Thirty five consecutive patients per day were screened irrespective of their psychiatric diagnosis for suspected ADRs on 3 fixed days in a week from January 2011 to December 2011. CDSCO form was used to record the ADRs. Causality was assessed by WHO causality assessment scale while severity was assessed using Hartwig and Siegel scale. Results: Out of 4410 patients were screened, 383 patients were suspected of having at least one ADR. Thus, 8.68 % of our study population reported ADRs. Of 407 events recorded, 369(90.60%) were "probable" and rest "possible" according to WHO-UMC causality assessment scale. According to Hartwig and Siegel scale, 268 ADRs (65.85%) were "moderate" category. Twenty one different kinds of ADRs were noted. Conclusion: This study enables to obtain information on the incidence and frequency of ADRs in the local population that allows opportunity for education to the physicians to improve the patient's quality of life. [Prajapati H et al NJIRM 2013; 4(2) : 102-106]

Key Words: Adverse drug reaction, Causality assessment scale, Psychotropic drugs, Severity assessment scale

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Introduction: Antipsychotic drugs can be of great benefit in a range of psychiatric disorders, including schizophrenia and bipolar disorder, but all are associated with a wide range of potential adverse effects. These can impair quality of life, cause stigma, lead to poor adherence with medication, cause physical morbidity and, in extreme cases, be fatal. Adverse effects are usually dose dependent and can be influenced by patient characteristics, including age and gender. These confounding factors should be considered in clinical practice and in the interpretation of research data. Selection of an antipsychotic should be on an individual patient basis. Patients should be involved in prescribing decisions and this should involve discussion about adverse effects [1]. Knowledge of how the prevalence and severity of adverse effects vary for different antipsychotics allows clinicians to reduce the occurrence of these effects [2]. Pharmacovigilance in psychiatry units can play vital role in detecting adverse drug reactions (ADRs) and allowing physician to possibility and circumstances of such events, thereby protecting the user population from avoidable harm [3]. In India, pharmacovigilance activities still in nascent stage and there are few reports available on the ADR profile of psychotropic drugs [4]. This inspired us to evaluate the ADR profile of psychotropic drugs used by the OPD based psychiatry patient of tertiary care hospital.

Materials And Methods: A prospective study was conducted in the psychiatry out-patient department (OPD) of Guru Gobindsingh hospital, Jamnagar, Gujarat from January 2011 to December 2011. The study was approved by the Institutional Ethics Committee. Thirty five consecutive patients per day were screened during the OPD hours from 9:00 A.M to 12:30 P.M., 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 4410 patients were screened of whom 383 patients were suspected of having at least one ADR (Incidence of 8.68%). Total of 407 ADRs were noted. Out of 383 patients, males represented 66.05% (n=253) of the cases while females represented 33.95% (n=130). On an average day, about 62% of the patients attending the concerned OPD were males. Mean age of our study population was 36.85 years. (95% confidence interval: 31.09-42.61 %). Schizophrenic spectrum disorder (42.51%; n=407) was the commonest clinical diagnosis among these ADRs, followed by mood disorder (23.03%; n=407). [Table 1]

Table 1 : Psychiatry disorders associated with adverse drug reaction

Clinical diagnosis	No. (% of all ADRs , n=407)
Schizophrenic spectrum disorder (including schizophrenia(m.c), brief psychotic disorder, schizophreniform disorder)	173(42.51%)
Mood disorder	110(27.03%)
Depression	63(15.48%)
Mania	33(8.11%)
Epilepsy	21(5.16%)
Mental Retardation	4(0.98%)

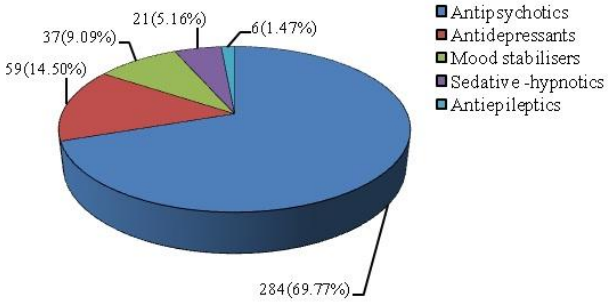
Twenty one different kinds of treatment emergent ADRs were encountered in the patients [Table 2].

Table 2: Spectrum of suspected ADRs noted among 383 patients

Type of Adverse Drug Reaction	No. (% of all ADRs, n=407)
Tremor	113(27.76)
Weight gain	63(15.48)
Hypersalivation	43(10.56)
Extrapyramidal reactions	34(8.35)
Constipation	27(6.63)
Sedation	23(5.65)
Increase appetite	21(5.16)
Dry mouth	15(3.69)
Anorexia	13(3.19)
Headache	12(2.95)
Impaired liver function (liver enzymes over twice normal)	7(1.72)
Insomia, vertigo	6(1.47) each
Amenorrhoea, galactorrhoea, impaired glucose tolerance	4(0.98) each
Polyuria, polydypsia, increased prolactine level	3(0.74) each
Postural hypotension	2(0.49)
Sexual dysfunction	1(0.25)

Tremor (27.76%) was the commonest ADR noted followed by weight gain (15.48%) (of ≥7% weight gain from baseline weight) and hyper salivation (10.56%). Antipsychotics (69.77%) (typical and atypical) were the commonest group of agents causing ADRs followed by antidepressants (14.50%) [Figure 1]. Olanzapine (31.20%) was the commonest drug incriminated followed by risperidone (26.78%) [Table 3].

