Original Article

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A Prospective Study on Monitoring and Reporting of Adverse Drug Reactions Associated with Psycholeptic and Psychoanaleptic Drugs in a Tertiary Care Teaching Hospital

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Abstract

Background: Psycholeptic and psychoanaleptic drugs are associated with adverse effects which can affect the patient compliance and course of treatment. Psychiatrist awareness about this can facilitate rational and safe use of these medicines. Pharmacovigilance studies for psychiatric drugs are found to be very low in our country. *Objectives:* To assess the types, severity, causality, preventability, predictability and management of Adverse Drug Reactions (ADRs) among Psycholeptics and Psychoanaleptics. *Method:* A Prospective spontaneous reporting study was carried out for 6 months in the patients of psychiatry department. The study includes the ADRs among the Psycholeptics and Psychoanaleptics in any age of either sex from in-patients. The medication charts of patients were analysed for ADRs. *Results:* Among the 141 admitted psychiatric patients, 35 ADRs were reported during the course of study. Risperidone and Olanzapine were the frequently used drugs having the highest number of ADRs and tremor was the commonest ADR. Number of ADRs was found to affect the neurological system. Type A reactions were found to be more in males than in females. The causality assessment was done using Naranjo scale and majority of the reports were rated as possible (85.71%). Mild and moderate reactions accounted for 31.43% and 62.86% respectively as per Hartwig scale and only 5.71% of the reactions were found to be severe. Preventability assessment using Schumock and Thornton scale showed that most of the ADRs were definitely preventable (48.57%). *Conclusion:* Continuously monitoring the safety profile of psychiatric drugs fosters the rational and safe use of the medicines.

Keywords: Adverse Drug Reactions; Psycholeptics; Psychoanaleptics; Antipsychotics.

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Introduction

The WHO defines an adverse drug reaction (ADR) as any response to a drug that is noxious and unintended and occurs at doses normally used in humans for the prophylaxis, diagnosis, and treatment of disease, or for modification of physiological function.[1] The detection of an ADR is crucial to the management of any patient since failure to recognise an AD Rmay result in continuing patient morbidity.

Psycholeptic drugs like antipsychotics, anxiolytics and mood stabilizers; psychoanaleptic drugs like antidepressants, psychostimulants and antidementia are associated with adverse effects which can affect the medication adherenceand treatment outcome in mental disorders. Many of these adverse effects are preventable. Clinician's awareness about the adverse effects of psychotropic drugs can establish rationality and safety profile of these medicines.[2] There are many case reports involving ADRs among psychiatric drugs but there

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is a lack of Indian studies on pharmacovigilance activities in a mental health setting.[3]

Antipsychotic medications are widely prescribed and have a tendency to cause weight gain and subsequently hyperglycaemia, hypertension and hyperlipidemia. These metabolic risk, along with poor life style habits and smoking, are known to occur around two to five times more often in patients suffering from psychosis as compared to the general population. Judicious tailoring of the usage of antipsychotic medications and early detection and intervention for cardio-metabolic risks, may help in improving the long term outcomes in these patients.[4] Several reports are published regarding causation of myocarditis or cardiomyopathy by the antipsychotic drug, Clozapine. Other drugs in the same therapeutic class may share similar toxicity.[5] Taking all this in to consideration, this study was undertaken as there were very few studies in this part of the region.

Materials and Methods

Study design:

This is a prospective, spontaneous reporting study.

Study location:

This study was conducted at the Psychiatry department of S.N. Medical College and HSK Hospital, Bagalkot.

Study population:

Study was based only on those patients who experienced an adverse reaction to medicine use during their stay at the psychiatry department of HSK Hospital and ultimately reported to student clinical pharmacist.

Inclusion criteria:

ADRs of drugs like psycholeptic and psychoanaleptic in any age of either sex from in-patients.

Exclusion criteria:

The ADR that is due to

1) Medication errors, over prescribing, over dosing/ excess consumption.
2) Drug-Drug interaction, Drug-Food interaction, Drug interaction with the use ofalternative system of medicine.
3) ADR from out-patients.
4) ADRs of drugs other than psycholeptic and psychoanaleptic.

Recording of data:

The data collected in the six months period was analyzed for the following parameters.

- The total number of ADRs that are reported.
- Reports received from different departments of the H.S.K. Hospital & research centre.
- Age groups and gender of the patients.
- Different organ systems affected by reactions.
- Classification of drugs that causing reaction.
- Assessment of causality based on Naranjo scale.(ANNEXURE III)
- Severity of the reaction based on Hartwig scale. (ANNEXURE IV)
- Assessment of causality based on WHO. (ANNEXURE V)
- Assessment of preventability based on Schumock and Thorntonscale.(ANNEXURE VI)

Results

During the 6 months of study, 35 ADRs were found from 23 patients. The total number of patients during this study period was 147 from which the 35 ADRs were reported. The overall incidence of ADRs during hospitalization in this patient group was 15.65%.

