Original Article

A Drug Utilization Study of Antidepressants in the Psychiatry Unit of a Tertiary Care Hospital

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This study aims at analyzing the drug utilization pattern of the different classes and individual antidepressant drugs used in the therapy of Major Depressive Disorder. Major Depressive Disorder (MDD) is an extremely common psychiatric condition. Antidepressant class of drugs are commonly used to treat this condition. In my study, analysis of prescription patterns of antidepressants was carried out for patients suffering from MDD.The prescribing patterns of antidepressants have changed globally over the last few years and therefore we wanted to observe the prescribing pattern of antidepressant drugs in our hospital.The drug utilization study was an observational cross-sectional study carried out in the Department of Pharmacology and Psychiatry, Hi-tech Medical College & Hospital, Bhubaneswar, India from 1st November 2015 to 30th October 2017 with a sample size of 262 patients suffering from Major Depressive Disorder and being treated with antidepressant class of drugs. Socio-demographic details of the patients, clinical features of each case were analysed in the study. Several quality indicators of drug use and standard parameters were observed. In my study it was seen that antidepressants were prescribed more in women (67.2%) as they comprised a majority of the patients.The mainstay of this study was to analyse the current prescription pattern of antidepressants at our hospital. A total of 492 antidepressant drugs were prescribed to the 262 patients enrolled in this study. It was seen that the average number of antidepressants per prescription was 1.87. It was seen that in this study 14.63% of the antidepressant drugs prescribed were from the Essential Medicines List (EML). This study revealed that that 77.24% of the antidepressants used were prescribed in their generic name. In this study it was seen that the SSRI class of antidepressant drugs was used most times comprising 45.7% of the total drugs used. This was followed by use of TCA class of drugs and SNRI class of drugs accounting for 23.8% and 17.9% of the total drugs used respectively. Escitalopram (SSRI) was used most times (36.99%) followed by Amitriptyline (TCA) (14.63%) and Mirtazapine (Atypical) (11.59%). The patients at the time of presentation were graded by HDRS score according to severity of illness. Choice of antidepressant drug prescribed and from which group is based on individual patient aspects, clinician's judgement and previous response to treatment. The newer drug classes such as SSRI, SNRI and Atypical class of drugs are more preferred now because other things being equal these are usually better tolerated and less dangerous in overdose. However, it must be kept in mind that even now TCA class of drugs is an effective and proven alternative and may be preferred in some cases of MDD.

Depressive disorders have plagued mankind since the earliest documentation of human experience. The earliest references, from ancient Greek descriptions of depression, refer to the Syndrome of Melancholia[1].

The World Health Organisation (WHO) defines drug utilization as the marketing, distribution, prescription and the use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences[19].

The prevalence of antidepressant usage in the community is rising in Western populations, with Iceland, Australia and Sweden having the highest consumption[9]. This trend has been replicated and documented in developing nations too like our own.

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> **Editor's Comment :**
> - Major Depressive Disorder (MDD) is an extremely common Phychiatric condition.
> - Most common anti depression are prescribed in generic name.
> - Escitalogram is one of the most preferred drug among the SSRIs.

Depressive disorders afflict one out of five women and one out of ten men at some point in their lives[2]. The depressive disorders are characterized by a lifelong vulnerability to episodes of the disease.

It was estimated that by the year 2020 if current trends for demographic and epidemiological transition continue, the burden of depression will increase to 5.7% of total burden of disease[3].

Depression is the most common type of mental illness. An estimated 7-10% of India's population

suffers from depressive illness[4].

This study will focus on the pharmacotherapy of unipolar major depression.

Depression is a clinical syndrome characterized by persistent sad mood, profound despair which persists 2 weeks or more and is associated with a change in previous functioning[1].

Many different antidepressants have established track records of efficacy for treating major depression. However, they all suffer some limitations in efficacy, since at least 20% of all depressed patients are refractory to multiple different antidepressants at adequate doses[7]. Therefore, a clinician's experience, insight and particular features of the case may have an effect on the drug(s) prescribed.

All drugs commonly used to treat depression share at some level, primary effects on serotonergic or noradrenergic neurotransmitter systems[8]. In general antidepressants enhance serotonergic and noradrenergic transmission, although the nature of this effect may change with chronic treatment.

