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A Prospective Observational Study of Prescription Pattern of Anti-Depressants in Psychiatric Department of a Tertiary Care Teaching Hospital

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Abstract

Background: Antidepressant drugs have had a remarkable impact in psychiatric clinical practices. Its prescription patterns have changed globally over the past few years. So, their utilization in actual clinical practice needs continuous study.

Materials & Methods: A prospective observational cross sectional drug utilization study which assesses the prescription pattern of antidepressant drugs was carried out for 1 year and 600 prescriptions were utilized. Patients aging between 18 to 60 years of both sexes attending psychiatric outpatient department were included in the study. Using world health organization's core drug prescribing indicators, the prescribing patterns were analyzed.

Results: Majority of patients received, Escitalopram and Fluoxetine from the Selective serotonin reuptake inhibitors class (SSRIs) and Amitriptyline from the Tricyclic antidepressants class (TCAs). Average number of drugs per prescription was 2.14. Percentage of drugs prescribed by generic name was 92.46%. Percentage of prescriptions for prescribing antidepressant by injectable route and FDCs were NIL. Percentage of drugs prescribed from National essential medicine list 36.80%. Percentage of drugs prescribed from WHO essential medicine list was 26.63%.

Conclusion: The newer groups of drugs, namely the SSRIs and the SNRIs seem to have replaced the older group, namely the TCAs. This seems to be in accordance with other research findings especially considering the fewer side effects of the newer group of drugs and the prolonged therapy which was needed to combat depression effectively.

Keywords: Drug utilization, Antidepressant drugs, prescribed daily dose, prescribing pattern, depression.

Introduction

The continuously expanding field of psycho pharmacology is challenging old traditional concepts of psychiatric treatment and is constantly seeking new and improved drugs to treat psychiatric disorders. By this way, psychiatric practitioners are continuously exposed to newly introduced drugs that are claimed to be safe and more efficacious.[1]

Drug utilization research is defined by WHO as "the marketing, distribution, prescription and use of drug in a society, with special emphasis on the resulting medical, social and economic consequences".

The principle aim of the drug utilization study is to facilitate rational use of drugs in population. For the individual patient, rational use of any drug implies the prescription of a well-documented drug in an optimal dose for a right indication, with the correct information.[2]

WHO defines "Depression is a common mental disorder, characterized by sadness, loss of interest or pleasure, feeling of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration" [3]. The accompanying signs include psychomotor retardation or at times withdrawal from interpersonal contact and vegetative symptoms such as anorexia and insomnia. [4]

Antidepressant prescribing patterns have changed globally over the last few years, with conventional drugs like tricyclic antidepressants (TCAs), selective serotonin reuptake inhibiters (SSRIs) and novel antidepressants. The recent proliferation of new drugs, the increasing recognition of delayed adverse effects and focus on pharmacoeconomical considerations have stimulated interest in the prescribing patterns of psychiatrists.

Material & methods

An observational cross sectional drug utilization study was carried out in Out Patient Unit of Psychiatry Department of a tertiary care teaching hospital. Total 600 cases were collected. The study was carried out for one year duration from January 2015 to December 2015.The study was started after approval from Institutional Ethics Committee (IEC). Patients from the age groups of 18 to 60 years and both the sexes, who were taking anti-depressant therapy & attending psychiatric outpatient department, were included in the study. Those patients of major depression who were receiving electroconvulsive therapy (ECT) were excluded from this study. Written informed consent was taken before enrolling all patients for the study. The patient's demographic data, clinical data and therapeutic data were collected from Patient's case notes, treatment charts, laboratory data reports and interviewing patients. Case record form included details like OPD registration number, date of attending OPD, patient initials, age, sex, diagnosis according to DSM-5 criteria, education, marital status, occupation, details of antidepressants and other drugs used to include its dose, route of administration, frequency, and duration & adverse drug reactions if any noted.

Statistical analysis

Recorded data were analyzed by Microsoft Office Excel 2013 and using descriptive statistics. Wherever necessary, the results were depicted in the form of percentages and graphs.