We observed more ADRs in females 20 (57.14%) than in males 15 (42.86%)during their hospital stay. The rate of ADRs in elderly patients was not considerably higher than in adult patients (Fig a).In present study majority of the reactions were Type A (97.15%), while Type B accounted (2.85%) very less in the observed patients (Table 1).Most of the reported ADRswere from psycholeptics (typical antipsychotics, atypical antipsychotics & anxiolytics) which accounted for 88.57% and psychoanaleptics (antidepressants) 11.43%. Psycholeptics such as Risperidone and Olanzapine were the most commonly involved drugs causing ADRs, whereas Escitalopram among psychoanaleptics (Fig. b).Antipsychotics with greater D2 receptor blockade potency showed 56.67% of ADRs while with lesser potency accounted 43.33% of ADRs (Table 2).During the time period of our study, the incidence of ADRs was found to be more in patients diagnosed with depression with psychotic symptoms (34.28%)

followed by paranoid schizophrenia (17.4%) as depicted in table 3.

We studied organ system affected with ADRs amongst which the neurological system ranked first with 54.29% followed by gastrointestinal (34.28%), endocrine (5.71%), haematology and CVS(Fig c).

Upon causality assessment using Naranjo scale, majority of the reports were rated as possible (85.71%) followed by probable (14.29%). According to Hartwig and Siegel scale, mild, moderate and severe reactions accounted for 31.43%, 62.86%and 5.71% respectively.Preventability assessment was done usingSchumock and Thornton scale showed that most of the ADRs were definitely preventable (48.57%) and 25.71% were probably and not preventable ADRs (table 4). Upon assessment of the type of prescription causing ADRs, the majority of the reports showed that the polypharmacy acts as the predisposing factor of ADR in both adults and elderly. Polypharmacy showed statistically significant difference between adults and elderly in causing ADRs (table 5).

In the majority of reported ADRs, the drug was not withdrawn for 71.43% of cases and managed by altering the dose for 31.43% of cases. The ADRs were also managed by instituting additional treatment for 62.86% of cases (Fig d).An improvement in the patients with ADRs was observed majorly (74.29%), because of the drug withdrawal, dose alteration and institution of additional treatment (Fig e).

Table 1: Types and incidence of reported ADRs

Type	% of ADRs reported	Incidence rate (%)	Number of ADRs	ADRs %
Type A	97.15 %	>10%	15	44.11
		1-10 %	16	47.05
		<1 %	3	8.82
Type B	2.85 %	>10%	00	00
		1-10 %	00	00
		<1 %	01	100

Table 2: ADRs based on D2 receptor blockade potency

Name of drug	Dopamine D2neuroreceptor potency	No. of ADRs	Total %
Haloperidol	High	05	56.67
Risperidone	High	12	
TOTAL		17	
Olanzapine	Low	11	43.33
Quetiapine	Low	02	
TOTAL		13	

Table 3: Distribution of ADRs based on the disorders diagnosed

Disorders	No. of patients with ADR	No. of ADRs	% of ADR
Paranoid schizophrenia	05	06	17.14
Depression without psychotic symptoms	05	12	34.28
Catatonia	01	01	2.86
OCD	01	01	2.86
Depression with psychotic symptoms	03	03	8.57
Adjustment disorder	01	01	2.86
Dementia	01	01	2.86
Psychosis	01	04	11.43
Somatoform disorder	01	01	2.86
BPAD	04	05	14.28

Table 4: Analysis of ADRs for selected parameters

Parameter	Number of ADRs	ADRs %
Causality		
Definite	00	00
Probable	05	14.29
Possible	30	85.71
Severity		
Mild	11	31.43
Moderate	22	62.86
Severe	02	05.71
Preventability		

Table 5: Influence of polypharmacy in adults and elderly

Age	Type of prescription			Chi-square test	P- value
	Number of drugs(>5)	Number of drugs (≤5)	Total		
Adults	03	24	27	9.243	0.0024 Statistically significant
Elderly	05	03	08		
Total	08	27	35		

