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Original Research Article

Drug utilization study and adverse drug monitoring of antidepressant drugs in a tertiary care hospital of Bihar

Raushan Kumar Ranjan[1], Manish Kumar[1], Rajesh Kumar[2], Saajid Hameed[1], Adil Ali Shakur[1,*], Lalit Mohan[1], Harihar Dikshit[1]

[1]*Dept. of Pharmacology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India*
[2]*Dept. of Psychiatry, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India*

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ABSTRACT

Background: Depressive disorders are amongst the most prevailing causes of morbidity and disability in the Indian population. Choosing suitable antidepressants for a particular patient is an imperative decision.
Aim: To study the drug utilization of antidepressantdrugs and their adverse drug reaction in the department of psychiatry of a tertiary care hospital.
Materials and Methods : It was an observational, prospective study conducted for a duration of 18 months, i.e., from February 2018 to July 2019. The first six months were for recruitment of patients and 12 months were for follow up and data compilation. The prescriptions of every alternate patient were collected on a twice-weekly basis.
Results: In our study, 21–30 years of age group accounted for majority (31.98%) of all depressive disorders**.** Males (52.28%) were found to be more affected than females. SSRIs (73.26%) were most frequently prescribed, followed by TCA (20%) and SNRI (6.33%). The average number of drugs per prescription was 2.49. The most commonly reported ADR was insomnia (21.23%). ADRs were more commonly found with nortriptyline; a tricyclic antidepressant drug. PDD/DDD values of most of the drugs were close to one.
Conclusions: Through this study, we found that SSRIs were the most commonly prescribed group of antidepressants because of their better efficacy, safety, tolerability, and fewer side effects as compared to TCAs. PDD/DDD ratio signifies that the drugs were neither under-utilized nor over-utilized. Since no prescription had more than five drugs; we can say that polypharmacy was avoided.

1. Introduction

Depressive disorders are amongst the most prevailing causes of morbidity and disability in the Indian population. They are generally accompanied by negative thinking, sense of guilt or worthlessness, reduced interest to work, psychomotor anxiety, unhappy married life due to reduced libido, weight loss or gain because of altered eating patterns, etc.[1] They are also accompanied by other medical conditions such as chronic pain and ischemic heart disease.[2] Antidepressants are primarily used for the management of depressive disorders and many anxiety disorders. However, these are also used in the pharmacotherapy of a range of psychiatric disorders including obsessive-compulsive disorders, attention deficit hyperactivity disorder, eating disorders, personality disorder, impulse control disorders, enuresis, chronic pain, neuropathic pain, etc. irrespective of the existence of co-morbid depression in these situations.[3,4] Choosing suitable antidepressants for a particular patient depends on many factors like; patient's demographic profile, comorbidities, side-effects of the drugs, and cost-effectiveness. In the last decade, there has been a gradual shift in the prescribing patterns of antidepressants from tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAO inhibitors) to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake

* *Corresponding author*.
E-mail address: adilshakur04@gmail.com (A. A. Shakur).

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Inhibitor (SNRIs).[5] The study of prescriptions can thus help in identifying the drug utilization pattern of these antidepressants. Drug utilization studies have been defined by the World Health Organization (WHO) as marketing, distribution, prescription, and use of drugs in a society, with consideration of its medical, social and economic consequences.[6] It has been estimated by WHO that depressive disorder will become the second most leading cause of morbidity and disability by the end of the year 2020.[7] In addition to this, the proliferation of new drugs, increasing recognition of delayed adverse effects and the increased focus in pharmacovigilance has stimulated interest in the study of prescription patterns.[8] Therefore, keeping these facts into consideration, we planned was to study the drug utilization of antidepressantdrugs and their adverse drug reaction in the department of psychiatry of a tertiary care hospital.

2. 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 2018 to July 2019. The first six months were for recruitment of patients and 12 months were for follow up and data compilation. The prescriptions of every alternate patient were collected on a twice-weekly basis. The study was commenced after getting approval from Institutional Ethics Committee.

2.1. Inclusion criteria

1. Patients of depressive disorder (diagnosed as per the International Classification of Diseases – ICD 10 criteria)[9] visiting O.P.D. of the psychiatry department.
2. Patients between 12 to 60 years of age
3. Patients of either gender
4. Patients receiving antidepressant drugs

2.2. Exclusion criteria

1. Patients below 12 years and above 60 years of age.
2. Prescriptions without any antidepressant drugs.
3. Patients suffering from malignancies and terminally ill patients.
4. Patients who were judged clinically to be at a suicidal risk.
5. Patients who had a history of substance abuse.
6. Patients taking antidepressant drugs, prescribed from outside of our hospital.

