Original Article

Pharmacology Section

Prescribing Trends in Depression: A Drug Utilization Study Done at a Tertiary Healthcare Centre

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ABSTRACT

Introduction: Depression is one of the most prevalent forms of mental illnesses.The 'Global Burden of Disease' study showed that depressive disorders were the fourth leading cause of burden among all the diseases. Depression accounted for 4.46% of the total DALYs (Disability Adjusted Life Years) and 12.1% of the YLDs (Years Lived with Disability) in 2002, as opposed to 3.7% of the DALYs and 10.7% of the YLDs in 1990.With the increase in the number of patients, there has been an increase in the number and the type of antidepressants which are available to the psychiatrists and other clinicians. This study was aimed to assess the current prescribing practice.

Materials and Methods: The data which was collected included information on the age, sex and the drug prescribed, including the group, subgroup, trade name, dosage and distribution in 50 outpatients who attended the psychiatry OPD.

Results: In this study, 82% of the subjects were females whereas 18% were males. Most of the patients were in the age group of 41-60 years followed by the 21–40 years age group, the above 60 years age group and the below 21 years age group. Most of the patients were prescribed selective serotonin reuptake inhibitors (SSRIs), followed by serotonin nor-epinephrine re-uptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs). The most prescribed SSRI was Escitalopram.

Conclusion: In this study on depression, most of the subjects were females. Most of the patients were in the age group of 41–60 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.

Key Words: Depression, Antidepressants, Prescribing patterns

KEY MESSAGE

- Significant changes in the antidepressants being prescribed. SSRIs are more popular than the TCAs.

INTRODUCTION

Depression is an important global public health problem due to both its relatively high lifetime prevalence and the significant disability that it causes. In 2002, depression accounted for 4.5% of the worldwide total burden of diseases (in terms of disability-adjusted life years). It is also responsible for the greatest proportion of burden which is attributable to non-fatal health outcomes accounting for almost 12% of the total years which were lived with disability worldwide [1]. The WHO defines depression as a pessimistic sense of inadequacy and a despondent lack of activity.

Depression can be defined as a mental state which is characterized by feelings of sadness, loneliness, despair, low self-esteem and self-reproach. The accompanying signs include psychomotor retardation or at times withdrawal from interpersonal contact and vegetative symptoms such as anorexia and insomnia [2]. Depression affects different people in different ways – not everyone has the same symptoms. The symptoms of depression have an impact on patients both mentally and physically, typically preventing the sufferers from leading normal lives. The symptoms may be chronic or recurrent and in severe cases can lead to suicide. The symptoms may include any or a combination of the following: Those which have been experienced for more than two weeks [3,4] low/sad, irritable or indifferent mood , loss of interest and enjoyment in daily life and lack of energy. The physical symptoms of depression include fatigue and reduced activity, disturbed sleep or excessive sleep, changes in appetite and weight, loss of sex drive, unexplained aches and pains and changes in the menstrual cycle. Other symptoms of depression include poor concentration or reduced attention, difficulty in making decisions, tearfulness, restlessness, agitation or anxiety, low self-confidence and self-esteem, feelings of guilt, inability to cope with life as before, etc [3].

Depression accounted for 4.46% of the total DALYs (Disability Adjusted Life Years) and 12.1% of the YLDs (Years Lived with Disability) in 2002, as opposed to 3.7% of the DALYs and 10.7% of the YLDs in 1990 [4].

General population surveys which were conducted in many parts of the world including some which were conducted in the south-east Asian region countries showed that 15% to 20% children and adolescents suffered from depression and that the causes were mostly similar to that of the adult populations. Isolation from peers, family and other emotional relationships or the inability to keep one's disappointments in his/her perspective and academic stress may lead to mental health problems [5].

Age standardized DALYs per 100000 population 2004 WHO figures for India [4] [Table/Fig-1].

Disorder	DALYs
Neuropsychiatric disorders	3228
Depression	1401
CVS diseases	3521
Hypertensive heart disease	72
CVA	837
Cancer	984
DM	305

[Table/Fig-1]: Age standardized DALYs per 100000 population 2004 WHO figures for India

A drug utilization study is aimed at evaluating the factors which are related to the prescribing, dispensing, administering and the taking of medication and its associated events. These factors analyze the trend of drug usage at various levels in the healthcare system irrespective of whether it is national, regional, local or institutional. They evaluate drug usage at a population level according to the age, sex, social class and morbidity among other characteristics. They also crudely estimate the disease prevalence to plan drug production and procurement.

Many studies have pointed to significant changes in the types of antidepressants that are being prescribed [6].The outpatient and medication based therapy for depression is becoming much more popular for the treatment of depression than for psychotherapy [7]. Thus, it is important to know the current trend of drug usage and the effectiveness of the drugs which are used for depression.

MATERIALS AND METHODS

The data was collected as per the proforma which included age, sex and the drug which was prescribed including the subgroup, the trade name, the dosage and the distribution.

