Original Article

Comparison of Adverse Drug Reactions among Antidepressant Drugs in the Outpatients Department of Psychiatry in a Tertiary Care Hospital of Eastern India

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ABSTRACT

Introduction: The antidepressants used can cause several adverse drug reactions (ADRs), some of which are fatal. Despite significant progress in understanding depressive disorders over the last decade, several issues related to disease diagnosis and effective clinical management remain unrecognized. Therefore, monitoring and evaluation of prescribing practices and pharmacovigilance studies is essential to underscore the rationality of medical care and to guide prescribing physicians and regulators to take corrective action.

Aims/ objective: To highlight patterns of adverse drug reactions associated with antidepressant drug use.

Materials and Method: Patients were screened for suspected ADRs and adverse event information was collected from patients and recorded in suspected drug reaction reporting form issued by the Indian Pharmacopoeia Commission. Reported adverse reactions were analyzed for suspected drug causality using the WHO-UMC causality categories. ADR preventability was analyzed using the modified Schumock and Thornton scales and severity was analyzed using the modified Hartwig and Siegel scales.

Results: SSRIs (72.35%) were the most frequently prescribed, followed by TCA i.e., nortriptyline (19.92%) and SNRI (7.72%). Insomnia and restlessness (14.81%) were the most commonly reported side effects in our study. One report of orthostatic hypotension was found in a patient taking nortriptyline. Five cases of sexual dysfunction have been reported in patients taking SSRIs (selective serotonin reuptake inhibitors). Most of the side effects were probably drug-related, and most of them were moderate in severity and unpreventable.

Conclusion: Side effects of dry mouth and blurred vision are more common with TCAs, whereas agitation and sexual dysfunction are more common with SSRIs, and nausea and fatigue are more common with newer antidepressants. Both clinicians and emergency medical staff should be aware of the various ADRs caused by antidepressants to reduce the morbidity.

Keywords: Depressive Disorders, Anti-depressants, Adverse Drug Reactions.

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INTRODUCTION

Depressive disorders are one of the most common causes of morbidity and disability in the Indian population. It is commonly associated with negative thoughts, feelings of guilt and worthlessness, decreased interest in work, psychomotor anxiety, unhappy marriages due to low libido, and weight loss or gain due to dietary changes.[1] It also accompanies other conditions such as chronic pain and ischemic heart disease.[2] Antidepressants are used primarily to treat depressive disorders and many anxiety disorders. However, these are also utilized in the treatment of various other psychiatric disorders comprising obsessive-compulsive disorders, attention deficit hyperactivity disorder, eat disorders, disorder of personality, impulse control disorders, enuresis, chronic pain disorder, neuropathic pain, etc. regardless of whether comorbid depression is present in these situations. [3,4]

Over the past decade, antidepressant prescribing patterns have shifted from tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) to selective serotonin reuptake inhibitors (SSRIs) and serotonin nor-epinephrine reuptake inhibitors. (SNRI). [5]

An adverse drug reaction (ADR) is defined by the World Health Organization (WHO) as "any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function."[6] ADRs are the most common drug-related adverse events occurring worldwide. [7]

Adverse drug reaction (ADR) detection has gained in importance due to the large number of drugs introduced over the last two decades. Side effects that occur daily in hospitals affect patient health, are often unreported, and lead to serious illness and death. We should be alert for the occurrence of suspicious signs and symptoms in patients who take large doses and have many co-morbidities. Drugs that frequently cause ADRs should be placed in the "high

suspicion" category. The growing supply of medicines on the market, increasing non-scientific advertising campaigns by pharmaceutical company representatives, and a growing trend toward polypharmacy based on individual medicines for individual conditions are contributing to evidence of ADR worldwide. It is increasing and becoming more complex. Adverse drug reactions can reduce patient confidence in treatment leading to negative feelings toward physicians further leading to treatment discontinuation and engagement with other treatment options that further lead to more ADRs and increase in mortality and morbidity in the population. [8] Psychiatric patients require lifelong treatment with psychotropic medications that predetermine the ADR network. [9]

The antidepressants used can cause several adverse drug reactions (ADRs), some of which are fatal.[10,11] Despite significant progress in understanding depressive disorders over the past decade, several issues related to disease diagnosis and effective clinical management remain undetected. In recent years, different classes of different drugs have flooded the market for better treatment of this common disease. [12] Therefore, monitoring and evaluation of prescribing practices and pharmacovigilance studies is essential to underscore the rationality of medical care and to guide prescribing physicians and regulators to take corrective action.