The optimistic expectations of a drug, based on the results of clinical trials, may not materialize when they are used outside controlled settings[5].

Long term effects of antidepressant drugs evoke adaptive or regulatory mechanisms that enhance effectiveness of therapy[9].

Depression often requires long term therapy as well as multi drug treatment in many cases. This becomes important because antidepressant use is often associated with a wide spectrum of adverse effects.

The recent proliferation of new drugs, the increasing recognition of delayed adverse effects and the focus on pharmacoeconomic considerations have stimulated interest in the antidepressant prescribing patterns of physicians[6].

Rational drug prescribing is the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost[18]. Goal of treatment should revolve around achieving a sustained and consolidated improvement in the mood of the patient, guarding against relapse and with minimal possible adverse effects.

This paper is a qualitative and quantitative critical analysis of the treatment of depression and the use of anti-depressants in Hi-Tech Medical College and Hospital, Odisha over the stipulated time frame.

MATERIALS AND METHODS

Study Design :

The drug utilization study was an observational cross- sectional study.

Sampling Technique :

The sampling technique was 'purposive' in nature.

Inclusion criterion :

All consenting patients with clinical diagnosis of Major Depressive Disorder (MDD) attending Psychiatry OPD of Hi-Tech Medical College and Hospital, Bhubaneswar, Odisha during the stipulated time frame.

Exclusion criterion :

Co-morbid diagnosis (eg, Schizophrenia, substance abuse), Bipolar disorder, Post-Partum psychosis, Clinical conditions with depressive symptoms (eg, Hypothyroidism, Parkinsonism)

Parameters studied :

1. Name of Drugs prescribed
2. Class of Drugs prescribed
3. Monotherapy or Combination therapy of different drug classes
4. Grading of patients according to severity of illness (i.e. depression; HDRS)
5. Average number of drugs per prescription
6. Percentage of drugs in generic name
7. Percentage of drugs from essential medicine list

Instruments :

Age, Sex, Marital status, Rural/Urban, Caste, Family Type, Socio Economic status

Study Technique :

Descriptive statistics was used to calculate mean and percentages.

Chi-square test was used to compare categorical variables and t-test (ANOVA) was used to compare continuous variables.

Features of this study :

Patient data for this study was collected in a pre-designed proforma. The first part of which was for collecting socio-demographic details of the patient. The next part dealt with recording details about the name of drugs prescribed, duration of therapy, number of drugs in generic name, number of drugs from essential medicine list and total number of anti-depressants drugs used for each patient. The Hamilton Depression Rating Scale (HDRS) (reference) was used to grade the severity of depression. The difference in HDRS score for each patient before and after therapy gave us an idea of the clinical efficacy of the different therapy options used and a measure of improvement they provided for each patient.

The data collected in the above format was then analysed using both qualitative and quantitative statistical techniques. The results and analysis have been discussed.

Ethical clearance :

The study was approved by the Institutional Ethics committee of Hi-Tech Medical College, Bhubaneswar

(Utkal University)

Study duration :

The data was collected for a period of 2 years from 1st November 2015 to 30th October 2017.

Study location :

The drug utilization study was carried out in the Department of Pharmacology and Psychiatry, Hi-Tech Medical College and Hospital, Bhubaneswar, India.

Sample size :

The sample size was of 262 patients suffering from Major Depressive Disorder (MDD) and being treated with anti-depressant class of drugs.

RESULTS

Data was collected for 262 patients as per the protocol of the study and was analysed through IBM SPSS 24.0 software. The analysis along with interpretations is presented in three sections.

Section 1 deals with the demographic and socio-economic profile of the patients, Section 2 analyses the prescription patterns of anti-depressants prescribed in the OPD of Psychiatry department, Section 3 deals with the clinical effectiveness of different therapy options

Demographic and Socio-economic profile
Age and Gender distribution

Figs 1&2 present age and gender distribution of patients suffering from MDD. It was found that maximum patients were in the age group 35-49 years (39.3%). The age group 19-34 years and 50-64 years shared nearly a quarter of the cases. The distribution was significantly concentrated in the age group 35-49 years (p=0.000). The mean age was 44.22± 12.54 years.

It was found that females constituted a majority of the cases with a share of little above 2/3rd of the total cases (p=0.000).