Inclusion Criteria

Patients of both the sexes in age group of 18-60 years.

The patients with an established diagnosis of depression were included.

Th Criteria for a Major Depressive Episode in Adults [8]

A. Five (or more) of the following symptoms were present during the same two-week period and they represented a change from the previous functioning and at least one of the symptoms was (1) depressed mood or (2) loss of interest or pleasure.

   (1) Depressed mood for most part of the day, nearly every day, as indicated by the subjective report (e.g., feeling sad or empty) or by the observation made by others (e.g., appearing tearful).
   (2) Markedly diminished interest or pleasure in all or almost all the activities most of the day or nearly every day (as indicated by the subjective account or by the observation made by others).
   (3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in the appetite nearly every day.
   (4) Insomnia or hypersomnia nearly every day.
   (5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective, feeling of restlessness or being slowed down).
   (6) Fatigue or loss of energy nearly every day.
   (7) Feeling of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
   (8) Diminished ability to think or concentrate or indecisiveness nearly every day (by the subjective account or as observed by others).
   (9) Recurrent thoughts of death (not just the fear of dying), recurrent suicidal ideation without a specific plan or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet the criteria for mixed bipolar disorder.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not caused by the direct physiological effects of a substance (e.g., drug abuse or medication) or a general medical condition (e.g., hypothyroidism).
E. The symptoms are not caused by bereavement—i.e., after the loss of a loved one; the symptoms persist for longer than two months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

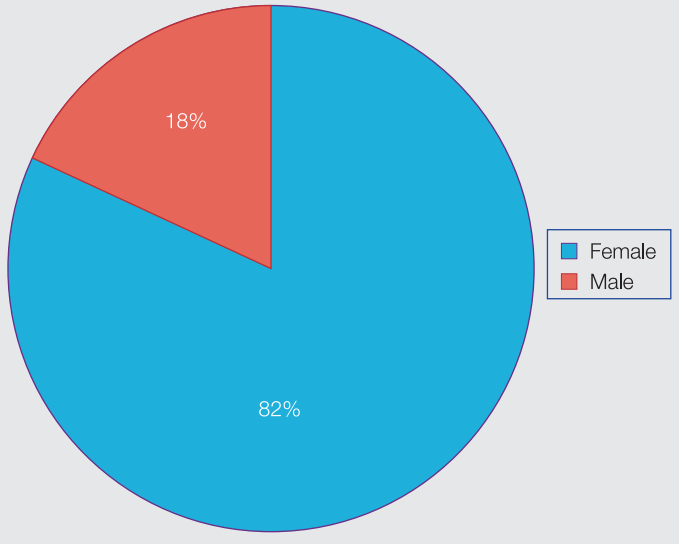
Exclusion Criteria

Depression existing with other disorders likes bipolar disorder.

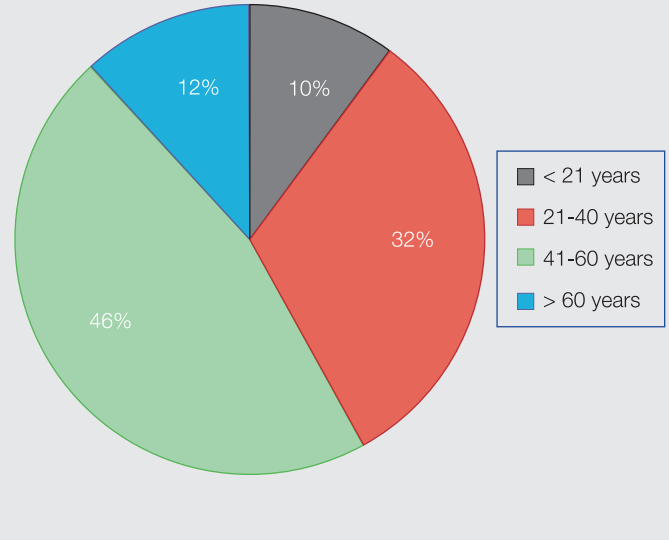
Patients with cardiovascular or any other comorbidity.

