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A Prospective Study of Adverse Drug Reactions to Antipsychotic Agents and its Causality Assessment in Psychiatry Ward of a Tertiary Care Hospital

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ABSTRACT

Adverse Drug Reactions (ADRs) is one of the most common reasons for discontinuation of antipsychotic treatment. The aim of the present study is to identify the pattern of ADRs in psychiatric in-patients on antipsychotic drugs and to assess the causality, severity, predictability and preventability of adverse events. The present study was a descriptive cross-sectional study conducted among the inpatients in the Psychiatry ward for a study period of one and half year. The sample size included all the ADRs due to anti psychotics medications which were reported by patients and confirmed by the physician. A total of 220 ADRs were collected from 83 inpatients. The incidence of ADR was slightly more in females (51.80%) and the majority of them were diagnosed with schizophrenia subtype (56.36%). The maximum number of ADRs reported was by patients being treated with an atypical agent clozapine (35%) followed by a typical agent chlorpromazine (19.54%). Using WHO-UMC criteria, the majority of ADRs (72.27%) in our study belonged to the category of possible. Specific treatments were required for management of ADRs consisting of extra-pyramidal syndromes (EPS). According to WHO ART system organ class, central and peripheral nervous system were the most affected classes. The study supports the importance of baseline investigations and active surveillance for early detection and prevention of ADRs. Also poly pharmacy should be avoided as far as possible and percentage method should be used in case where higher dose of antipsychotic is required.

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Key Words
Adverse drug reactions, antipsychotic agents, causality assessment

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INTRODUCTION

Newer Anti psychotics drugs are being introduced from time to time and are used to treat a wide range of psychotics symptoms and disease conditions like schizophrenia, bipolar disorder, major depressive disorders, organic psychosis, drug induced psychosis etc. But both FGA (first generation anti psychotics) and SGA (second generation anti psychotics) are associated with a wide range of potential adverse effects. So there is an essential need for an improvement in the awareness of pharmacovigilance among the clinicians and patients. ADRs are one of the most common reasons for discontinuation of antipsychotic treatment. SGAs significantly outperformed FGAs with regard to lower discontinuation rates, irrespective of indication (positive or negative symptoms or cognitive disorders), even though associated with higher metabolic side effects[1]. A study of the pattern, the severity of reactions, and pharmacological class of drugs involved can help us understand and develop patient targeted safety initiatives. A better understanding of the probability, predisposing factors can lead to development of a more personalized approach to antipsychotic treatment which can help us overcome the individual variation on long-term treatment[2]. So there is a need for collection data regarding response, tolerability and variations to anti psychotics among Indian psychiatric inpatients. The aim of the present study is to identify the pattern of ADRs in psychiatric in-patients on antipsychotic drugs and to assess the causality, severity, predictability and preventability of adverse events.

MATERIALS AND METHODS

This was a descriptive cross-sectional study conducted among the inpatients in the Psychiatry ward of a tertiary care hospital. The sample size included all the ADRs due to antipsychotics medications during the study period of one and half year based on the following inclusion and exclusion criteria:

Inclusion Criteria:

- (a) All in-patients of any age and either sex admitted in psychiatry ward with a psychiatric disorder as per ICD 10 criteria and receiving treatment with at least one antipsychotic drug were included.
- (b) ADRs reported by patients and confirmed by the treating physician were included.

Exclusion Criteria:

- (a) ADRs due to drugs other than anti psychotics.
- (b) Patients treated with anti psychotics in other wards.

The study got approval from the Institutional Review Board and Institutional Ethics Committee of the hospital. Each documented ADR was included in the study after getting a written informed consent from all study participants or their guardians. In addition to the demographic details of patient, a questionnaire Glasgow Antipsychotic Side effect Scale, asking patient specific questions related to the likely ADR was collected[3]. Details of adverse events, suspected drug, concomitant medications, management of ADRs as well as lab investigations was were recorded in the Standard CDSCO format of Pharmacovigilance program of India and causality of adverse events was assessed using WHO-UMC Causality criteria. Modified Schumock and Thornton scale for preventability and Hartwig siegel criteria to assess severity of ADR was used[4,5].

Statistical Analysis: The collected data was entered into Microsoft excel version 2010 and analyzed using descriptive statistics.

