Analysis of adverse reactions associated with use of psychiatric medications in a teaching hospital - A retrospective study

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ABSTRACT

Drug therapy for psychiatric disorders is frequently associated with various adverse drug reactions (ADRs). Our study was based on analyzing the reports received by spontaneous ADR reporting program. Collected data were evaluated to understand the pattern with respect to patient demographics, nature of the reactions, characteristics of the drugs involved and outcome of the adverse drug reactions. Causality, severity, and preventability of reactions were analyzed. Most of the ADRs were reported in the age group of 31-45 (36 %) and female preopondarance (53.6 %) was observed. Most of the reported ADRs were of Type A 68.8%. Phenytoin (23.2%) was found to be the most common drug which caused ADRs. Skin and appendages disorders (56.8%) were the most affected system. Our

current study supports the need of pharmacovigilance in psychiatry practice to promote early detection of ADRs and passing on information on drug safety to psychiatrists regarding the probability of ADRs to promote patient safety.

Keywords: Adverse drug reactions, Psychiatric Medications and Pharmacovigilance.

1. INTRODUCTION

Drug therapy for psychiatric disorders is frequently associated with various adverse drug reactions (ADRs). As far as treatment is concerned there is a need for trying different drugs in a patient to control the symptoms, which increases the risk of ADRs. Patients with psychiatric illnesses require long-term therapy with psychotropic drugs which lead them to an array of ADRs.[1] The second generation antipsychotic medications are the most widely used antipsychotic drugs in psychiatric practice because the conventional first generation drugs are associated with unwanted extrapyramidal signs and symptoms (EPS)[2]. Pharmacovigilance activities continuously update the medical community about the adverse events associated with medications and inform clinical practioners about the nature and severity of adverse drug reactions.[3] Spontaneous reporting of ADRs has played a major role in the identification of the safety issues to Antipsychotic drugs and thereby help in ensuring safer use. Periodic evaluation of ADR-related data generated is equally important in characterizing the pattern of ADRs and thereby help in designing steps to improve the safety of drug use in the clinical set up. Data generated from the tertiary care hospital contributes to the national and international safety database thereby contributing to the common goal of a safer drug use. The present study was aimed to analyze the pattern of ADRs implicated to Antipsychotic drugs reported spontaneously to the ADR monitoring Centre.

2. MATERIALS AND METHODS

This retrospective study was carried out toanalyze the pattern of ADR caused by psychiatric medication.ADR received through the Spontaneous reporting form fromPharmacovigilance Programme of India (PVPI) was used to analyze the Data. ADRs notified and receivedover a period of 2 years (January 2018–Dec 2019) were selected for analysis. All suspected ADRswere initially assessed by the Pharmacovigilance Associate for its validness and then by the Causality assessment committee in the Department of Pharmacology. Collected data was evaluated to understand the pattern with respect to patient demographics, type of the reported reactions, nature of the medicinal product involved and outcome of the reactions. Causality, severity, andpreventability of reaction were analyzed. Patient's age and sex were considered for evaluation. In agreement with previous published research articles.[4] patients were subdivided into six age groups; infants, children and adolescents (0–15 years), young adults (16– 30years),adults(31–45years),olderadults(46–60years),elderlyadults(61–75years), andveryelderly adults (over 75 years). The received reportwasdifferentiated as type A (Augmented) and type B (Bizarre) based on the classification by Rawlins and Thompson [5]. Based on the literatures available the reported ADRs were classified as common, uncommon, rare, and very rare based.[6]Reactions were codified and were further classified to various system organ classes depending on World Health Organization adverse reaction terminology (WHO-ART) [7].

Causality assessment was carried out using the ''WHO causality assessment scale''. In the WHO causality assessment, the drug reaction is classified as Certain, Probable/Likely, possible, unlikely, Inaccessible/ unclassifiable. For preventability assessment, ADR's ADRs were categorized into definitely preventable, probably preventable and not preventable by using the modified Schumock and Thornton method [8]. Depending upon the severity, ADRs were classified into mild, moderate and severe reactions using the criterion developed by Hartwig et al for severity assessment [9].