Result & Observations

In our study, out of 600 patients, 223 patients fall into age group of 41-50 years (37.16%), 151 patients into age group of 31-40 years (25.16%), 106 patients into age group of 51-60 years (17.66%), 99 patients into age

group of 21-30 years (16.5%) and only 21 patients into age group of 11-20 (3.5%). The mean ± SD of age of all patients was 40.93±10.72.

Out of total 600 prescriptions noted 313 patients were Female (52.16%), and 287 patients were Male (47.83%).

As shown in table-1 out of 600 patients attended OPD, 375 patients were diagnosed as Major Depressive Disorder (62.5%) followed by 63 patients having Generalized Anxiety Disorder (10.5%) and so on according to DSM-5 criteria.

*MDD= Major depressive disorder

*OCD= obsessive compulsive disorder

*DSM-= Diagnostic and Statistical Manual of Mental Disorder.

Table 1: Primary diagnosis acc. to DSM 5 criteria in patients receiving antidepressants

Diagnosis	No. of patients (%) (n=600)
Major Depressive Disorder	375 (62.5)
Generalized Anxiety Disorder	63 (10.5)
Unspecified Anxiety Disorder	16 (2.66)
Schizophrenia	16 (2.66)
Obsessive Compulsive Disorder	15 (2.5)
Epilepsy + secondary depression	27 (4.5)
Major Depressive Disorder+ Anxiety	21 (3.5)
Major Depressive Disorder+ Panic attacks	17 (2.83)
Bipolar mood disorder	7 (1.16)
Other	43 (7.1)

Table-2 shows prescribing indicators. Total number of drugs prescribed in 600prescription was 1288. Average number of drugs per prescription was 2.14. Percentage of drugs prescribed by generic name was 92.46% while no single prescription containing injectable antidepressant or FDC of was there. 36.80% drugs were prescribed from National essential medicine list while 26.63% drugs were prescribed from WHO essential medicine list.

Table 2: Prescribing Indicators

Average no. of drugs per prescription	2.14 (1288/600)
Percentage of drugs prescribed by generic name	92.46%
Percentage of prescriptions for prescribing antidepressant by injectable route	NIL
Percentage of FDCs* of antidepressants	NIL
Percentage of drugs prescribed from National essential medicine list	36.80%
Percentage of drugs prescribed from WHO essential medicine list	26.63%
*FDCs= Fixed Dose Combinations	

As shown in table-3, From Selective serotonin reuptake inhibitors group Escitalopram 428(71.33%), Fluoxetine 121 (2.16%), Sertraline 6 (1%) were prescribed. From Tricyclic antidepressants group Amitriptyline 119 (19.83%), Imipramine 9 (1.5%) was prescribed. From Atypical antidepressants Mirtazapine 12 (2%) and Bupropion 2(0.33%) were prescribed. From Serotonin and noradrenalin reuptake inhibitors Duloxetine 3 (0.5%) and Venlafaxine 1 (0.16%) were prescribed.

Table 3: Drug distribution in different class

Drug class	Drug	No. of Prescription (%) [n=600]
Selective serotonin reuptake	Escitalopram	428 (71.33)
	Fluoxetine	121 (20.16)
	Sertraline	6 (1)

inhibitors (SSRIs)		
Tricyclic antidepressants (TCAs)	Amitriptyline	119 (19.83)
	Imipramine	9 (1.5)
Atypical antidepressants	Mirtazapine	12 (2)
	Bupropion	2 (0.33)
Serotonin and noradrenaline reuptake Inhibitors (SNRIs)	Duloxetine	3 (0.5)
	Venlafaxine	1 (0.16)

Table 4: shows Antidepressants with their ATC code and WHO DDD measures with calculated DID* values.

Drug	No. of prescription	ATC* CODE	WHO DDD* MEASURE	DDD/1000PTs/DAY
Escitalopram	428	N06AB10	10mg	0.000381
Fluoxetine	121	N06AB03	20mg	0.000102
Sertraline	6	N06AB06	50mg	0.0000055
Amitriptyline	119	N06AA09	75mg	0.0000404
Imipramine	9	N06AA02	100mg	0.0000059
Mirtazapine	12	N06AX11	30mg	0.0000062

*ATC= Anatomical therapeutic classification

*DDD= Defined Daily Dose

*DID= Defined Daily Dose (DDD) per thousand inhabitants per day (DID)

Table 5: shows Antidepressants with their PDD and calculated values of PDD/DDD.

