

Original Research Article

A pharmacovigilance study of anti-depressant agents in psychiatric patients at a tertiary care teaching hospital

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ABSTRACT

Background: Anti-depressant drugs have great benefit in treating a many psychiatric disorders, including schizophrenia and bipolar disorder, although all these drugs are associated with many potential adverse effects. In this study, the occurrence of adverse effects like weight gain, sleep disturbances, dry mouth were assessed and reported in drug naïve patients Anti-depressant drugs.

Methods: It is a prospective observational study of patients attending Psychiatry department in NRI General Hospital of age 10 to 80 years who were prescribed with anti-depressant drugs. The study was conducted for a period of 8 months from June 2018 to February 2018.

Results: Among 86 patients prescribed with antidepressants, the occurrence of adverse drug reactions due to antidepressants was 60.78% with Selective serotonin reuptake inhibitors being the most common class of drugs implicated for adverse drug reactions followed by 24.49% with Tricyclic antidepressants. A total of 51 adverse drug reactions were noted of which weight gain was most common, closely followed by sleep disturbances and drowsiness. Out of 52 adverse drug reactions assessed for causality, 88.2% of the adverse drug reactions cases were probable, while 11.7% were possible. According to Hartwig and Siegel's Scale 84.3% of the cases are found to be mild, 15.68% moderate.

Conclusions: The study allows knowing information about the occurrence and pattern of adverse drug reactions associated with Anti-depressant drugs in the population thus reducing its incidence and protecting the user population from available harm.

Keywords: Adverse drug reactions, Anti-depressants, Causality assessment scale, Prospective, Weight gain

INTRODUCTION

Adverse drug reaction is defined as any response to the medicinal product that was potentially harmful and unintentional occurs at doses when used for diagnosis, prophylaxis and therapy of disease or for the modification of physiological function where individual factors may play an crucial role.¹ Adverse drug reactions are most

commonly occurred in a hospital setting, attributed to the severity and complexity of the disease process, the use of poly pharmacy. Moreover, abundance of new drugs is available, for which reporting of unexpected and rare adverse drug reactions depends on the alertness of the practicing physicians.² The problem of adverse drug reactions is not unique to any particular population group or age range, Poly pharmacy and alterations in drug

clearance place them at an increased risk for adverse effects associated with therapy.³ Adverse drug reactions surveillance and documentation, reporting of adverse drug reactions, mechanism for the safety monitoring of drug use in high-risk patient populations, and educating the health professionals regarding potential adverse drug reactions can be encouraged by monitoring of adverse drug reactions and reporting programs.⁴

Depression is a major heterogeneous disorder that affects a person's mood, physical health and behaviour. Depression is a mental health disorder that was declared by the World Health Organization as the 4th leading cause of disability and premature death in the world in 2001.⁵ Antidepressant drugs, though having a great benefit in range of psychiatric disorders is also associated with comprehensive of potential adverse effects. Adverse drug reactions are the important factors for non-adherence to anti-depressant treatment, but due to lack of self-report measures and overlap with depressive symptoms the assessment is complicated.⁶

In early 1990s new classes of antidepressants, Selective Serotonin Reuptake Inhibitors, serotonin-norepinephrine reuptake Inhibitors and second generation antipsychotics were introduced and are widely prescribed. Therefore, prevention of side effects should be the vital part of treatment, as the severity and frequency of the side effects may play a role in the effectiveness and tolerability of a particular drug.⁷

However, adverse drug reaction can perhaps be reduced by using less medication and with adequate knowledge of drug interactions and by collecting reliable information about their frequencies and possible risk factors. Monitoring of adverse drug reactions helps in detecting adverse drug reactions and alerting physicians about the and occurrences of such events, thereby protecting patients from avoidable harm.⁸

METHODS

The study was a hospital based prospective observational study conducted for a period of 8 months in both outpatients and in-patient who were prescribed with antidepressant medications in the department of Psychiatry at a tertiary care hospital, Guntur, A.P, India. The ethical approval was obtained from institutional ethical committee of the hospital and informed consent from the attendants of the patients who are willing to participate in the study. Based on inclusion and exclusion criteria patients were recruited into study and patient data collection form was used to collect the adverse drug reactions during the ward rounds and at the out-patient visit. This form include all information regarding the patient's admission status and other details like patient's age, sex, information regarding reaction, date of onset of reaction and the list of suspected drug/drugs. The past medical and medication history data collected includes the patient's previous allergies, co-morbidities and the

drugs received previously. To assess the causality, Naranjo adverse drug reaction probability scale, Hartwig's Severity Assessment Scale was used. Data collected was analysed using Microsoft Excel for Univariate analysis and Chi square test for proportions.

RESULTS

Total of 86 study subjects attending department of psychiatry as in-patient and out-patients of were recruited and are followed during the study follow up period. After completion of follow up study subjects were evaluated for the incidence of adverse drug reactions.