Setting standards through performance assessment and assessing treatment safety should be part of routine clinical practice. With this in mind, the present study was conducted to highlight patterns of adverse drug reactions associated with antidepressant use.

MATERIALS AND METHODS

It was an observational, prospective study done on patients visiting the outpatient department (OPD) of Psychiatry in a tertiary health care centre. The study was conducted for a duration of 18 months, i.e., from February 2022 to July 2022. The first 3 months were used for patient recruitment and the next 3 months for follow-up and data collection. Each alternate patient's prescriptions were collected twice a week. This study was initiated after institutional review board approval.

Inclusion criteria

- Patients with depressive disorders (diagnosed according to the criteria of the International Classification of Diseases - ICD 10) from O.P.D. of Psychiatry department. [13]
- Patients aged 12 to 60
- Patients of both sexes
- Patients taking antidepressants

Exclusion criteria

- Patients under the age of 12 and over the age of 60.
- Prescriptions that do not contain antidepressants.
- Patients suffering from malignancies and terminally ill patients.
- Patients clinically identified as at risk for suicide.
- Patients with a history of substance abuse.
- Patients taking antidepressants prescribed outside our hospital.

In 3 months, approximately 710 patients attended the OPD of psychiatry. Approximately 232 patients visited the OPD on our days of visit (twice weekly). In the recruitment phase, after interviewing every alternate patient, we gathered prescriptions of 215 patients. Of these 215 patients, 31 patients were ruled out as per the exclusion criteria. In the follow up period, 83 patients were lost to follow up. So finally, we were left up to 101 patients.

In the follow-up phase, patients were evaluated for suspected ADR and information on adverse events such as date and time ADR started or ended. Information on dosage, frequency, route and duration of administration of the suspect drug; actions taken after response; other concomitant medications; relevant laboratory test data and relevant history were collected from patients and recorded in suspected adverse drug reaction reporting form issued by IPC (Indian pharmacopoeia commission).[14] Reported adverse reactions were analyzed for suspected drug causality using the WHO-UMC causality categories. ADR preventability was analyzed using the modified Schumock and Thornton scales and severity was analyzed using the modified Hartwig and Siegel scales.[15-17]

Statistical Analysis

Results from this study were presented in tabular format and data were interpreted using Microsoft Excel 365 software. Descriptive analysis was performed for comparative analysis of data using numbered analysis.

RESULTS

In our study, the 21- to 30-year-old age group accounted for the majority of all depressive disorders. When we analyzed gender, we found that men were more susceptible than women. [Table 1]

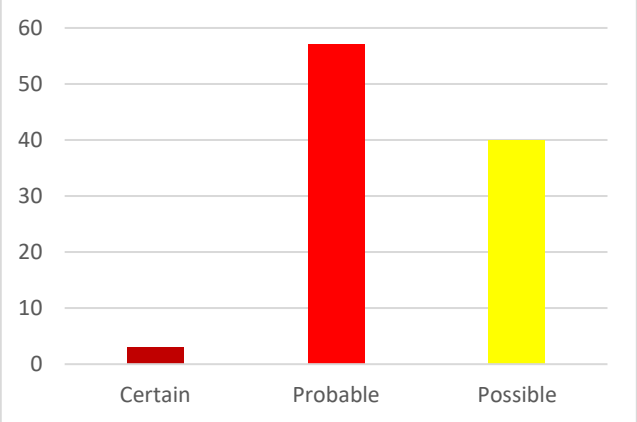

Figure 1: Distribution of ADRs in Various WHO-UMC Causality Categories

Table 1: Baseline demographic and clinical characteristics of 101 patients

Parameters	Values
Age in years (mean ± SD)	25.63 ± 9.84
Gender	
Male, n (%)	53 (52.48)
Female, n (%)	48 (47.52)
Lifestyle	
Living alone, n (%)	38 (37.62)
Living with family, n (%)	63 (62.38
Employment status	
Employed, n (%)	32 (31.68)
Un-employed, n (%)	69 (68.32)
Duration of illness in years (mean ± SD)	4.68 ± 2.24