Distribution by place of residence :

The major chunk of the cases was from urban areas with a share of 76% (Fig 3).

Education :

Graduate and above qualified individuals comprised 44.3% cases while matric pass was 38.2%, under matric and illiterate together constituted 17.6% cases. The proportion of cases was found significantly higher in graduate and above category (p=0.000).

Marital Status and Family Type (Figs 4&5) :
Prescription pattern of anti-depressants :
Drugs used in generic name and from EML :

Figs 6&7 present distribution of anti-depressants used in generic name and from essential medicine list (EML). 262 patients were prescribed 492 drugs. Of these 492 drugs 380 (77.24%) were prescribed in their generic name. The remaining 112 drugs (22.76%) were
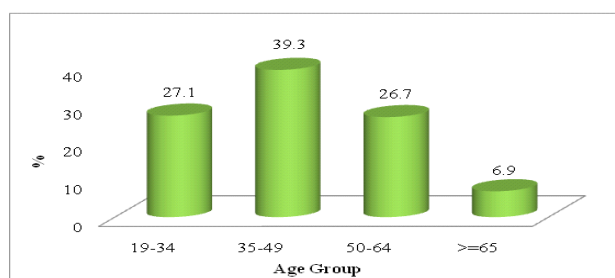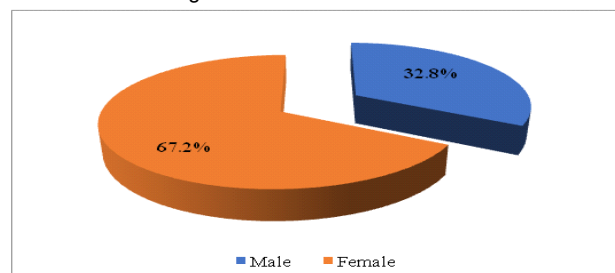

Fig 1 — Distribution of Patients
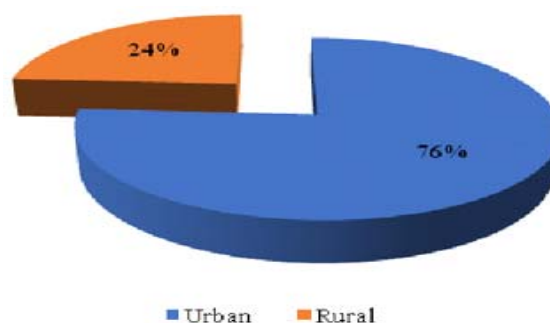

Fig 2 — Gender Distribution of Patients

Fig 3 — Distribution of Patients by place of residence

prescribed using their trade name. The study also showed that of the 492 drugs used only 72 (14.63%) were from the essential medicine list (EML) while the remaining 420 (85.36%) were not from the EML.

Class of drugs used :

The total of 492 drugs used were distributed among four class of anti-depressant drugs namely Atypical Antidepressants, SNRI, SSRI and TCA. The majority class of drugs was SSRI with a share of 45.7% followed by TCA (23.8%). The other two categories, Atypical and SNRI, comprised of 12.6% and 17.9% respectively (Fig 8).
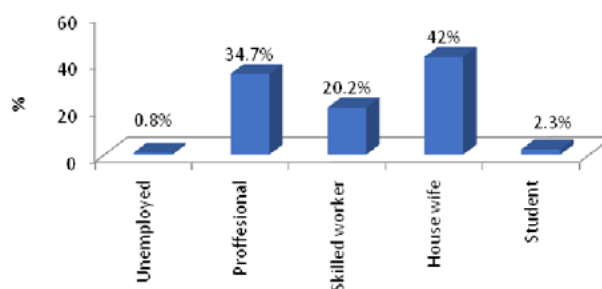

Fig 4 — Gender Distribution of Patients

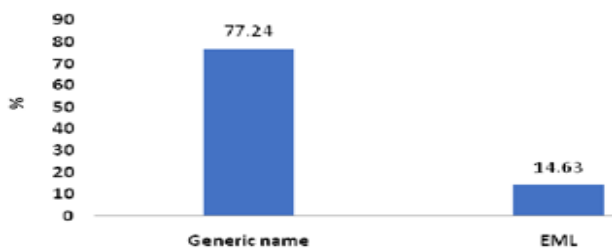Fig 5 — Distribution of Patients by Family Income