RESULTS AND DISCUSSION

A total of 220 ADRs were collected from 83 inpatients which included 40 males and 43 females (Table 1). The incidence of ADR was slightly more in females (51.80%) than males. Higher numbers of patients were identified in the age group of 21-40 years. The mean age of the patient in the study was 38.12 with a range of 11-76. The morbidity pattern of psychiatric illness among the inpatients at the time of occurrence of ADRs was categorized as per ICD-10 coding. (Table 2). The maximum number of ADRs was reported in patients who were on antipsychotic drugs especially the atypical anti psychotics. (Table 3). Using WHO probability scale, majority of ADRs were categorized as possible (72.27%) and 13.63% ADR were found to be of the category probable and unlikely each. On severity assessment using Hartwig and Siegel scale, 66.36% were mild level 1, 12.27% were mild level 2 and 21.36% were moderate level 3. As part of management of the ADRs with respect to suspected antipsychotic drug, in 3.18 % required drug withdrawal, 10.45% required dose alteration and in 86.36 % no changes in therapy was required. As part of management of the ADRs with respect to treatment stratergy, in 64.54% required no treatment, 18.63% required symptomatic treatment and in 16.81% required specific treatment. It was found that that there was 100% improvement as an outcome of ADRs on dose alteration and drug withdrawal. As per the preventability assessment using Modified Schumock and Thornton's Scale, it was found that 83.18% and 16.81% of the reported ADRs were not preventable and probably preventable respectively. 38% and 50% of antipsychotic drugs were prescribed from WHO essential drug list and the National list of Essential Medicine India (NLEM) respectively. It was found that 59% of the ADRs to be of predictable (Type A). The CNS and GIT were the two most common system involved when the suspected

ADRs were classified according to WHO ART SOC code as shown in (Table 4). Clozapine was the most common suspected drug followed by Chlorpromazine as shown in (Table 5). Drowsiness was the most common adverse drug reaction seen followed by constipation as shown in (Table 6).