SD = Standard Deviation

Table 2: Utilization of antidepressant drugs in 101 patients

Name of Drug	Number of prescriptions	Percentage of prescriptions
Nortriptyline	49	19.92
Venlafaxine	11	4.47
Duloxetine	8	3.25
Paroxetine	25	10.16
Sertraline	56	22.76
Fluoxetine	51	20.73
Fluvoxamine	19	7.72
Escitalopram	27	10.98
Total	246	100

Table 3: Frequency of different ADRs of antidepressant drugs

ADRs	Total (%)	Nortriptyline	Venlafaxine	Duloxetine	Paroxetine	Sertraline	Fluoxetine	Fluvoxamine	Escitalopram
Insomnia	12 (14.81)	4			1	3	3		1
Blurring of Vision	4 (4.94)	2				1		1	
Fatigue	5 (6.17)	3	1	1					
Sweating	1 (1.23)						1		
Postural Hypotension	1 (1.23)	1							
Tachycardia	1 (1.23)	1							
Dry mouth	8 (9.88)		2	2	1	1	1		1
Nausea	8 (9.88)		2	1	1	2	1	1	
Loss of Appetite	2 (2.47)					1	1		
Headache	3 (3.7)	1			1			1	
Tremor	3 (3.7)		2						1
Agitation	12 (14.81)			1	1	4	3	1	2
Nervousness	5 (6.17)					2	1	2	
Anxiety	10 (12.35)		2	1	1	2	3		1
Urinary hesitancy	1 (1.23)	1							
Sexual Dysfunction	5 (6.17)				1	2	2		
Total	81	13	9	6	7	18	16	6	6

DISCUSSION

Our study found that the 21- to 30-year-old age group accounted for most of all depressive disorders, consistent with several other studies.[18,19] In a study by Kessler et al., it was shown that the median and interquartile range (IQR) ages for some anxiety and impulse control disorders were very low. The age-of-onset distribution was more for mood disorders, substance use disorders and other anxiety disorders. [19] When we analyzed gender, we found that men were more susceptible than women. This may be due to fewer visits of female patients due to illiteracy. [20] Our findings highlight the high prevalence of depressive disorders among unemployed people living apart from their families.

In our study, among antidepressants, SSRIs (72.35%) were most frequently prescribed, followed by TCA i.e., nortriptyline (19.92%) and SNRI (7.72%). Among SSRIs present drug utilisation was most in sertraline (22.76%) followed by fluoxetine (20.73%), escitalopram (10.98%), paroxetine (10.16%) and, fluvoxamine (7.72%). SSRIs are the most commonly prescribed antidepressants because they are generally non-sedating, safer at high doses, and well tolerated with mild side effects. [21] In many other studies, including tripathi et al. SSRIs accounted for the majority of prescribed antidepressant drugs. [22-25]