Fig 6 — Distribution of cases by no of anti depressants used in generic name and from EML
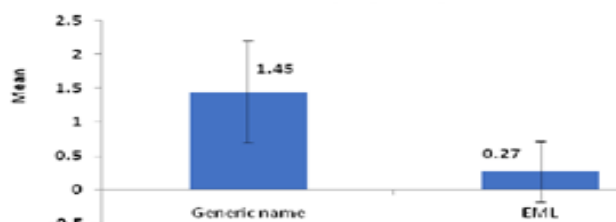

Fig 7 — Mean no of anti depressants used in generic name and from EML per prescription
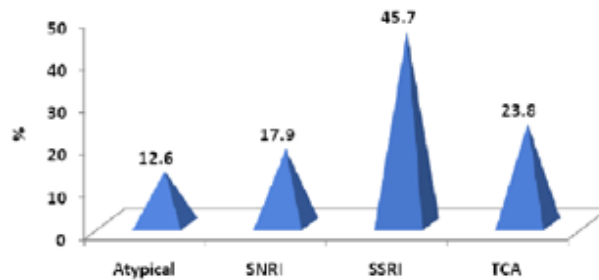

Fig 8 — Distribution of cases by class of drugs

range of 1 month to 120 months with a mean ± SD of 11.53 ± 12.05 months. Maximum proportion of patients were under therapy for 6-11 months (42%).

Efficacy of Treatment

Severity of presenting illness

The patients at the time of presentation were graded by HDRS score according to severity of illness. HDRS score within 8-13 were classified as mild depression; HDRS score within 14-18 as moderate depression while HDRS score within 19-22 was classified as severe depression; HDRS score $\geq$23 was classified as very severe depression. The results are presented on Fig 11. Nearly 2/3rd of cases (63.4%) had moderate level of depression while 34% presented with severe level of depression. Mild depression was of the order 1.9% while 0.8% cases presented with very severe depression.

HDRS score before and after therapy (clinical improvement) :

The comparison of HDRS score before and after therapy for the different treatment options used is presented on Fig 12. It was found that 262 patients were administered 11 types of therapy options. Single therapy with SNRI, SSRI and TCA was given to 5, 31 and 17 patients respectively. Combination therapies given were Atypical + SSRI, SNRI + SSRI, SSRI + TCA, TCA + SNRI, SSRI + SNRI + Atypical, SSRI + SNRI + TCA, SSRI + TCA + Atypical and SSRI + TCA + SSRI. In each of these therapies there was significant
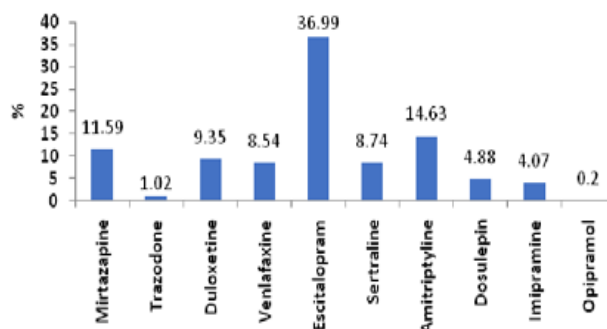
Fig 9 show the distribution of cases by the individual drugs used from different classes. Out of 225 drugs prescribed from SSRI class 182 were Escitalopram while the remaining 43 were Sertraline. These two drugs had a share of 36.99% and 8.74% respectively of the total drugs used. Under TCA class 117 drugs were prescribed of which Amitriptyline was 72, Dosulepin 24, Imipramine 20 and Opipramol 1. The respective proportions were 14.63%, 4.88%, 4.07% and 0.2% of the total drugs prescribed. In the SNRI class 88 drugs were prescribed of which 46 were Duloxetine while Venlafaxine was used 42 times with a share of 9.35% and 8.54% of the total drugs prescribed respectively. In the Atypical class 62 drugs were prescribed of which 57 were Mirtazapine and the remaining 5 were Trazodone with a share of 11.59% and 1.02% of the total drugs respectively. Escitalopram was prescribed most times followed by Amitriptyline and Mirtazapine. These three drugs together constituted 63.21% of the total drugs prescribed.