Several studies are published on ADRs of antipsychotics from India[6-8]. Compared with our study the majority of studies were of outpatient and among the inpatient ones most had a sample size of about 50 only. Also, very few studies have assessed the strategies for the management of ADRs. The incidence of ADR was slightly more in females (51.80%) than males. This is in concordance with another large prospective study done among Indian psychiatric inpatients where the incidence in females was 54.85%[9]. The exception to our finding, few studies have reported a male preponderance in which the total number of ADRs collected were about 50 only[10]. Higher numbers of patients were identified in the age group of 21-40 years (Table 1). Majority of the in patients who were prescribed antipsychotics in the psychiatry ward were diagnosed to have psychosis due to schizophrenia (Table 2). This finding is similar to that of the study by Lucca[9]. In our study, the maximum number of ADRs were reported in patients who were on antipsychotic drugs especially atypical antipsychotics which were most frequently prescribed among the inpatients (Table 3) which is comparable to other studies[9-11]. Over the last few years, atypical antipsychotics are been increasingly prescribed in the treatment of schizophrenia. First-generation antipsychotics (FGA) generally have a higher incidence of movement disorders than SGAs. FGAs may be slightly less efficacious than some SGAs with regard to negative symptoms[12]. Although the CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) and CUtLASS (Cost Utility of the Latest Antipsychotic drugs in Schizophrenia Study) studies showed that no difference in psychosocial outcomes was evident[13,14]. In 32.72% of ADRs, patients were taking the combination of a typical and atypical antipsychotic agent. These patients required swapping of their antipsychotic agent and were subjected to Cross-tapering as per guideline. During Cross-tapering the dose of the first drug is slowly reduced (anything over anything up to 8 weeks), whilst the new agent is being introduced. Although Cross-tapering has the potential disadvantage for combined side-effects and interactions but was preferred by the clinicians in our study due to a lesser risk of relapse associated with it. Many inpatients in psychiatry ward will require polypharmacy for acute and long- term management of psychiatric illnesses and this may lead to higher incidence of ADRs, nonadherence, medication errors and drug interactions[6,7,15]. In our study majority of the ADR occurred in patients on four or more drugs and in order to check polypharmacy, the clinicians prescribed small quantities initially and reviewed the patients regularly. Using World Health Organization-Uppsala Monitoring Center (WHO-UMC) criteria, the majority of ADRs in our study belonged to the category of possible. The study by Sengupta *et.al* also found that majority of ADRs were possible[16]. Regarding causality assessment, our study had no "certain" cases since the suspected ADRs were mostly of mild to moderate severity and hence usually did not require the withdrawal of therapy. In cases where de-challenge was done, re-challenge was not attempted with the offending drug. This is in contrast to the Brazilian study where 24 cases were found to be "definite" as re-challenge was attempted[17]. The differences in the results of probability scale in various studies may be due to the different scales used for causality assessment or because of individual differences in the interpretation of data. In the present study WHO criteria was preferred over the Naranjo algorithm as its less time consuming and based on clinical judgment. On severity assessment using Hartwig and Siegel scale, the 78.63% of ADRs were mild. This is because the majority of the ADRs in study neither required a change in treatment with respect to suspected drug nor required an antidote/other treatments or increase in the length of stay in the hospital. Similarly, assessment of ADR by Juno *et al.* and Solanke *et al.* reported that maximum patients were in the mild category[11,14]. None of the ADRs during the study were lethal. In general, the management approach of ADRs begins with a consideration of the likely ADRs for psychiatric as well as co-prescribed non-psychiatric drugs. Management of this side-effect predominantly depends on severity, type of ADRs and body system they affect rather than by specific antipsychotic medication. In this study, approximately 86.36% of the ADRs did not require any interventions with respect to the suspected drug for the management. In ADRs in which the antipsychotic drug was withheld were clozapine-induced agranulocytosis, risperidone-induced hyper pro lactinemia, olanzapine-induced mask-like face, chlorpromazine-induced drowsiness and haloperidol-induced dystonia. For 19.9% ADRs patients were reassured and given no treatment. The ADRs for which specific treatment was required were EPS like akathisia, dystonia, tremors, rigidity, gait disturbance and mask face. Anticholinergic drugs, benzodiazepine and propranolol were used for their treatment. 18.63% of ADRs required symptomatic treatment. This include symptoms like diarrhea, constipation, vomiting, sialorrhoea, hyperglycemia, hypoglycemia, hypotension, generalized itching, fever which were managed with intravenous fluids, lactulose, metoclopromide, dextrose and antihistaminic, with or without dose reduction of the suspected drug. In our study weight gain case very low as we enrolled only

Table 1: Age and Gender Wise Distribution of Patients Under Study

Age range(yrs)	Males	Females	Total
≤20	4	5	9
21-40	25	22	47
41-60	9	12	21
61-80	2	4	6
Total	40	43	83

Table 2: Morbidity Pattern of Psychiatric Illness among the Study Population at the Time of Occurrence of ADR Based on ICD-10 Coding

ICD-10 code	Disease	Number of ADRs (%)
F 20.0	Paranoid schizophrenia	15 (6.81)
F20.3	Undifferentiated schizophrenia	1 (0.45)
F20.5	Residual schizophrenia	2 (0.90)
F20.9	Schizophrenia, unspecified	124 (56.36)
F22.0	Persistent delusional disorders	10 (4.54)
F22.9	Persistent delusional disorders, unspecified	6 (2.72)
F23.1	Acute polymorphic psychotic disorder with symptoms of schizophrenia	3 (1.36)
F25.2	Schizoaffective disorder, mixed type	1 (0.45)
F29	Unspecified nonorganic psychosis	14 (6.36)
F31.1	Bipolar affective disorder, current episode manic without psychotic symptoms	2 (0.90)
F31.2	Bipolar affective disorder, current episode manic with psychotic symptoms	14 (6.36)
F31.4	Bipolar affective disorder, current episode severe depression without psychotic symptoms	3 (1.36)
F32.3	Severe depressive episode with psychotic symptoms	2 (0.90)
F33.3	Recurrent depressive disorder, current episode severe with psychotic symptoms	23 (10.45)

Table 3: Distribution of ADRs with Respect to Anti Psychotics with or without Antidepressant Drugs