Figure 1 : Association of drug class with 407 ADRs



Causality assessment revealed that 369 ADRs (90.66%; n=407) were "probable" category according to WHO-UMC scale [6] [Figure-2] while

378 ADRs (92.87%; n=407) were "probable" category according to Naranjo's scale [7] [Figure-3]. Not a single case of "certain" category was noted as rechallenge was not attempted by the consultant psychiatrist, once a drug was withdrawn.

Figure 2 : WHO causality assessment scale

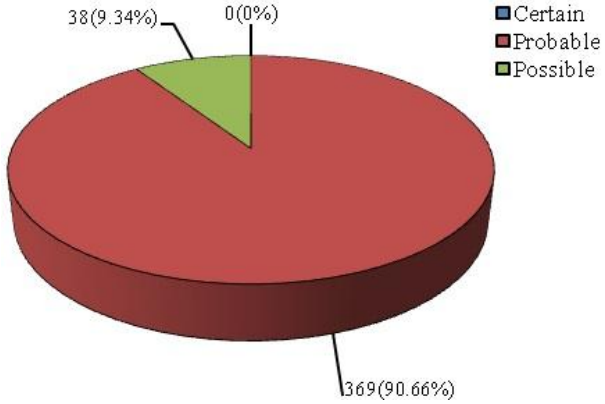


Figure 3: Naranjo's assessment scale

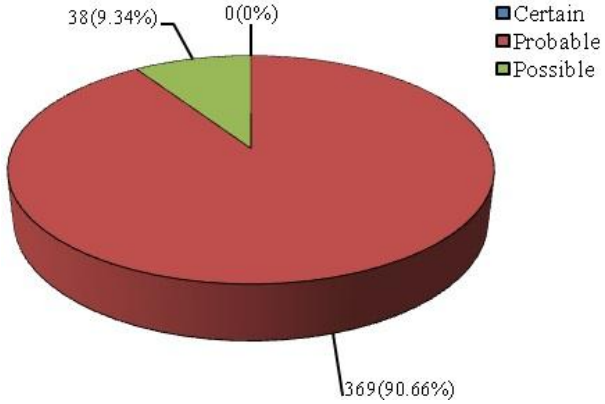
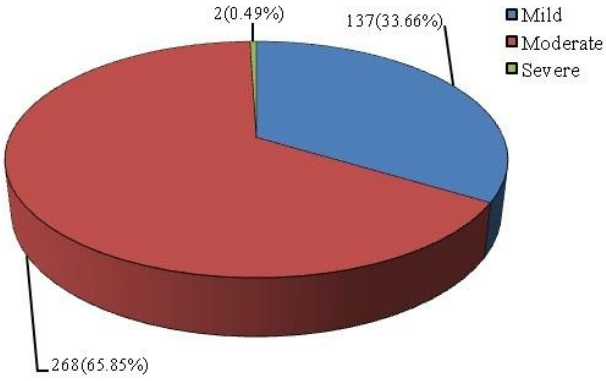


Figure 4: Hartwig and Siegel severity scale



Hartwig and Siegel severity scale revealed that 268 ADRs (65.85%; n=407) were "Moderate" category while 137ADRs (33.66%; n=407) were "Mild" category [8]. Only two cases (0.49%; n=407) of "Severe" category were recorded. Schumock and Thornton scale revealed that 399 ADRs (98.03%; n=407) were "Nonpreventable" while 8 ADRs (1.97%; n=407) were "Preventable" [9]. The preventability factors involved in our study were inappropriate dose according the patient's clinical condition and poor patient's compliance.

Table 3:Drugs responsible for 407 ADRs noted among 383 patients

Name of Drug	No. (% of all ADRs, n=407)
Olanzapine	127(31.20)
Risperidone	109(26.78)
Amitriptyline	31(7.62)
Lithium	28(6.88)
Haloperidol	20(4.91)
Imipramine	19(4..67)
Diazepam	16(3.93)
Sodium valproate	13(3.19)
Trifluoperazine	9(2.21)
Chorpromazine	6(1.47)
Paliperidone	5(1.23)
Fluoxetine,Sertraline	4(0.98) each
Clonazepam,Clozapine,Amisulpride	3(0.74) each
Aripiprazole,Quetiapine,Escitalopram	2(0.49) each
Lorazepam	1(0.25)

Some interesting ADRs were noted during the course of study. One case of acute muscular dystonia was noted on the first single dose of the tablet paliperidone 6 mg orally. Two cases of neuroleptic malignant syndrome [one case of haloperidol and one case of olanzapine] were noted during the course of study that required hospitalization for management by clinicians. One case of drug induced parkinsonism had been reported with haloperidol. Some of the events, such as tremor, rigidity, dyskinesia were managed by the clinicians with corrective medication like trihexiphenidyl or by dose modification.

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". 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 [10]. 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.

Table 4 : Classification of adverse drug reactions (ADRs) according to System Organ Class (SOC) using *Med DRA version 14.1 English (n=407).*

System Organ Classification(SOC)	No. (% of all ADRs, n=407)
Nervous system disorder	194(47.67)
Gastrointestinal disorder	106(26.04)
Metabolic and nutritional disorder	83(20.39)
Endocrine disorder	7(1.72)
Hepatobiliary disorder	7(1.72)
Reproductive and breast disorder	4(0.98)
Renal and urinary disorder	3(0.74)
Vascular disorder	2(0.49)
Psychiatric disorder	1(0.25)

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 [4]. 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 [11]. 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 [12]. 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 [11]. 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: Our study builds up the ADR profile of psychotropic drugs likely to be encountered in outdoor patients of an Indian tertiary care hospital. Any therapeutic process involving administration of medications has the inherent possibility of producing undesirable adverse reactions to the patients. Taking this truism into consideration, psychiatrists as well as other healthcare professionals should be constantly reminded of that possibility and thus, advised to prescribe the drugs in cases of real clinical necessity. 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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