Duration of Therapy :

Distribution of cases by duration of therapy is presented in Fig 10. Duration of therapy was in the

Fig 9 — Distribution of cases by individual drug used in different classes

reduction in HDRS score after therapy (p<0.001).

Comparison of difference in HDRS score (clinical improvement) among different class of therapies may be seen in Fig 13. ANOVA suggested mean reduction in HDRS score differed significantly among different therapy options used (p=0.000). Highest mean reduction (11.2±1.64) was observed in the three combination therapy "SSRI + SNRI + Atypical" followed by "SSRI + TCA + Atypical" (9.2±1.92). Two combination therapy like Atypical + SSRI, SNRI + SSRI, SSRI + TCA resulted in mean reduction of HDRS score in the range of 7.11±2.01 to 8.75±1.8. Single drug therapy with SNRI, SSRI and TCA had a mean reduction in HDRS score in the range of 4.41 to 6.94. The two combination therapy TCA + SNRI had a low mean reduction of 5±0.71.

Comparison of single, two drug and three drug therapy is presented in Fig 14.

Significant difference was found in the reduction of HDRS score in the therapy options used (p=0.000). The mean reduction in single drug therapy was 6.11±1.85 with a range of 2-10. Two drug therapy resulted in mean decrease of 7.73±2.14 in HDRS score with a range of 3-12. Three drug therapy resulted in a mean reduction of 8.81±2.04 with a range of 6-13. Two drug therapy was found to be significantly more effective than single drug therapy (p<0.05). Three drug therapy also caused greater reduction of HDRS (p=0.075). Use of greater number of anti-depressants
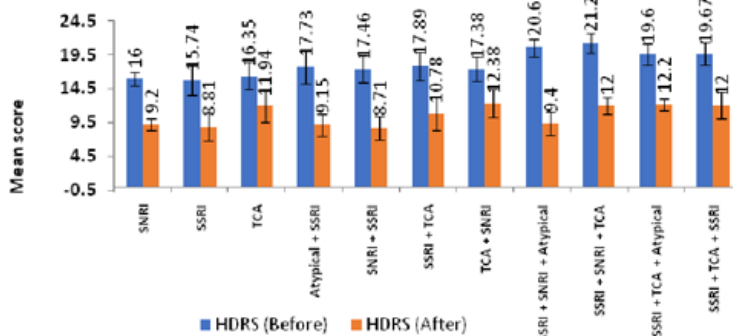

Fig 12 — Comparison of HDRS score (before/after) by class of therapy
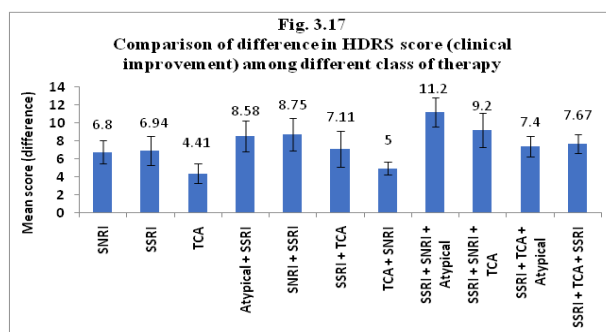

Fig 13 — Comparison of difference in HDRS score (clinical improvement) among different by class of therapy

was generally consistent with a greater reduction in HDRS score however this also came with increased incidence of adverse effects. It was seen that milder cases of depression could be adequately treated with fewer drugs while the more severe or resistant cases may require use of multiple drugs from different classes.

These findings need to be verified with further experiment.

Comparison of therapy according to severity of illness is presented in Fig 15. It is observed that mild depression was commonly treated with single drug therapy (80%). Moderate depression was commonly treated with two drug therapy (73.5%). Severe depression cases had 71.9% two drug therapy and 19.1% three drug therapy with anti-depressants. This implied that as the severity of depression increases combination therapy is the preferred option (p=0.000).