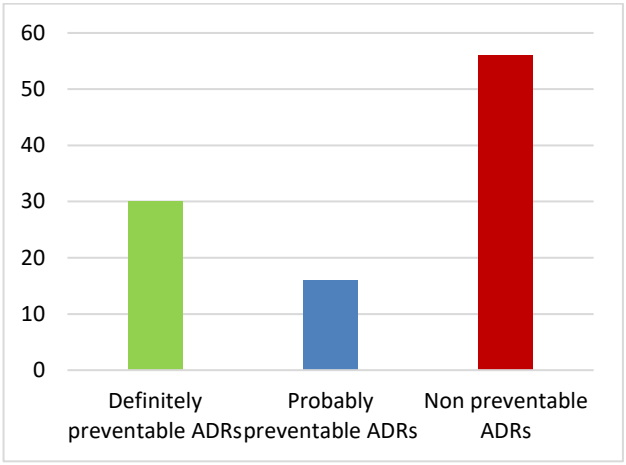

Figure 2: Preventability of ADRs using Modified-Schumock and Thornton scale

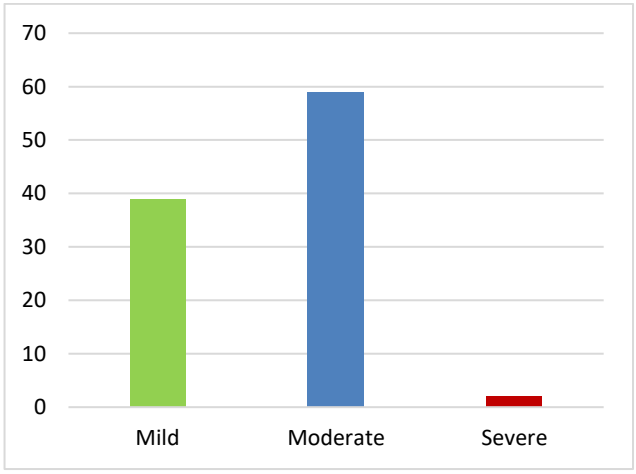

Figure 3: Severity of ADRs using Modified Hartwig and Siegel scale

Since most of the research related to antidepressants only analyzes patterns of drug use, there is known objective data that favours certain groups over others. This study determined the frequency and type of adverse drug reactions associated with antidepressants and established a correlation between ADRs and drug use patterns. Of all the side effects, the study found that common side effects such as blurred vision, insomnia, sweating, and fatigue were more common in the study population. Of these side effects, insomnia was more common with patients taking TCAs than with patients taking SSRIs. However, sweating and anorexia were only observed in patients receiving SSRIs.

Cardiovascular side effects such as tachycardia and orthostatic hypotension are associated with TCAs. When examining gastrointestinal side effects, we found that TCAs were most often associated with dry mouth than SSRIs, and nausea was most commonly associated with SSRIs. Neurological side effects such as headache were often associated with TCAs, and tremors were associated with SSRIs.

SSRIs have shown more psychiatric side effects such as restlessness, nervousness, and anxiety. A similar study concluded that 52% of the study population receiving fluoxetine and escitalopram experienced agitation compared to newer antidepressants such as venlafaxine. [26]

Sexual dysfunction was most commonly associated with SSRIs-treated patients than with the patients who were taking TCAs in our survey. But urinary hesitancy was reported in patients which were taking TCAs. Similar studies conducted have reported that sexual dysfunction is a frequent adverse effect of nearly all the standard antidepressant drugs including SSRIs and of some of the newer drugs. [27] Some of the newer antidepressants such as Bupropion, may be effective alternatives without as high a risk for this problem.[28] Some newer antidepressants, such as bupropion, may be effective alternatives without increased risk for this problem.[29] ADR rates are higher in TCAs (attributed in 1.0% of patients), was lower in SNRIs and SSRIs. [30]

TCAs were associated with known risks such as elevated liver enzymes, urinary retention, and orthostatic hypotension. Psychological and neurological ADRs were most prominent in patients treated with SSRIs.[30]

Antidepressants, antipsychotics, and mood stabilizers are associated with side effects that can affect compliance and the course of treatment for psychiatric disorders.[31]

Our study had some limitations. The sample size was small, study participants were limited to OPD, and the study was conducted at a single centre for a short period of time. At the same time, however, many common antidepressant-induced ADRs can be avoided by knowing the incidence, demographic profiles, and causative agents of different ADRs. This study presented a side effect scenario in East Indian patients and provided baseline data for comparison with other similar studies conducted in different parts of the country. Both physicians and emergency medical staff should be aware of the different ADRs caused by antidepressants so that morbidity can be reduced. Finally, this study strengthens pharmacovigilance activities, provides information on how to address ADR, and may be a further step towards making pharmacotherapy safer and more rational.

CONCLUSION

This study was a candid attempt to identify antidepressant use and its ADRs. SSRIs have been found to be the most commonly prescribed group of antidepressants due to their greater efficacy, safety, compliance and fewer side effects than TCAs. Restlessness, anxiety, and insomnia are the most common side effects associated with antidepressant use. This study provided a representative profile of ADR expected in a psychiatric outpatient clinic. The adverse effects like dry mouth and blurred vision are more common with the use of TCAs, whereas restlessness and sexual problems are frequent with the use SSRIs and nausea and tiredness are more frequent with the use of newer antidepressants.

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