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Original Research Article

Safety Profile of Antidepressant Drugs in Tertiary Care Teaching Hospital, Haldwani

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Abstract:

Objective: This prospective observational study was carried out to identify the safety profile of antidepressant drugs in a tertiary care teaching hospital.

Materials and Methods: New patients aged above 18 years prescribed with at least one antidepressant reporting to outpatient and inpatient unit of Department of Psychiatry of Dr. Susheela Tiwari Government Hospital, Haldwani, meeting the inclusion criteria and consenting to participate in the study were recruited.

Results: Of the 205 patients who received antidepressants, 44 patients (21.4%) experienced 69 ADRs. Maximum ADRs were reported from the central nervous system (46.3%) followed by gastrointestinal system (44.9%). Sleep disturbance (15.9%), dyspepsia (11.6%) and headache (10.1%) were the most common ADRs reported. The rate of occurrence of adverse drug reactions was highest with fluoxetine (20.3%) followed by paroxetine (17.4%) and desvenlafaxine (14.5%) utilization. WHO-UMC scale and Naranjo scale showed similar causality assessment scale. Most cases were of possible category (74%) followed by probable (26%). According to modified Hartwig and Siegel severity assessment scale, most of the ADRs were mild in severity (31.9%) and on Schumock and Thornton preventability scale, the occurrence of maximum number of ADRs was definitely preventable (68.1%). Most of the ADRs reported were Type A category. Severity of the ADRs was rendered mild due to the judicious use of the antidepressant drugs.

Conclusion: Antidepressant drugs were safe to use in psychiatric patients as most of the ADRs were of mild severity.

Keywords: Adverse drug reaction, antidepressants, psychiatry, causality.

Introduction

Depression, one of the most widespread illnesses, often co-exists with other serious illnesses like cancer, cardiovascular disorders and chronic kidney disorders.[1,2] Although the antidepressant drugs which are currently available are effective but they are not devoid of any adverse effect.[3,4] The prevalence of adverse drug reactions (ADRs) in the psychiatric patients is very high varying from 17.25% to 60.7%.[5-7] There are wide number of studies which provide the evidence that antidepressants and antipsychotics among all psychiatric drugs are most frequently associated with ADRs i.e. approximately 90%.[5,8,9] ADRs due to antidepressants decreases adherence as well as delay recovery and sometimes also cause treatment failure.[10,11,12] In context of increased number of newer antidepressants in the market and the use of different class of antidepressants in the psychiatric patients, it is very imperative to assess the safety profile of antidepressants. As there is only limited data available regarding the safety of psychotropic agents especially on antidepressants in the Kumaon region, this study is intended to assess the incidence and pattern of ADRs to antidepressants in Haldwani, Uttarakhand.

Materials and Methods

This was an observational, prospective, hospital based study conducted after taking approval from Institutional Ethical Committee of Government Medical College and Dr Susheela Tiwari Government Hospital, Haldwani. Written Informed Consent was obtained from the patients. Patients enrolled for the first time, aged 18 years and above prescribed with at least One antidepressant Psychiatry OPD and IPD were included in the study. In total 218 patients were recruited, out of which 13 patients who were lost to follow up were

excluded from the study. Therefore, the following study was done in 205 patients. Follow up for ADR was done on the day 1st, 14th and 28th of patients visit.

The safety of antidepressant drugs was analyzed by monitoring the occurrence and severity of adverse drug reactions. The adverse drug reactions were reported on the day of patient's visit using the adverse drug reaction form provided by CDSCO. All the credentials provided in the adverse drug reaction form were recorded namely patient initials, onset and type of adverse drug reaction, suspected drug; reduction, continuation or withdrawal of drug therapy and finally causality assessment of adverse drug reaction. Later, ADRs were reported to the National Coordination Centre (NCC) of Pharmacovigilance Programme of India (PvPI).

Our study assessed adverse drug reactions (ADRs) using WHO-UMC causality assessment scale, Naranjo scale, Modified Hartwig and Siegel Severity Assessment Scale, and Schumock and Thornton Preventability Scale.

Collected data was coded appropriately, entered in Microsoft Excel (MS Excel) spreadsheet and later cleaned for any possible errors in SPSS (Statistical Package for Social Studies} for Windows version 16.0. Categorical data was presented as percentage (%). The descriptive analysis of data was presented in graphs, percentages.

Results

In the sample size of 205 patients, 69 ADRs were reported in 44(21.4%) patients whereas 161(78.6%) patients presented with no ADRs (Table 1).

Table 1: Number of adverse drug reactions reported

ADR	No.
Present	44 (21.4%)
Absent	161 (78.6%)

These adverse drug reactions were classified according to the various body systems and maximum adverse drug reaction were reported from central nervous system 32(46.4.7%), followed by gastrointestinal system 31(44.9%) and metabolic system 4(5.6%). Other body systems from which adverse drug reaction reported were dermatological 1(1.4%) and genitourinary 1(1.4%) (Table 2).