Out of 86 study subjects willing to participate the study 52 (60.46%) were male and 34 (39.53%) were female (Table 1). In our study 27.9% study subjects are in 21-30 years age group followed by 26.9% in 31-40 years age group. This specifies that the patients who have psychiatric illness were more in age group between 20-40 years as compared with other age groups (Table 2).

Table 1: Gender wise distribution of patients.

Gender	Number of patients (n=86)	Percentage (%)
Male	52	60.46
Female	34	39.53

Table 2: Age wise distribution of patients.

Age groups (yrs)	Number of patients (n=86)	Percentage (%)
10-20	7	8.13
21-30	24	27.90
31-40	23	26.74
41-50	15	17.44
51-60	13	15.11
61-70	2	2.32
71-80	2	2.32

Table 3: Utilization pattern of different groups of antidepressant drugs.

Group of drug	Frequency of drug (n=99)	Percentage (%)
SSRI's	49	49.49
SNRI's	6	6.06
TCA's	6	6.06
Atypical anti-depressants	18	18.18
SSRI and Anti-convulsants	18	18.18
SNRI and atypical anti psychotics	2	2.02

Selective serotonin re-uptake inhibitors followed by Serotonin and nor-epinephrine re-uptake inhibitors,

Tricyclic anti-depressants, Atypical antipsychotics, Selective Serotonin Reuptake Inhibitors and Anti-convulsants and Selective Serotonin- norepinephrine Reuptake Inhibitors and Atypical Anti-psychotics combinations were the most common class of drugs prescribed to the inpatients (Table 3).

Fluoxetine was prescribed in higher proportion with 17.82%, followed by 16.83% were prescribed with Mirtazapine, 14.85% were prescribed with combination of Escitalopram+ Clonazepam, 12.87% were prescribed with Paroxetine, 8.91% were prescribed with Sertraline, 5.94% were prescribed with Escitalopram, 3.96% were prescribed with Desvenlafaxine and Imipramine each, 2.97% were prescribed with Fluvoxamine, 1.98% were prescribed with Duloxetine, Desvenlafaxine and Clonazepam, Paroxetine and Clonazepam each, 0.99% were prescribed with Opipramol, Fluoxetine+ and Olanzapine (Table 4).

Table 4: Prescribing pattern of individual and combination antidepressant drugs.

Drug	Frequency (n=101)	Percentage (%)
Sertraline	9	8.91
Escitalopram	6	5.94
Fluoxetine	18	17.82
Fluvoxamine	3	2.97
Paroxetine	13	12.87
Duloxetine	2	1.98
Desvenlafaxine	4	3.96
Imipramine	4	3.96
Clomipramine	3	2.97
Opipramol	1	0.99
Mirtazapine	17	16.83
Tianeptine	1	0.99
Escitalopram and Clonazepam	15	14.85
Desvenlafaxine and Clonazepam	2	1.98
Paroxetine and Clonazepam	2	1.98
Fluoxetine and Olanzapine	1	0.99

Adverse drug reactions were encountered in the patients as listed in (Table 5). Weight gain (23.52%) was the commonest followed by drowsiness and sleep disturbances (13.7%) each, constipation(11.7%), dry mouth(9.8%), sweating(7.84%), loose stools, generalized weakness, loss of appetite (3.92%) each. 1.96% with facial edema, numbness of body, palpitations and vision changes.

Adverse drug reactions were observed in patients prescribed with specific class of drugs (Table 6). In patients prescribed with Selective Serotonin re-uptake Inhibitors a total of 30 adverse drug reactions were

reported. Among them drowsiness (23.3%) and sleep disturbances (23.3%) were in higher proportion followed by sweating (13.3%), weight gain (10%), constipation (10%), dry mouth (6.6%), loose stools (6.6%), palpitations (3.3%) and generalized weakness (3.3%). Among Tricyclic anti-depressants a total of 12 adverse drug reactions were reported and majorly dry mouth (25% and constipation (25%) were observed followed by weight gain(16.6%), numbness of body(8.3%), generalized weakness (8.3%), loss of appetite (8.3%) and vision changes (8.3%). Patients who are prescribed with other classes of drugs reported weight gain (77.7%) as major adverse drug reaction and followed by facial edema (11.1%), loss of appetite (11.1%).

Table 5: Frequency of various ADR's observed among 86 patients.

Adverse drug reaction	Frequency (n=51)	Percentage (%)
Weight gain	12	23.52
Drowsiness	7	13.7
Sleep disturbances	7	13.7
Constipation	6	11.7
Sweating	4	7.84
Dry mouth	5	9.8
Loose stools	2	3.92
Facial edema	1	1.96
Numbness of body	1	1.96
Palpitations	1	1.96
Generalized weakness	2	3.92
Loss of appetite	2	3.92
Vision changes	1	1.96

Table 6: ADR's observed for specific class of drugs.