Patients Medication details	Number of ADRs(%)	Total(%)
Only on typical antipsychotics	20 (9.09)	20(9.09)
On typical antipsychotics with antidepressant	4 (1.81)	
On typical without antidepressant	16 (7.27)	
Only on atypical antipsychotics	128 (58.18)	128(58.18)
On atypical antipsychotics with antidepressant	13 (5.90)	
On atypical without antidepressant	105 (47.72)	
On both typical & atypical	72 (32.72)	72(32.72)
Both with antidepressant	10 (4.54)	
Both without antidepressant	62 (28.18)	
	Total	220

Table 4: Classification of Suspected ADRs among in-Patients in Psychiatry Ward on Anti Psychotic Medications as Per WHO ART SOC Code

System Organ Class (WHO ART SOC code)	Number of ADRs (%) (n=220)	Suspected ADRs (Number of ADR)
Central and peripheral nervous system (0400)	61 (27.72)	Extra pyramidal syndrome (24), tremors (7), blurring of vision (7), headache (7), giddiness (6), slurring of speech (5), dizziness (4), tingling sensation (1),
Gastrointestinal system disorders (0600)	57 (25.90)	Constipation (18), sialorrhoea(13), diarrhea (7), vomiting(5), heart burn(6),dryness of mouth (3),abdominal pain (2), dysphagia (1), nausea (2)
Psychiatric disorders (0500)	46 (20.90)	Drowsiness(21),Sedation (15), agitation (5), disturbed sleep (1), increased appetite (4)
Body as a whole general disorders (1810)	17 (7.72)	Fever (8),tiredness(5),lethargy(2), fatigue (1), body ache (1),
Metabolic and nutritional disorders (0800)	10(4.54)	Hyperglycemia (5), hypoglycemia (1), weight gain (1), hyperprolactinemia (1), hyperuricemia (1), anorexia(1),
Respiratory system(1100)	8 (3.63)	Cough (3), nasal blockade (2), rhinitis (2), dyspnoea (1)
Cardiovascular disorders (1000)	6 (2.72)	tachycardia (2), hypotension (2), Angina (1), orthostatic hypotension (1)
Urinary system disorders (1300)	4 (1.81)	Difficulty in urination (2), polyuria (1), enuresis (1)
Skin and appendages disorders (0100)	3 (1.36)	Sweating (2), furuncle (1)
Miscellaneous	8(3.63)	Agranulocytosis (2), generalized itching (1), hoarseness of voice (1), hiccups (1), heaviness of head (2), menstrual cycle abnormality (1)

Table 5: Suspected Anti Psychotic Drugs Responsible for the Adverse Drug Reactions Noted among the Study Population

Suspected antipsychotic drug	Number of ADRs (%)
Clozapine	77 (35)
Chlorpromazine	43 (19.54)
Risperidone	42 (19.09)
Olanzapine	31 (14.09)
Haloperidol	16 (7.27)
Trifluoperazine	7 (3.18)
Quetiapine	4 (1.81)
Fluphenazine	3 (1.36)
Aripiprazole	2 (0.90)

Table 6: Spectrum of Suspected Adverse Drug Reactions with Suspected Drugs Seen During the Study Period