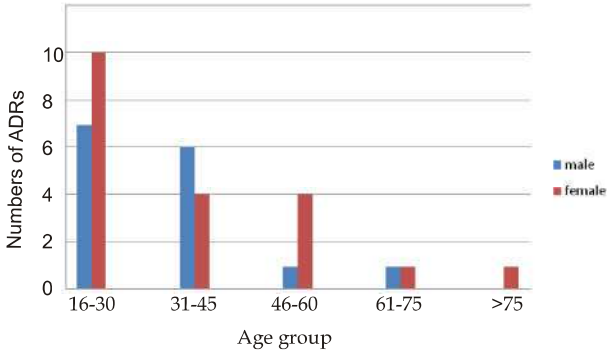


Fig. a: Percentage of the patients and patient characteristics

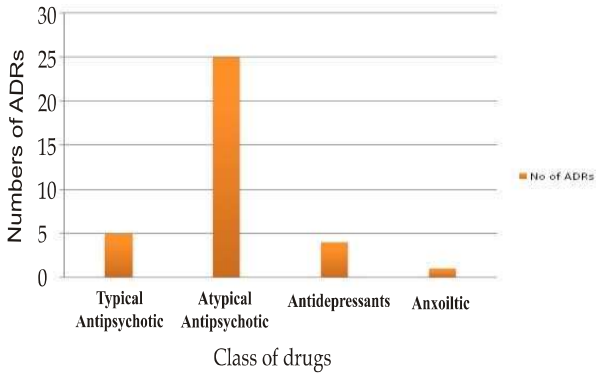


Fig. e: Percentage outcome of ADRs

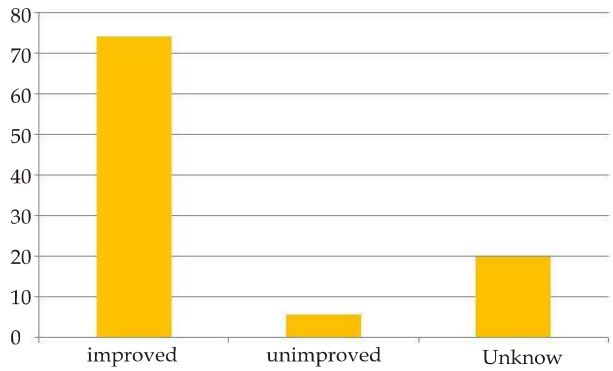


Fig. e: Percentage outcome of ADRs

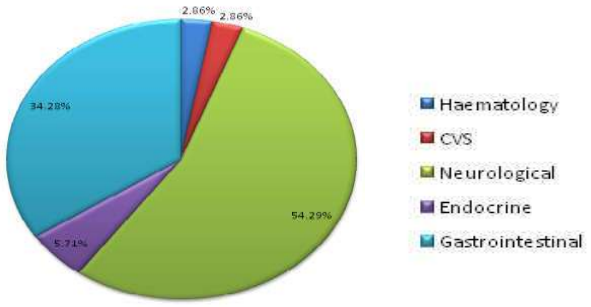
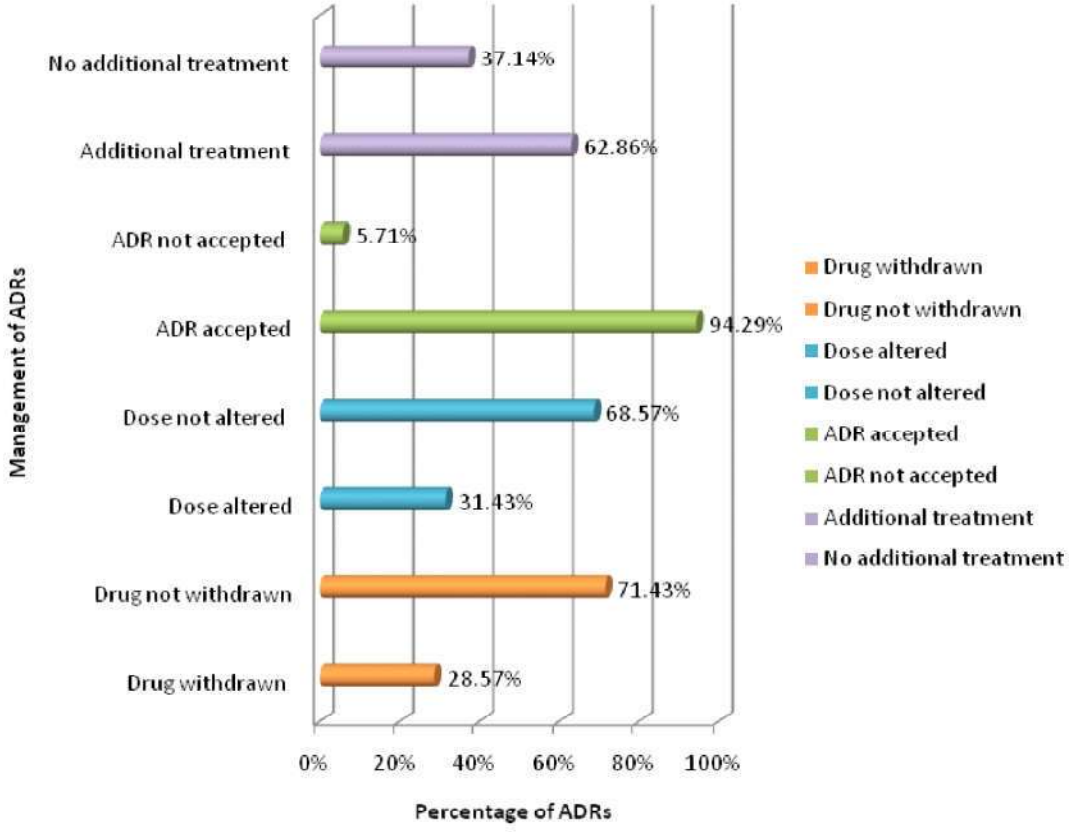