Duration of therapy :

Comparison of therapy according to duration is furnished in Fig 16. It was revealed that when the duration is 1-5 months single drug therapy was 33.3% and two drug therapy was 64.8%. When the duration becomes 6-11 months single drug therapy was 14.5% and two drug therapy was 85.4%. When the duration increased to 12-17 months single drug therapy was 18%, two drug therapy was 64% while three drug therapy was 18%. When the duration becomes 18-23
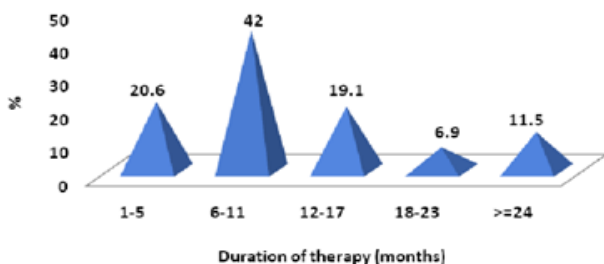

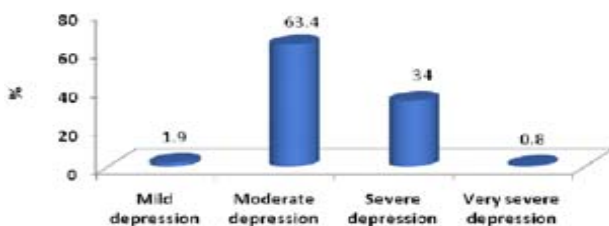
Fig 10 — Distribution of cases by duration of therapy

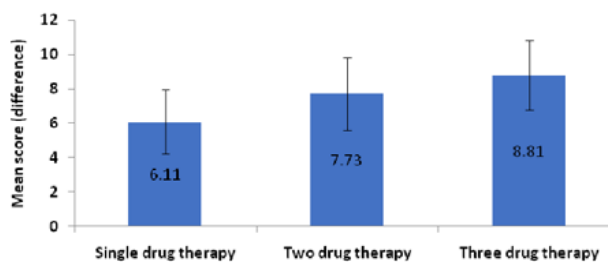Fig 11 — Grading of patients by severity of presenting illness (HRDS)

Fig 14 — Comparison of difference in HDRS score (clinical improvement) among different by class of therapy
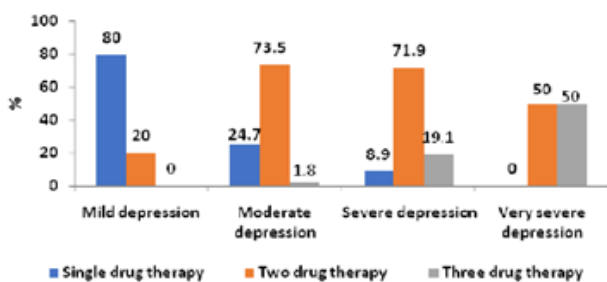

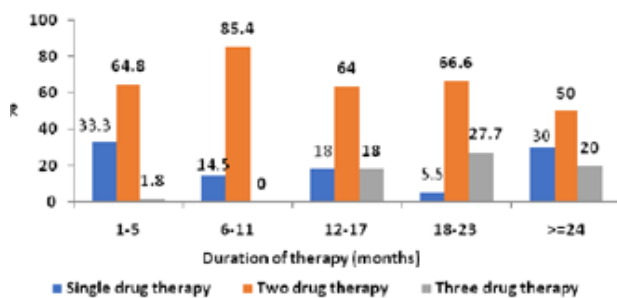Fig 15 — Comparison of therapy according to severity

Fig 16 — Comparison of therapy according to duration of therapy

months single drug therapy was 5.5%, two drug therapy was 50% and three drug therapy was 27.7%. This clearly indicated a higher trend of multidrug therapy with increased duration of therapy (p=0.000).

DU90 % :

DU90% presented in Table 1 presents the list of drugs in descending order of frequency and which cumulatively make up 90% of the prescriptions; these are Escitalopram which was used most times (36.99%) followed by Amitriptyline (14.63%), Mirtazapine (11.59%), Duloxetine (9.35%), Sertraline (8.74%) and Venlafaxine (8.54%).

Table 1 — DU 90%			
Drug/Class	No.	%	Cumulative %
Escitalopram	182	36.99	36.99
Amitriptyline	72	14.63	51.62
Mirtazapine	57	11.59	63.21
Duloxetine	46	9.35	72.56
Sertraline	43	8.74	81.3
Venlafaxine	42	8.54	~ 90.0

DISCUSSION

Usually, the term antidepressants refer to mainstream prescribed antidepressants; the qualitative and quantitative assessment of which in the Psychiatry department at Hi-Tech Medical College and Hospital, Bhubaneswar was the focus of this study.