ADR	Number of ADRs (%)	Suspected drug (number of ADRs)
Drowsiness	21 (9.54)	Chlorpromazine (11), clozapine (5), haloperidol (3), risperidone (1), trifluoperazine (1)
Constipation	18 (8.18)	Clozapine (8), chlorpromazine (4), risperidone (2), olanzapine (2), haloperidol (2)
Sedation	15 (6.81)	Haloperidol (6) , chlorpromazine (5), Clozapine (3), olanzapine (1)
Sialorrhoea	13 (5.90)	Clozapine (11), olanzapine (1), Risperidone (1)
Akathisia	10 (4.54)	Clozapine (3),chlorpromazine (3), risperidone (1), olanzapine (1), trifluoperazine (2)
Dystonia	9 (4.09)	Clozapine (5), haloperidol (2), fluphenazine (1), chlorpromazine (1)
Fever	8 (3.63)	Clozapine (4), olanzapine (2), quetiapine (1), haloperidol (1)
Blurring of vision	7 (3.18)	Chlorpromazine (2), clozapine (1), risperidone (1), olanzapine (1), fluphenazine (1), trifluoperazine (1)
Tremors	7 (3.18)	Chlorpromazine (2), clozapine (2), risperidone (2), trifluoperazine (1)
Diarrhea	7 (3.18)	risperidone (4), Olanzapine (2), clozapine (1)
Headache	7 (3.18)	Clozapine (3), olanzapine (2), risperidone (2)
Heart burn	6 (2.72)	Risperidone (2), olanzapine (1),clozapine (1), quetiapine (1), chlorpromazine (1)
Giddiness	6 (2.72)	Chlorpromazine (3), clozapine (2), risperidone (1)
Vomiting	5 (2.27)	Aripiprazole (2), trifluoperazine (1), risperidone (1), olanzapine (1)
Hyperglycemia	5 (2.27)	Clozapine (2), olanzapine (1), risperidone (1), quetiapine (1)
Tiredness	5 (2.27)	Clozapine (3), risperidone (2)
Agitation	5 (2.27)	Risperidone (3), clozapine (1), olanzapine (1)
Slurring of speech	5 (2.27)	Chlorpromazine (4), clozapine (1)
Dizziness	4 (1.81)	Chlorpromazine (2), olanzapine (1), clozapine (1)
Increased appetite	4 (1.81)	Risperidone (2), clozapine (1), olanzapine (1)
Cough	3 (1.36)	Olanzapine (3)
Drying of mouth	3 (1.36)	Olanzapine (2),chlorpromazine (1)
Agranulocytosis	2 (0.90)	Clozapine (2)
Lethargy	2 (0.90)	Clozapine (1)
Abdominal pain	2 (0.90)	Risperidone (1), clozapine (1)
Hypotension	2 (0.90)	Clozapine (1), olanzapine (1)
Difficulty in urination	2 (0.90)	Quetiapine (1), clozapine (1)
Rhinitis	2 (0.90)	Olanzapine (2)
Nausea	2 (0.90)	Chlorpromazine (1), risperidone (1)
Nasal blockade	2 (0.90)	Risperidone (1), clozapine (1)
Tachycardia	2 (0.90)	Clozapine (1), risperidone (1)
Heaviness of head	2 (0.90)	Chlorpromazine (1), haloperidol (1)
Sweating	2 (0.90)	Clozapine (2)
Dysphagia	1 (0.45)	Risperidone (1)
Tardive dyskinesia	1 (0.45)	Fluphenazine (1)
Frequency of micturition	1 (0.45)	Clozapine (1)
Lip smacking	1 (0.45)	Chlorpromazine (1)
Hypoglycemia	1 (0.45)	Haloperidol (1)
Mask face	1 (0.45)	Olanzapine (1)
Hiccups	1 (0.45)	Clozapine (1)
Angina	1 (0.45)	Clozapine (1)
Anorexia	1 (0.45)	Clozapine (1)
Rigidity	1 (0.45)	Trifluoperazine (1)
Enuresis	1 (0.45)	Clozapine (1)
Weight gain	1 (0.45)	Olanzapine (1)
Hoarseness of voice	1 (0.45)	Clozapine (1)
Body ache	1 (0.45)	Risperidone (1)
Menstrual cycle abnormality	1 (0.45)	Risperidone (1)
Generalized itching	1 (0.45)	Risperidone (1)
Tingling sensation	1 (0.45)	Olanzapine (1)
Orthostatic hypotension	1 (0.45)	Clozapine (1)
Gait disturbance	1 (0.45)	Risperidone (1)
Disturbed sleep	1 (0.45)	Risperidone (1)
Furuncle	1 (0.45)	Clozapine (1)
Hyperprolactinemia	1 (0.45)	Risperidone (1)
Dyspnoea	1 (0.45)	Clozapine (1)
Hyperuricemia	1 (0.45)	Olanzapine (1)
Fatigue	1 (0.45)	Chlorpromazine (1)

ADRs caused during inpatient stay, while in other outpatient based studies weight gain contributed to a major bulk in metabolic symptoms[9,16]. There was an improvement in all the ADRs in which either the dose was tapered or the drug withdrawn. This ADRs include mask like face induced by olanzapine, agranulocytosis, giddiness, sedation, drowsiness dystonia, slurring of speech and dryness of mouth induced by clozapine and hyperprolactinemia induced by respiration. In our study preventability was assessed using modified