3. RESULTS

In our study most of the ADRs were reported in the age group of 31-45 (36 %) followed by 46-50 years of age which is about 27.2 %. The results were provided in Table 1. Considering the Gender female preopondarance (53.6 %) was observed in our study (Table-2). Considering the type of Reaction, most of the reported ADRs were of Type A 68.8% followed by Type B (31.2%). Phenytoin (23.2%) was found to be the most common drug which caused ADR followed by Haloperidol (16.8%), Carbamazepine (16.8%) and Risperidone (16.8%) results are presented in table-4. While analyzing the systems affected, Skin and appendages disorder 56.8% was the most affected system followed by Central and peripheral nervous system disorders 32.8%, Psychiatric disorders 4.8%. Majority of the suspected ADRs were probable and mild in nature. On severity assessment 14.5% of the reactions were seemed to be severe. Majority of the suspected ADRs were of a predictable and probably preventable.

Table 1 Age wise distribution of ADR's

AGE	
Age group	**Number (%) of ADR reports**
0-15	7(5.6%)
16-30	12 (9.6%)
31-45	45 (36 %)
46-60	34 (27.2%)
61-75	19 (15.2%)
>75	8 (6.4%)
Total	**125**

Table 2 Analysis of ADRs based on Gender

Gender	
Gender	**Number (%) of ADR reports**
Female	67 (53.6%)
male	58 (46.4%)
Total	125

Table 3 Analysis of ADRs based on Type of Reaction

Type of Reaction	
Type	**Number (%) of ADR reports**
Type A	86 (68.8%)
Type B	39 (31.2%)
Total	125

Table 4 Analysis of ADRs based on Individual Drugs involved

Drugs Involved	
Drug name	**Number (%) of ADR reports**
Phenytoin	29 (23.2%)
Haloperidol	21 (16.8%)
Carbamazepine	21 (16.8%)
Risperidone	21 (16.8%)
Sodium Valproate	08 (6.4%)
Fluoxetine	05 (4.0%)
Amitriptyline	03 (2.4%)
Chlorpromazine	02 (1.6 %)
levetiracetam	02 (1.6 %)
Clozapine	03 (2.4%)
Olanzapine	02 (1.6 %)
Trihexyphenidyl	03 (2.4%)
Diazepam	02 (1.6 %)
Quetiapine	02 (1.6 %)
Phenobarbitone	01 (0.8 %)
Total	125

Table 5 Analysis of ADRs based onType of Reaction

Drugs Implicated	Reaction	Number (%) of ADRs
	Itching	3 (2.4%)
	Vomiting	1 (0.8 %)

Phenytoin	Skin lesion/oral erosion	4 (3.2%)
	Rash	14 (11.2%)
	Gum hypertrophy	6 (4.8 %)
	Stevens - Johnson Syndrome	1 (0.8 %)
Haloperidol	Tremor	4 (3.2%)
	Extrapyramidal symptoms	7 (5.6%)
	Itching	3 (2.4%)
	Rash	4 (3.2%)
	Sedation	1 (0.8 %)
	Excessive Salivation	2 (1.6 %)
Carbamazepine	Rash	11(8.8 %)
	Skin erosion/lesions	3 (2.4%)
	Itching	3 (2.4%)
	Erythema	1 (0.8 %)
	Swelling of Lips/eyes	2 (1.6 %)
	Stevens - Johnson Syndrome	1 (0.8 %)
Risperidone	Extrapyramidal symptoms	9 (7.2%)
	Giddiness	1 (0.8 %)
	Galactorrhea	2 (1.6 %)
	Anxiety	2 (1.6 %)
	Skin erosion	1 (0.8 %)
	Rash	3 (2.4%)
	Hypotension	1 (0.8 %)
	Tremor	2 (1.6 %)
Sodium Valproate	Itching	3 (2.4%)
	Fixed drug eruption	2 (1.6 %)
	Skin rash	2 (1.6 %)
	Loose stools	1 (0.8 %)
Fluoxetine	Rash	1 (0.8 %)
	Anxiety	1 (0.8 %)
	Slurring of speech	2 (1.6 %)
	Gastritis	1 (0.8 %)
Amitriptyline	Sedation	1 (0.8 %)
	Giddiness	1 (0.8 %)
	Rash	1 (0.8 %)
Chlorpromazine	Slurring of Speech	1 (0.8 %)
	Rash	1 (0.8 %)
levetiracetam	Skin Lesion	1 (0.8 %)
	Rash	1(0.8 %)
Clozapine	Headache	1 (0.8 %)
	Tremor	1 (0.8 %)
Olanzapine	Giddiness	1 (0.8 %)
	Amenorrhea	1 (0.8 %)
Trihexyphenidyl	Extrapyramidal symptoms	2 (1.6 %)
	Constipation	1 (0.8 %)
Diazepam	Skin lesion	1 (0.8 %)
	Anxiety	1 (0.8 %)
Quetiapine	Extrapyramidal symptoms	1 (0.8 %)
	Drowsiness	1 (0.8 %)