Antidepressants were prescribed more in females than in males. This was consistent with the findings of other studies[10,11]. Antidepressants were prescribed more in women as they comprised a majority of the patients. This greater incidence of depression in women is the most consistent finding inepidemiology studies conducted on depression all over the world. In my study of the 262 patients (n=262) enrolled 67.2% were females. Similar result on gender distribution was found in a study on 'Drug use pattern of antidepressant agents in psychiatric patients- a prospective study' conducted in Ahmedabad[15] where almost 60% of the patients were females. Similar findings of higher incidence of depression in females compared to males have been stated in community based epidemiological study according to National Institute of Mental Health (2007).

In this study it was seen that the greatest proportion of patients were in the age group 35-49 years and comprised 39.3% of the total cases. The age distribution in the retrospective drug utilization study of antidepressants in Pondicherry showed that the majority of patients who received the antidepressants belonged to the 21-40 years age group[16], in contrast to the results of a study on antidepressant use in East Asia, wherein the mean age of the patients who received antidepressant prescriptions was more than 40 years[17].

Rational prescribing was followed as per the principles of prescription order writing[12]. 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[13].

One of the strengths of this study was the detailed analysis of socio-demographic profile of each of the patients enrolled. Few studies in India have taken such a close analytical look in this aspect.

The mainstay of this study was to analyse the current prescription pattern of antidepressants at our hospital.

As per WHO prescribing indicators, we observed:

A total of 492 antidepressant drugs were prescribed to the 262 patients enrolled in this study. It was seen that the average number of antidepressants per prescription was 1.87. It must be mentioned here that records were kept only of the drugs strictly classified as antidepressants in the prescription. The average number of drugs per prescription which was 1.87

reflected only the antidepressant medication used per prescription as we wanted to study their particular effect on efficacy caused to patient. A 'Retrospective Drug Utilization Study of Antidepressants in the Psychiatry Unit of a Tertiary Care Hospital' in Pondicherry showed that the average number of drugs per prescription according to their data was 2.32[16]. This was slightly higher in this study compared to our study as they also included other psychiatric medication (eg, sedative-hypnotics, antipsychotics) which was in some cases prescribed to the patients in addition to antidepressants. As per the inclusion and exclusion criteria of this study patients with co-morbid diagnosis like psychosis, bipolar disorder etc. were not included in the study; only the patients with a frank diagnosis of Major Depressive Disorder (MDD) and receiving antidepressant therapy were included in the study. Another study which was conducted on drug use patterns of antidepressant agents in psychiatric patients in Ahmedabad showed a still higher average number of drugs per prescription of 2.72[15]. Again co-morbid psychiatric diagnosis and concomitant medication were a part of this study while our study focussed solely on depression and the use of antidepressants.

This study revealed that a total of 380 (77.24%) of the 492 antidepressants used were prescribed in their generic name. The retrospective study conducted in Pondicherry had shown that 88.54% of the antidepressants used in that study were prescribed in their generic name. Our results in this aspect was comparable to the above mentioned study.

In this study it was observed that Escitalopram from the SSRI class of antidepressants was the most highly used antidepressant 36.99%. Amitriptyline from the class TCA was second accounting for 14.63% of the antidepressants used. Mirtazapine from the Atypical class 11.59% and Duloxetine from the SNRI class 9.35% were also used in a significant number of patients. In accordance with this study many other studies have reported that selective serotonin reuptake inhibitors (SSRIs) account for the bulk of the prescribed antidepressants, with high prescribing rates.

Among the SSRIs, Escitalopram was the preferred drug. Again, this was in contrast to findings of the east Asian study on antidepressant use, wherein Fluoxetine and Sertraline were prescribed more frequently than Escitalopram and the use of Escitalopram was lower than that of Trazodone, Mirtazapine, Imipramine and Amitriptyline[17].

There is need for more research on this topic to improve efficacy of therapy and find ways to consolidate improvement and guard against relapse.

To conclude newer class of anti depressant drugs are currently being used more in pharmacotherapy of depression. However older antidepressant class of drugs has also significant role to play in the treatment of this condition.

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