In six months, approximately 2840 patients attended the OPD of psychiatry. Approximately 947 patients visited the OPD on our days of visit (twice weekly). In the recruitment phase, after interviewing every alternate patient, we gathered prescriptions of 473 patients. Of these 473 patients, 71 patients were ruled out as per the exclusion criteria. In the follow up period, 205 patients were lost to follow up. So finally, we were left up to 197 patients. In the follow up phase, patients were screened for suspected ADRs and were consequently reported to the adverse drug reaction monitoring centre (AMC), Department of Pharmacology of our Institute.

Prescriptions were analysed on the basis of:

1. Age distribution.
2. Gender distribution.
3. Age group based utilisation of antidepressant drugs.
4. The prescribed drugs were classified according to the Anatomical Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) Classification.
5. The Prescribed Daily Dose (PDD) was calculated by taking the average of the daily doses of psychotropic drugs. Then the PDD to DDD ratio was calculated.

3. Results

In our study, 21–30 years of age group accounted for the majority (31.98%) of all depressive disorders [Table 1]

Table 1: Distribution of patients on basis of age group

Age Group	Number of patients (%) (n = 197)
12-20	14 (7.11)
21-30	63 (31.98)
31-40	43 (21.82)
41-50	50 (25.38)
51-60	27 (13.70)

In gender based analysis we found that males were more affected than females. [Table 2]

Table 2: Distribution of patients on basis of gender

Gender	Number of patients (%) (n=197)
Male	103 (52.28)
Female	94 (47.72)

In our study, among antidepressants, SSRIs (73.26%) were most frequently prescribed, followed by TCA i.e. nortriptyline (20%) and SNRI i.e. venlafaxine (6.33%). [Table 3]

The most commonly reported ADR was insomnia (21.23%) followed by dizziness (12.33%) and weight gain (10.96%). ADRs were more commonly found in nortriptyline; a tricyclic antidepressant drug. [Table 4]

In our study, PDD/DDD values of most of the drugs were close to one which signifies that drugs were not under-utilized or over-utilized. [Table 5]

PDD/DDD value of sertraline, fluoxetine and nortriptyline was greater than 1. PDD/DDD values of most of the drugs were less than one and close to one.

Table 3: Age group based utilisation of antidepressant drugs

Name of Drug	Number of patients (%)	12-20 years	21-30 years	31-40 years	41-50 years	51-60 years
Fluvoxamine	37 (7.55)	3	14	10	7	3
Paroxetine	49 (10)	0	1	5	27	16
Sertraline	113 (23.06)	12	44	24	21	12
Fluoxetine	103 (21.02)	8	40	30	18	7
Nortriptyline	98 (20)	8	38	30	16	6
Venlafaxine	33 (6.73)	5	12	7	6	3
Escitalopram	57 (11.63)	3	14	8	16	16
Total	490 (100)	39	163	114	116	63

Table 4: Suspected ADRs of antidepressant drugs

ADRs	Drugs							
	Total (%)	Fluvoxamine	Paroxetine	Sertraline	Fluoxetine	Nortriptyline	Venlafaxine	Escitalopram
Weight Gain	16 (10.96)	-	3	-	-	6	-	7
Sedation	9 (6.16)	-	1	4	4	-	-	-
Dizziness	18 (12.33)	3	3	6	6	-	-	-
Insomnia	31 (21.23)	-	-	8	7	6	-	10
Headache	16 (10.96)	2	3	2	2	7	-	-
Akathisia	2 (1.37)	-	-	-	-	-	-	2
Tremor	2 (1.37)	-	-	-	-	-	2	-
Fatigability	11 (7.53)	-	-	-	-	11	-	0
Anorexia	9 (6.16)	1	2	4	2	-	-	-
Sexual Dysfunction	4 (2.74)	-	1	1	-	-	2	-
Nausea	11 (7.53)	1	-	3	2	3	1	1
Abdominal Pain	9 (6.16)	4	-	1	1	2	1	-
Constipation	6 (4.11)	-	-	-	-	3	3	-
Rash	2 (1.37)	-	-	-	-	2	-	-
Total	146	11	13	29	24	40	09	20
ADR/Drug	0.30	0.30	0.26	0.26	0.23	0.41	0.27	0.35

Table 5: ATC/DDD classification, PDD values and PDD/DDD ratio of antidepressantdrugs

Drugs	ATC Code	DDD	PDD	PDD/DDD
Fluvoxamine	N06AB08	100	85	0.85
Paroxetine	N06AB05	20	17.5	0.875
Sertraline	N06AB06	50	80	1.6
Fluoxetine	N06AB03	20	25	1.25
Nortriptyline	N06AA10	75	79	1.05
Venlafaxine	N06AX16	100	77	0.77
Escitalopram	N06AB10	10	13.5	1.35