Shumock and Thronton criteria, 16.81% ADR were probably preventable, of which 3.18% of the preventable ADR were due to drug to drug interaction, among which patient who were on chlorpromazine along with an atypical agent developed ADR like sedation, drowsiness. Considering the fact that preventative measures were not prescribed prophylactically ADRs like tremor, akathisia and dystonia were assessed as probably preventable (13.63%) and ADRs like agranulocytosis, increase blood sugar level etc. were assessed as not preventable (57.58%). Out of the 9 antipsychotic drugs prescribed during the study, 4 (44.44%) drugs were prescribed from NLEM and 5 (55.55%) drugs were prescribed from WHO Essential Drug List. These findings support rational drug use as per WHO drug utilization study guidelines[18]. Among the ADRs 59% were categorized as type A (Predictable). For the purpose of reporting to WHO–UMC, ADRs were coded based on WHO-ART (WHO Adverse Reaction Terminology) (Table 4). The most common organ system (SOC-system organ class) affected by ADRs was the CNS and peripheral nervous system (27.72%). These results were similar to other such studies from India[6-8]. The reason for this is due to the blockage of dopamine receptors by antipsychotic drugs. Extra pyramidal syndrome (EPS) accounted for almost 50% of the central and peripheral nervous system ADRs. Specific treatments such as anticholinergic, benzodiazepines and beta-blockers were given for it. The other common ADR in CNS were tremors, blurring of vision and headache. For most of patients, tremors were self-limiting and reassurance was sufficient. Only in patients with distressing and troublesome tremors, central anticholinergic drug was prescribed with or without a dose reduction of the suspected antipsychotic drug. The gastrointestinal system was the second most common system organ class with constipation accounting for the majority of patients (30%). This was followed by psychiatric disorder system organ class with sedation being the most common (78.26%). The common metabolic adverse effects observed in our study included hyperglycemia, hypoglycemia, weight gain, hyper prolactinemia, hyperuricemia and anorexia. This finding is immensely correlated with the other published studies[6,9,16]. Drug wise cataloging was made to categorize the highest number of ADRs reported by each drug during the study period. We observed that clozapine caused the highest number of ADRs (35%) followed by chlorpromazine (19.54%), risperidone (19.09%) and olanzapine (14.09%). The particulars of other suspected drugs are presented in (table 5). These results are similar to other studies where atypical antipsychotic drugs were associated with the majority of ADRs[9,10]. The higher use of Clozapine in the study is justifiable because the majority of patients were treatment-resistant schizophrenia. Considering the cost, Chlorpromazine was prescribed commonly leading it to be the second most common suspected drug in our study. Patients were considered on high dose antipsychotic medication if the total daily dose of a single antipsychotic exceeds the upper limit stated in the summary of product characteristics (SPC) or British National Formulary (BNF) with respect to age and indication and a total daily dose of two or more anti psychotics exceeds the SPC or BNF maximum using the percentage method[19]. In percentage method the doses of each antipsychotic drug prescribed should be expressed as a percentage of their respective recommended maximum dose and then these percentage values are added together, if the cumulative dose of greater than 100% is obtained then it should be considered as 'high dose. In our study, the total daily dose of all antipsychotic medications was lesser than their respective prescribed upper limits. Also, the clinicians kept a check on high dose anti psychotics prescription by restricting it use mainly for control of acute emergency symptoms, avoiding the combination of depot with oral, typical with atypical drugs and by not prescribing anti psychotics on a PRN basis. The crossover strategy as mentioned above was adopted in cases where combinations of anti psychotics were required to prevent high dose antipsychotic prescription. The entire spectrum of ADRs observed during the study period of one year with respect to their suspected drug seems bit exhaustive as was noted in other studies (Table 6)[11,20]. These findings support the need to warn the patients and their care givers about these ADRs which they may encounter while consumption of antipsychotic drugs and thus help them from discontinuing the drugs unnecessarily. In addition, these findings support the rationale for ordering various investigations by the physicians at baseline during the initial visit and also on an ongoing basis for early detection and preventions of ADRs. Hence the initial visit should consist of investigative work ups like full blood count including hemoglobin, serum creatinine, serum urea, thyroid function tests, liver function tests, blood glucose, body weight, blood pressure, fasting lipid profile, serum prolactin and ECG.

CONCLUSION

The study supports the importance of baseline investigations and active surveillance for early detection and prevention of ADRs. Poly pharmacy may

be avoided whenever clinically feasible and percentage method which defines what constitutes a high dose should be used in cases where higher doses of antipsychotic are required.