Fig. c: Organ system affected with ADRs

Discussion

Adverse Drug Reactions and Drug-drug interactions to psychotropic agents are common and can lead to noncompliance and at times discontinuation of therapy.In our study, we found number of ADRs was more in females than in males and majority of patients were found to be in the median age 35 years. However this finding is in contrast with the study done byLashmi Pet.al, which reported ADRs were noted more in males than females and the median age was 31.5 years.[6]

Depression without psychotic symptoms and paranoid schizophrenia were found to be the



commonest clinical diagnosis. Among them, more ADRs were with depression than with paranoid schizophrenia. This finding is similar to the study by Venkatesh K et.al, which reported paranoid schizophrenia as the commonest clinical diagnosis.[6]

Class of drugs responsible for ADRs included atypical antipsychotics, typical antipsychotics, antidepressants and anxiolytics. Among these, the ADRs caused by atypical antipsychotics and typical antipsychotics were preventable. Previous studies done by Courtney et.al, showed more ADRs among mood stabilizers followed by typical antipsychotics, atypical antipsychotics and antidepressants. Out of these mood stabilizers, atypical antipsychotics and typical antipsychotics were commonly associated with preventable ADRs.[7]

In previous studies, the causality assessment of suspected ADRs done by using Naranjo Scale and WHO Scale revealed that majority of the ADRs were possible than probable. We also accounted the similar result.

The severity assessment of ADRs was done by using Hartwig and Siegel Scale in which 58.93% were found to be moderate and 41.43% mild. This is similar to our study where we found ADRs of moderate severity.6

We studied organ system affected with ADRs amongst which the neurological system (tremor) ranked first followed by gastro intestinal, endocrine, haematology and CVS. Sengupta et.al, had also found that neurological ADRs (tremor) were the commonest followed by metabolic (weight gain) and gastro intestinal effects (constipation).8In this study most of the reactions were type A (97.15%), while type B (2.85%) accounted very less in the observed patients.

In our study, we found an incidence of ADRs as 32.91%. The highest number of ADRs was shown by Risperidone and Olanzapine, tremor the most recurrent one. Pritom Ket.al also found an incidence of ADRs as 9.19% in their study. Olanzapine was the commonly used drug having the highest number of ADRs and tremor the frequent ADR.[9]

The preventability of the ADRs was assessed using Schmock and Thornton Scale, in which definitely preventable ADRs came as the highest one. But in another study not preventable ADRs like agranulocytosis, increased blood sugar level etc were noted more than probably preventable ADRs like tremor, akathisia, dystonia.[9]

No ADR found turned out to be fatal, life-threatening or required hospitalization for management. Some of the events, such as tremor were temporarily disabling but were managed by clinicians with appropriate medicines (such as trihexyphenidyl for EPS) or dose modification (for example, the doses of antipsychotics can be decreased for the management of sedation and drowsiness cases).

Conclusion

By this study, it is evident that ADRs with psycholeptics and psychoanaleptics are common in the psychiatric population of HSK hospital,Bagalkot. But the involvement of the clinical pharmacist in monitoring and reporting ADRs will help the patients for medication adherence and the psychiatrists to provide better treatment outcome.

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Conflict Of Interest

Authors declareno conflict of interest

Abbreviations Used

ADR	: Adverse Drug Reaction
WHO	:World Health Organisation
D2 Receptor	: Dopamine 2 Receptor
CVS	: Cardio Vascular System
EPS	:Extra Pyramidal Symptoms
OCD	: Obsessive Compulsive Disorder
BPAD	: Bipolar Affective Disorder

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