ADR's	SSRI's	TCA's	Others	Total
Weight gain	3	2	7	12
Drowsiness	7	-	-	7
Sleep disturbances	7	-	-	7
Constipation	3	3	-	6
Sweating	4	-	-	4
Dry mouth	2	3	-	5
Loose stools	2	-	-	2
Facial edema	-	-	1	1
Numbness of body	-	1	-	1
Palpitations	1	-	-	1
Generalized weakness	1	1	-	2
Loss of appetite	-	1	1	2
Vision changes	-	1	-	1

Based on Causality assessment according to Naranjo's scale 45 were judged as probable and 6 were possible and no patient was found to be certain (Table 7).

The Severity of the adverse drug reactions were assessed and 4 (87.32%) were found to be mild, while 8 (15.68%) moderate (Table 8).

Table 7: Severity assessment using Hartwig and Siegel's scale.

Severity	No of ADR's(n=51)	Percentage (%)
Mild	43	84.3
Moderate	8	15.68
Severe	0	0

Table 8: Causality assessment using Naranjo's Algorithm.

Causal association	Frequency (n=51)	Percentage (%)
Probable	45	88.2
Possible	6	11.7

DISCUSSION

Spontaneous reporting is the best and most common method used in pharmacovigilance to generate signals on new and rare ADRs. Lack of awareness in patients as well as health care professionals is the major drawback of this system causing under reporting. In the present study the gender distribution of patient was male 52 (60.46%) and female 34 (39.53%). This is similar study was conducted by Kiran G Piparva¹⁰ males were in higher proportion with 70.27% while females are with 22.72%.

The mean age of the male subjects who reported adverse drug events was 35.2 years while that of females was 32.4 years and it is similar to the study conducted by Sha Mukherjee et al.⁹ Selective Serotonin Reuptake Inhibitors were most commonly prescribed anti-depressant medication. This was followed by atypical anti-antipsychotics and Selective Serotonin Reuptake Inhibitors + Anticonvulsants, serotonin-norepinephrine reuptake Inhibitors, Tricyclic antidepressants and serotonin-norepinephrine reuptake Inhibitors + Atypical Antipsychotics. This was similar to the study conducted by Swathi Mishra et al in which Selective Serotonin Reuptake Inhibitors are mostly prescribed.¹¹

Among the study subjects, Fluoxetine, Mirtazapine, combination of Escitalopram and Clonazepam, Paroxetine was prescribed in higher proportion and other drugs like Escitalopram, Desvenlafaxine, Imipramine Fluvoxamine, Duloxetine, Opipramol, Clomipramine, Tianeptin, Desvenlafaxine and Clonazepam and Fluoxetine and Olanzapine were less frequently prescribed.

Among the adverse drug reactions in our study weight gain was observed in majority of the subjects prescribed with Selective Serotonin Re-uptake Inhibitors which is due to loss of control on appetite by serotonin which was

similar to the study conducted by Kingshuk Lahon et al in which 70% of the reported adverse drug reactions were weight gain.¹²

Tricyclic antidepressants causing dry mouth and constipation, numbness of body, generalised weakness loss of appetite and vision changes which was similar to the study conducted by Kingshuk Lahon et al.¹² Regarding causality assessment our study had no 'certain'. 45 adverse drug reactions reported were found to be 'probable', and 6 were 'possible' according to Naranjo scale. This was similar to study conducted Sha Mukherjee et al, 9 out of 130 adverse drug reactions evaluated for causality using Naranjo scale- for 116 of those adverse drug reactions, the causality was probable, remaining 14 it was possible.

Regarding severity of the adverse drug reactions 43 were mild, while 8 were moderate. Since none of the adverse drug reactions was found to be severe so ICU admission is not required in our study subjects. Our results are in agreement with the study carried by Sha Mukherjee et al, majority of adverse drug reactions were mild (83.99%), followed by moderate (14.97%) and none of the adverse drug reactions are severe.⁹

CONCLUSION

This prospective study provides a data representing the adverse drug reaction profile of the antidepressants likely to be occurred in psychiatric patients. Among 86 patients prescribed with antidepressants, a total of 51 adverse drug reactions were reported within 34 patients. The incidence of adverse drug reactions due to antidepressants was 60.78% with Selective Serotonin Reuptake Inhibitors being the most common class of drugs implicated for adverse drug reactions followed by 24.49% with tricyclic antidepressants. Constant vigilance in early detection and reporting of adverse drug reactions and subsequent management can make the therapy with antidepressants safe and effective. Educating the health care professionals as well as patients regarding the adverse events caused by the antidepressants helps in reducing the incidence.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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