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REFERENCES

1. Zhang, J.P., J.A. Gallego, D.G. Robinson, A.K. Malhotra, J.M. Kane and C.U. Correll, 2013. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: A systematic review and meta-analysis. Int. J. Neuropsychopharmacology, 16: 1205-1218.
2. Pakpoor, J. and M. Agius., 2014. A review of the adverse side effects associated with antipsychotics as related to their efficacy. Psychiatr Danub., 1: 273-284.
3. Schumock, G.T. and J.P. Thorn., 1992. Focusing on the preventability of adverse drug reactions. Hosp Pharm., Vol. 27.
4. Hartwig, S.C., J. Siegel and P.J. Schneider, 1992. Preventability and severity assessment in reporting adverse drug reactions. Am. J. Health-Syst. Pharm., 49: 2229-2231.
5. Pahari, N., S.K. Tripathi, T. Maity, B.K. Gupta, C. Bagchi and D.K. Mondal., 2012. Evaluation and analysis of adverse drug reactions of second generation antipsychotics in a psychiatry out-patient department.2012;4:158-62. Int J Pharm Pharm Sci., 4: 158-162.
6. Piparva, K.G., J.G. Buch and K.V. Chandrani, 2011. Analysis of Adverse Drug Reactions of Atypical Antipsychotic Drugs in Psychiatry OPD. Indian J. Psychological Med., 33: 153-157.
7. Lahon, K., H. Shetty, A. Paramel and G. Sharma., 2012. Adverse drug reaction monitoring of antipsychotics, antidepressants and mood stabilizers in the psychiatric outpatient unit of a teaching hospital-a retrospective study. Int J Pharma Bio Sci., 3: 470-478.
8. Lucca, J., R. Madhan, G. Parthasarathi and D. Ram, 2014. Identification and management of adverse effects of antipsychotics in a tertiary care teaching hospital. J. Res. Pharm. Pract., 3: 46-50.
9. Pritom, K. *et al.*, 2015. To Study the Pattern of Adverse Drug Reaction of Antipsychotic Drugs in a Tertiary Care Hospital of Assam. International Journal of PharmTech Research., 8: 101-105.
10. Juno J.J. et al., 2014. Evaluation of adverse drug reactions associated with the psychotropic drugs in the management of patients with schizophrenia. Der Pharmacia Lettre., 6: 129-134.
11. Leucht, S., C. Corves, D. Arbter, R.R. Engel, C. Li and J.M. Davis, 2009. Second-generation versus first-generation antipsychotic drugs for schizophrenia: A meta-analysis. The Lancet, 373: 31-41.
12. Keefe, R.S.E., R.M. Bilder, S.M. Davis, P.D. Harvey, B.W. Palmer and J.M. Gold, *et al.,* 2007. Neurocognitive Effects of Antipsychotic Medications in Patients With Chronic Schizophrenia in the CATIE Trial. Arch. Gen. Psychiatry, 64: 633-647.
13. Jones, P.B., T.R.E. Barnes, L. Davies, G. Dunn and H. Lloyd et al., 2006. Randomized Controlled Trial of the Effect on Quality of Life of Second- vs First-Generation Antipsychotic Drugs in Schizophrenia. Arch. Gen. Psychiatry, 63: 1079-1087.
14. Lakshmi, P., K. Venkatesh, G. Divya, T.S.D. Prasad, S. Ramand and V. Kishore, *et al*., 2014. A Study on Adverse Drug Reactions of Antipsychotics in Psychiatry Patients of South Indian Hospital. ResearchGate., 2014: 153-155.
15. Hazra, A., G. Sengupta, S. Bhowmick, A. Datta and M. Rahaman, 2011. Adverse drug reaction monitoring in psychiatry out-patient department of an Indian teaching hospital. Indian J. Pharmacol., 43: 36-390.
16. Carlini, E.L.D. and S.A. Nappo, 2003. The pharmacovigilance of psychoactive medications in Brazil. Rev. Bras. Psiquiatria, 25: 200-205.
17. Jayanthi, C.R. *et al.,* 2013. Adverse drug reactions in psychiatry outpatients: Clinical spectrum, causality and avoidability. J Chem Pharm Res., Vol. 5.