Table 2: Classification of adverse drug reactions

S No.	System	N = 69	%
1	CNS	32	46.4
2	GIT	31	44.9
3	Metabolic	4	5.6
4	Dermatology	1	1.4
5	Genitourinary	1	1.4

In the study, sleep disturbance 11(15.9%), dyspepsia 8(11.6%) and headache 7(10.1%) were the most common ADRs. Other common ADRs reported were sedation 6(8.7%), anorexia 6(8.7%), constipation 6(8.7%), increased appetite 4(8.7%) and nausea 4(5.8%) (Table 3).

Table 3: Systemic adverse drug reactions with antidepressant drugs

System	Reaction	N = 69	%
CNS	Sleep disturbance	11	15.9
	Headache	7	10.1
	Sedation	6	8.7
	Tingling and numbness	2	2.9
	Drowsiness	2	2.9
	Forgetfulness	1	1.4
	Odd behaviour	1	1.4
	Parasomnia	1	1.4
	Vertigo	1	1.4
GIT	Dyspepsia	8	11.6
	constipation	6	8.7
	Increased appetite	6	8.7
	Anorexia	6	8.7
	Nausea	4	5.8
	Vomiting	1	1.4
Metabolic	Weight gain	1	1.4

	Weight loss	1	1.4
	Decrease libido	1	1.4
	Vitamin B12 deficiency	1	1.4
Dermatology	Itching	1	1.4
Genitourinary	Difficulty in micturition	1	1.4

Most common ADR reported with fluoxetine are insomnia 3(6.8%) and constipation 2(4.5%) while headache 2(4.5%) and dyspepsia 2(4.5%) were the most common ADR reported by paroxetine. Desvenlafaxine caused insomnia and nausea in 3(6.8%) and 2(4.5%) patients respectively while most common ADR caused by mirtazepine is headache in 2(4.5%) patients. Most common ADR reported by both escitalopram and sertraline is dyspepsia in 2(4.5%) patients. (Table 4).

Table 4: Adverse drug reactions association with antidepressant drugs

Drugs	ADR	No. of Cases	WHO causality	Naranjo
Fluoxetine	Insomnia	3	Probable	Probable
	Constipation	2	Probable	Probable
	Odd Behaviour	1	Probable	Probable
	Wt Loss	1	Probable	Probable
	Nausea	1	Probable	Probable
	Drowsiness	1	Possible	Possible
	Dyspepsia	1	Possible	Possible
	Anorexia	1	Possible	Possible
	Vitamin B12 Deficiency	1	Possible	Possible
	Sedation	1	Possible	Possible
	Tingling & Numbness	1	Possible	Possible
Paroxetine	Headache	2	Possible	Possible
	Dyspepsia	2	Possible	Possible
	Insomnia	1	Possible	Possible
	Constipation	1	Possible	Possible
	Difficulty Micturition	1	Possible	Possible
	Nausea	1	Possible	Possible
	Itching	1	Probable	Probable
	Drowsiness	1	Probable	Probable
	Sedation	1	Possible	Possible
	Tingling & Numbness	1	Possible	Possible
Desvenlafaxine	Insomnia	3	Possible	Possible
	Nausea	2	Possible	Possible
	Forgetfulness	1	Possible	Possible
	Constipation	1	Probable	Probable
	Parasomnia	1	Possible	Possible
	Vomiting	1	Possible	Possible
	Anorexia	1	Possible	Possible
Mirtazepine	Headache	2	Probable	Probable
	Sedation	1	Possible	Possible
	Anorexia	1	Possible	Possible
	Vertigo	1	Probable	Probable
Escitalopram	Dyspepsia	2	Possible	Possible
	Headache	1	Possible	Possible
	Insomnia	1	Possible	Possible
	Decrease Libido	1	Possible	Possible
Sertraline	Dyspepsia	2	Possible	Possible
	Anorexia	1	Possible	Possible
	Headache	1	Possible	Possible
	Constipation	1	Possible	Possible
	Anorexia	1	Possible	Possible
	Insomnia	1	Probable	Probable
Bupron	Headache	1	Possible	Possible
	Insomnia	1	Possible	Possible

	Sedation	1	Possible	Possible
	Wt Gain	1	Probable	Probable
Duolexetine	Anorexia	1	Possible	Possible
	Dyspepsia	1	Probable	Probable
	Sedation	1	Possible	Possible
Amitryptyline	Sedation	1	Probable	Probable

Adverse drug reactions were analyzed by applying WHO-UMC, Naranjo causality scale, modified Hartwig and Siegel severity assessment scale and Schumock and Thornton preventability scale (Table 5, 6, 7 and 8).