Drug	WHO DDD Measure	PDD *	PDD/ DDD
Escitalopram	10mg	10mg	1
Fluoxetine	20 mg	20 mg	1
Sertraline	50 mg	50 mg	1
Amitriptyline	75 mg	25 mg	0.33
Imipramine	100 mg	50 mg	0.5
Mirtazapine	30 mg	15 mg	0.5

*PDD= Prescribed Daily Dose

Table 6 shows adverse drug reaction reported due to antidepressants. One patient complained erectile dysfunction, dryness of mouth and constipation due to amitriptyline and other patient reported of sexual dysfunction due to escitalopram.

Table 6: adverse drug reactions due to antidepressants

Drug	Adverse drug reaction
Amitriptyline	Erectile dysfunction, dryness of mouth, Constipation
Escitalopram	Sexual Dysfunction

Discussion

Although pharmacological intervention is the primary treatment modality for relieving depression, the efficacy and suitability of other therapeutic options should not also be overlooked. Other therapeutic options include:

1] Psychotherapy,

2] Somatic intervention and

3] Lifestyle adjustment.

Pharmacological intervention includes the use of TCAs, SSRIs, SNRIs and MAOIs (Monoamine oxidase inhibitors). All drugs share at some level the primary effect on the Serotonergic or the noradrenergic neurotransmitter system.[5]

Antidepressant drug therapy is divided into three phases: acute phase, continuation phase and maintenance phase. The acute phase starts from the initiation of therapy until remission (usually up to 6–12 weeks).The continuation phase is from remission to 6 to 9 months after the remission. The drugs of the acute phase are continued to prevent the relapse of depression. The maintenance phase is used in high-risk patients like those with multiple episodes of depression, those with a history of suicidal thoughts, etc. They may receive maintenance treatment for 2-3 years or for lifelong. [6]

TCAs, by inhibiting histamine receptors causes' sedation. By blocking muscarinic receptors, they cause blurred vision, dry mouth, constipation, tachycardia and difficulty in urination. Blockage of the alpha-1 receptors leads to orthostatic hypotension and sedation. They affect cardiac conduction and this limits their use in the CAD patients. SSRIs do not cause cardiovascular, histamine blocking or alpha-1 receptor side effects. But insomnia, anxiety, irritability and decreased libido result from the excess stimulation of the 5HT receptors. The stimulation of the 5HT receptors in the CNS and the periphery contributes to the GI side effects like nausea, diarrhea, emesis, etc. SNRIs have a similar side effect profile as the SSRIs (nausea, constipation, headache and sexual dysfunction). Immediate release Venlafaxine can cause sustained diastolic hypertension.[7]

In this study, the age group which was commonly affected was the middle age. Also, there has been a dramatic change in the prescription patterns since the advent of the newer group of drugs, namely the SSRIs, which are being prescribed more as also shown by some other studies [8].

In this study the (Male: Female) ratio was 1:1.1 correlating with the fact that prevalence of major depression is higher in females compared to males which is in accordance with finding stated in community based epidemiological study, according to National Institute of Mental Health (2007). [9]

Major depressive disorder was the most common diagnosis in this study (62.5%) associated with use of antidepressants. This finding correlates with drug utilization study in the UK where depression was the most common diagnosis associated with selective serotonin reuptake inhibitors (SSRI) use in all age groups. [10]

Prior to the introduction of first SSRI in 1987, pharmacological treatment of depression was limited primarily to tricyclic antidepressants (TCAs) and non-selective mono-amine oxidase inhibitors (MAOIs). But now SSRIs have gained popularity recently for treatment of depression compared to TCAs. So in our study, SSRIs were the most commonly prescribed group with escitalopram and fluoxetine being the most frequently used agents from the group with similar results found by many other studies. [11]

Although SSRIs are generally associated with higher drug acquisition costs than are TCAs, the total healthcare costs are at least offset if not decreased, by reductions in the costs which are associated with the use of SSRIs. Escitalopram has a high affinity for the serotonin transporters. Also, in a study which compared citalopram with escitalopram, the latter was found to have a superior effect in major depressive disorders [12].