4. Discussion

In our study, 21–30 years of age group accounted for the majority (31.98%) of all depressive disorders and is in accordance with several other studies, including by Dutta et al. who found that 68 patients (57.62%) were <30 years of age and 50 (42.37%) were >30 years [10–12] followed by 41-50 years (25.38%), followed by 31-40 years (21.82%), followed by 51-60 years (13.70%) and 12-20 years (7.11%). In a survey done by Kessler et al., median and inter-quartile range (IQR) of age of onset was very early for some anxiety disorders (7-14, IQR: 8-11) and impulse control disorders (7-15, IQR: 11-12). The age-of-onset distribution was later for mood disorders (29-43, IQR: 35-40), other anxiety disorders (24-50, IQR: 31-41), and substance use disorders (18-29, IQR: 21-26). [11] In gender based analysis we found that males were more affected than females. [13,14] In our study, among antidepressants, SSRIs (73.26%) were most frequently prescribed, followed by TCA i.e. nortriptyline (20%) and SNRI i.e. venlafaxine (11.63%). Among SSRIs present drug utilisation was most in sertraline (23.06%) followed by fluoxetine (21.02%), escitalopram (11.63%), paroxetine (10%) and, fluvoxamine (7.55%). SSRI is the

extensively prescribed antidepressants as they are generally free of sedative effects, safer at higher doses and have better tolerability with mild adverse effects.[15] In many other studies, including Tripathi et al. SSRIs accounted for majority of the prescribed antidepressants.[16–19]

A total of 490 antidepressant drugs were prescribed in 197 prescriptions. The average number of drugs per prescription was 2.49. It is somehow in conformity with the study of Lahon et al. and Piparva et al who acclaimed 2.32 and 2.96 average number of drugs per prescriptions in their study.[10,20] Polypharmacy can lead to poor compliance, drug interactions, adverse drug reactions, and medication errors.[21,22] Since no prescription had more than five drugs, we can say that polypharmacy was avoided. In our study 146 ADRs were found in 197 patients. Most commonly reported ADR was insomnia (21.23%) followed by dizziness (12.33%) and weight gain (10.96%). ADRs were more commonly found in nortriptyline; a tricyclic antidepressant drug.[23,24]

Defined Daily Dose (DDD) is the assumed average maintenance dose per day for a drug used for its indication in adults.[25] The prescribed daily dose (PDD) is the average dose, prescribed according to a representative sample of prescriptions. It is important to relate the PDD to the diagnosis on which the dosage is based. The PDD will give the average daily amount of a drug that is actually prescribed. PDD is especially important for drugs where the recommended dosage differs from one indication to another. When there is a substantial discrepancy between the PDD and DDD, it is imperative to take this into consideration when evaluating and interpreting drug utilization figures, particularly in terms of morbidity.[26] The ratio of PDD to DDD is often used as an indication of the adequacy of dosing. When this ratio is either less than or greater than one, it may indicate that there is either under or over utilization of drugs. Nevertheless, it is important to note that the PDD can vary as per patient and disease factors. In our study, PDD/DDD values of most of the drugs were close to one which signifies that drugs were not under-utilized or over-utilized.

The limitation of our study was that we did not study the appropriateness of prescribing antidepressant drugs with regard to diagnosis and comorbidities. We were not able to study certain factors, such as; patient compliance, patient care indicators, adherence to treatment guidelines, and cost, which can broaden the utility of a study. Further, in our study patients of depression with psychotic symptoms, elderly depressed patients, and patients in the child and adolescent age group were excluded. Future studies should try to overcome these limitations.

5. Conclusion

This study was a sincere attempt to see the drug utilization of antidepressants and their ADRs. We found that SSRIs were the most commonly prescribed group of antidepressants because of their better efficacy, safety, tolerability, and fewer side effects as compared to TCAs. Among SSRIs sertraline was most frequently prescribed. The average number of drugs per prescription was 2.49. Since no prescription had more than five drugs; we can say that polypharmacy was avoided. ADRs were more frequently found in nortriptyline; a tricyclic antidepressant group.

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Nil.

8. Conflicting Interest

Nil.

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Author biography

Raushan Kumar Ranjan, Senior Resident

Manish Kumar, Associate Professor

Rajesh Kumar, Professor and Head

Saajid Hameed, Junior Resident

Adil Ali Shakur, Assistant Professor

Lalit Mohan, Additional Professor

Harihar Dikshit, Professor and Head

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