Phenobarbitone	Rash	1 (0.8 %)

Table 6 Classification of Organ systems associated with adverse drug reactions

System organ class (WHO-ART SOC code)	Number (%) of ADRs (n=125)
Skin and appendages disorder (0100)	71 (56.8%)
Central and peripheral nervous system disorders (0410)	41(32.8%)
Gastro-intestinal system disorders (0600)	3 (2.1%)
Psychiatric disorders (0500)	6(4.8%)
Reproductive system disorders female (1420)	4 (3.2%)

Table 7 Analysis of ADRs based on Causality

Category	Number (%) of ADRs
Certain	1 (0.8 %)
Probable	63 (50.4%)
Possible	57 (45.6%)
Unlikely	4 (3.2%)

Table 8 Analysis of ADRs based on Severity

Category	Number (%) of ADRs
Mild	79 (63.2%)
Moderate	28 (22.4%)
Severe	18(14.4 %)

Table 9 Analysis of ADRs based on its Preventability

Category	Number (%) of ADRs
Definitely preventable	12 (50%)
Probably preventable	8 (33.33%)
Not preventable	4 (16.6%)

4. DISCUSSION

Pharmacotherapy for psychiatric disorders is frequently associated with adverse drug reactions. Monitoring and evaluation of ADRs associated with psychotropic drugs is essential as these medications differ from others as they often affect emotion and cognition [10]. Wide range of psychotropic drugs are available in the market for treating psychiatric disorders [11]. And the repeated use of these multiple psychiatric drugs in a single patient (polypharmacy) has now emerged into a common practice in clinical psychiatry which further potentiates the chances of developing ADRs.[12]

The most common method used in pharmacovigilance is the spontaneous reporting and it is the best method to generate signals on new and sometimes rare ADRs of established drugs.

A total of 125 ADRs associated with the use of Antipsychotic drugs were reported during the evaluation period. Upon evaluation of the patient characteristics in the reported ADR's, more reports were in females. This is in contrast to the male preponderance observed among patients visiting psychiatry OPD. Similarly, a higher incidence of 54.85% ADRs was identified among female psychiatric patients in a study conducted on identification and management of antipsychotics' ADR by Lucca et al.[13]

Majority of ADRs were observed in 31-45 (36 %) years of age group. In earlier studies there were varied reports on ADR prevalence among different age groups, namely, Mishra, et al. (36-50 years; 10.62%), Hemalatha et al., (21-30years; 24%), Lucca et al., (19-29years; 37.32%) and Sridhar et al., (18-28 years; 30.1%).[14-17] Most of the ADRs reported were Type A 68.8%. Phenytoin used as mood stabilizer caused the highest number of ADRs (23.4%). The system organ class most commonly affected was skin and appendages (56 %) and the most reported reaction was skin rash, Itching. Majority of the suspected ADRs were probable and mild in nature. This finding was in

accordance with two other studies in which most of the ADRs were mild to moderate in severity and had a probable causal relationship with antipsychotics.[18,19]On severity assessment 14.5% of the reactions seemed to be severe. Majority of the suspected ADRs were of a predictable and probably preventable type. In contrast to our findings, the study conducted by Kurmi et al [20]. reported the majority of ADRs as not preventable type followed by probably preventable.

5. CONCLUSION

ADRs to antipsychotics medications are more common in clinical practice. Our study was based on analyzing the reports received by spontaneous reporting program and includes patients who developed ADRs after receiving the psychiatric Medications. Our current study supports the need of pharmacovigilance in psychiatry practice to promote early detection of ADRs thereby improving patient safety. This study would help in further research in psychopharmacology and might add an insight towards developing personalized drugs with less ADRs.

Limitations of the study

The major drawback of pharmacovigilance system is "under reporting". It is due to the lack of awareness at both the level of healthcare professionals and patients being an OPD study, there are chances that we have missed ADRs that were transient or too mild that the patient would not be able to report.

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Peer-review

External peer-review was done through double-blind method.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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