Long term studies favor use of SSRIs over TCAs and the results indicate that the effect of SSRIs is mainly due to the prevention of relapse [13]. The popularity of SSRIs is mainly due to ease in their use, their safety in overdose, their relative tolerability, and the broad spectrum of their uses.

Rational prescribing was followed as per the principles of prescription order writing.[14] Considering the definitions of polypharmacy which are most commonly cited, there was no polypharmacy, because there was no prescription of antidepressant medication which did not match the diagnosis and there was no prescription with more than 5 drugs with average number of drugs per prescription being 2.14. [15] Other prescribing indicators like percentage of drugs prescribed with generic name was 92.46% while Percentage of drugs prescribed from National essential medicine list was 36.80% and 26.63% of drugs prescribed from WHO essential medicine list in our study.

A comprehensive application of drug utilization tools like the ATC/DDD classification and the calculation of the DID and the PDD/DDD ratios to assess the prevalence of antidepressant use in the community of the study population is the strength of this study.

Adverse events such as mania, hostile behavior and suicide have been reported in teenagers who had been treated with SSRIs. Suicidal tendencies however, have shown variation with respect to one SSRI to the other and fluoxetine has been shown to cause less suicidal tendencies [16]. A similar study in Sweden has shown a decrease in suicides as the effect of a primary care educational programme [17]. In our study adverse drug reactions like erectile dysfunction, dryness of mouth, constipation due to amitriptyline and sexual dysfunction due to escitalopram was reported.

Limitations and future perspectives

However, our study was undertaken at a tertiary care teaching hospital where most of the patients seeking treatment are from poor socioeconomic class. So, they are prescribed medications available a hospital pharmacy which they can avail free of cost. Hence prescribing depends on the drugs available at hospital pharmacy. A larger multi-centric trial would be more representative of the prescribing trends on a national and international level. Since SSRIs and SNRIs are relatively newer drugs, they may have some long-term side effects at a later date. As with any drug utilization study, it was not possible to monitor the actual use or compliance with the prescribed antidepressant.

The prescribing habits among psychiatrists should follow a standard treatment national or international guideline. They can be improved further by creating awareness about the choice of drugs from the Essential Medicines List and by reducing the prescription of sedative hypnotics. Such measures can decrease the number of drugs per prescription and also the cost of therapy. The prescribers should also be encouraged to check for the patients' compliance with the prescribed medications and to record them in the case sheets. Such measures will promote the rational use of medicines and ultimately, the quality of healthcare.

Summary & conclusion

Most of the patients receiving antidepressants were from the age of 30 -50 years with female predominance. Most of the patients taking antidepressants were primarily diagnosed as having Major Depressive Disorder followed by Generalized Anxiety Disorder and other diagnosis according to DSM-5Criteria.Majority of patients received, Escitalopram and Fluoxetine from the Selective serotonin reuptake inhibitors class (SSRIs) and Amitriptyline from the Tricyclic antidepressants class (TCAs). Among the concomitant drugs prescribed, most of the patients received anti-anxiety drugs and Antipsychotic drugs. Average number of drugs per prescription was 2.14. Percentage of drugs prescribed by generic name was 92. 46%. Percentage of prescriptions

for prescribing antidepressant by injectable route and FDCs were NIL. Percentage of drugs prescribed from National essential medicine list 36.80%. Percentage of drugs prescribed from WHO essential medicine list was 26. 63%. Amitriptyline produced adverse events of erectile dysfunction, dryness of mouth and constipation while one adverse event of sexual dysfunction due to escitalopram was reported.

In this study on Antidepressant drugs, most of the subjects were females. Most of the patients were in the age group of 30–50 yrs. By and large, the newer groups of drugs, namely the SSRIs and the SNRIs seem to have replaced the older group, namely the TCAs. This seems to be in accordance with other research findings especially considering the fewer side effects of the newer group of drugs and the prolonged therapy which was needed to combat depression effectively.

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