Table 5: WHO UMC Scale

Causality	N%
Probable	18 (26)
Possible	51 (74)
Total	69

Table 6: Naranjo Scale

Causality	N%
Probable	18 (26)
Possible	51 (74)
Total	69

Table 7: Modified Hartwig and Siegal Severity Assessment Scale

Causality	N%
Mild level 1	18 (26.1)
Mild level 2	4 (5.8)
Moderate level 3	47 (68.1)
Total	69

Table 8: Schumock and Thorton Preventability Scale

Causality	N%
Definitely preventable	47 (68.1)
Not preventable	22 (31.9)
Total	69

Most widely used causality scales are WHO-UMC scale and Naranjo scale. Adverse dug reaction due to antidepressant drugs were analyzed by using WHO-UMC and Naranjo causality scale. 44 ADRs were reported and the causality was probable in 18(26%) ADR and was possible in 51(74%). (Table 5 and 6) Severity of the adverse drug reaction was assessed by applying modified Hartwig and Siegel severity assessment scale. According to modified Hartwig and Siegel severity assessment scale, 18(26.1%) and 4(5.8%) ADRs were of mild level 1 and level 2 severity respectively whereas 47(68.1%) were of moderate severity. No severe ADR was reported.(Table 7) To assess preventability of ADR, Schumock and Thornton preventability scale was applied to all the reported forty four ADRs. According to this scale, 22(31.9%) ADRs were not preventable whereas 47(68.1%) ADRs were definitely preventable (Table 8).

Discussion

The total forty four adverse drug reactions were reported which was lower than Lucca et al (42.3%).[13] Maximum ADR were reported from the central nervous system 32(46.4%) followed by gastrointestinal system 31(44.9%). In contrast to study by Hussain et al, metabolic system was most commonly involved.[14] In the current study, sleep disturbance 11(15.9%), dyspepsia 8(11.6%) and headache 7(10.1%) were the most common ADRs reported. In other studies by Hussain et al, weight gain (17.85%), sedation (16.6%) and insomnia (14.3%) were the most common reported ADRs.[14] Most common ADR associated with fluoxetine are insomnia (6.8%) and constipation (4.5%) while headache (4.5%) and dyspepsia (4.5%) were the most common ADR caused by paroxetine. Desvenlafaxine caused insomnia and nausea in 3 and 2 patients respectively. Study done by Tejashwini et al revealed that main adverse reactions were nausea (0.83%), dry mouth (0.83%), and weight gain (0.83%) associated with amitriptyline treatment. With fluoxetine treatment, weight gain (1.67%) and nausea (1.5%) were more common while nausea (2.17%), weight gain (2.0%), gastritis (1.33%), and insomnia (0.83%) were the more common adverse effects seen with sertraline.[15]

Causality assessment is the analysis of probability of particular medications/treatment to cause an adverse event. It establishes relationship between them. It is an important component of Pharmacovigilance and helps in analysis of ADR reports, risk-benefit profile of medicines and taking regulatory actions. The causality of ADRs was found to be same with WHO-UMC scale and Naranjo scale. Overall, it was found to be probable in 18(26%) and possible in 51(74%) patients. None of the ADRs belonged to 'certain' in their causality category, as rechallenge was not attempted in any case.

This finding is in contrast to Brazilian study wherein 24 cases were categorized as 'definite' in their causality category after the positive rechallenge.[16] According to modified Hartwig and Siegel severity assessment scale, 18(26.1%) and 4(5.8%) ADRs were of mild level1 and level 2 severity respectively whereas 47(68.1%) were of moderate severity. Severe ADR was not reported. On Schumock and Thornton preventability scale, 22(31.9%) ADRs were not preventable whereas 47(68.1%) ADRs were definitely preventable.

This shows that in the current study, most of the ADRs reported were Type A category. Severity of the ADRs was rendered mild due to the judicious use of the antidepressant and concomitant drugs. ADR analysis was also done in the study by Jisha M. Lucca which reported that 61% of the ADRs were probable causality whereas 22.54% were preventable and 90.17% were mild in their severity.[13]

Conclusion

Antidepressant drugs were safe to use in psychiatric patients as most of the ADRs were of mild severity. Maximum ADRs were reported from the central nervous system (46.3%) The rate of occurrence of adverse drug reactions was highest with fluoxetine (20.3%) followed by paroxetine (17.4%) and desvenlafaxine (14.5%) utilization. The data about safety and efficacy of antidepressants is limited in psychiatric population due to paucity of clinical trials.

Limitations

- The current study was unicentric, hence the generalization of the results cannot be done, for this, multicentric studies need to be done.
- There may be recall bias in assessment of minor ADRs experienced by psychiatric patients.
- It was an observational study and follow-up of patients was done up to 28 days, therefore long-term side-effects of antidepressants in each patient was not evaluated.

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