RESULTS

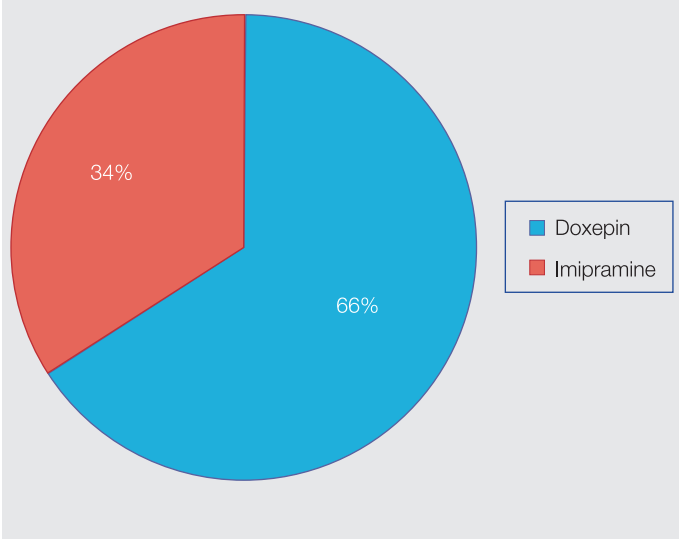
Females constituted 82% and males constituted 18% of the total patients [Table/Fig-2]. The patient distribution in the different age groups is shown in [Table/Fig-3]. Most were in the age group of 41-60 years. The most commonly prescribed group of antidepressants was SSRIs (70%), followed by SNRIs (18%) and then by TCAs (12%) [Table/Fig-4].The most prescribed SSRI was Escitalopram 85.7%. Duloxetine was the most prescribed SNRI ([Table/Fig-5] and Doxepin was the most prescribed TCA (66%) [Table/Fig-6]. The drugs which were prescribed other than the antidepressants were benzodiazepines, H_2 blockers and multivitamins. The duration of the treatment ranged from a minimum of three months to a maximum of three years ([Table/Fig-8].



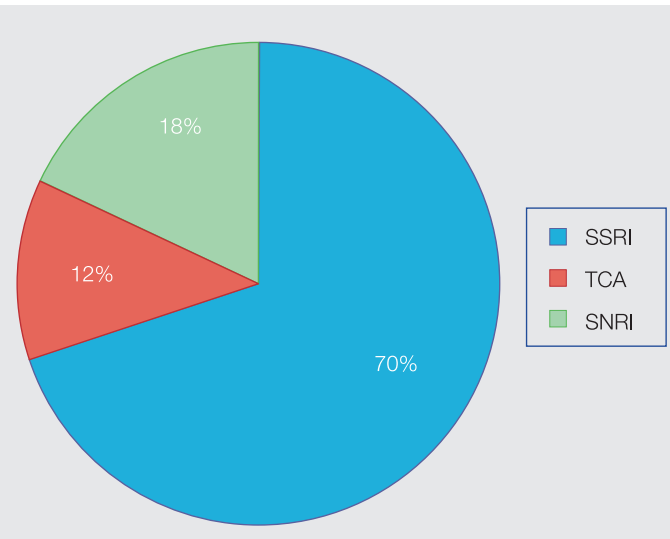
[Table/Fig-2]: Patient distribution in both sexes



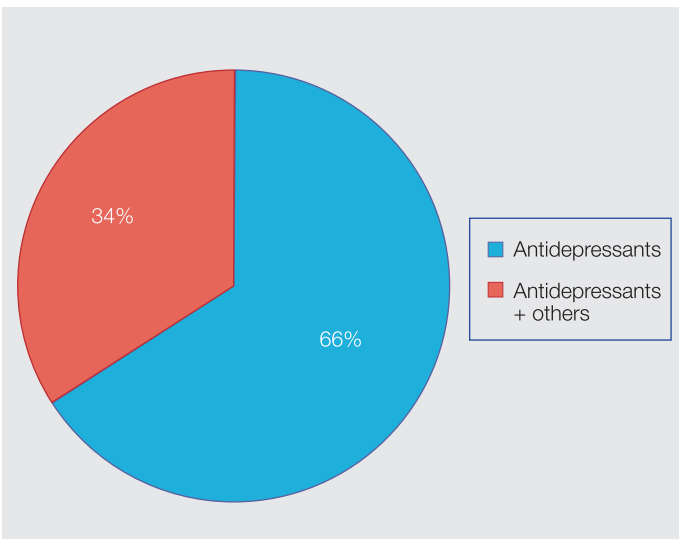
[Table/Fig-3]: Patient distribution in different age groups



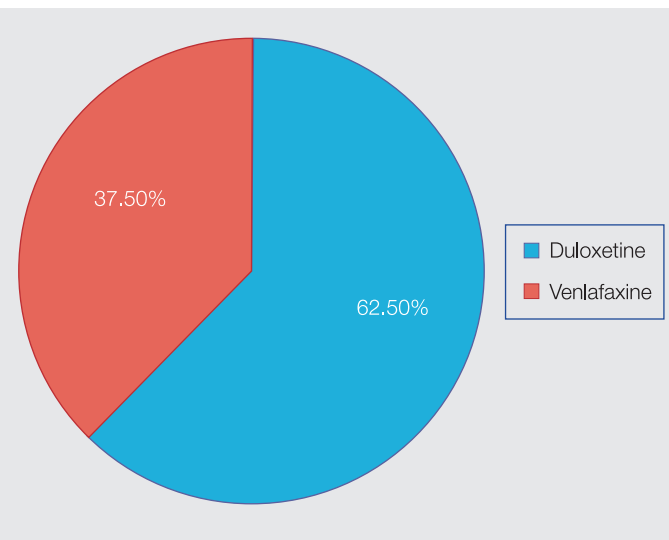
[Table/Fig-6]: TCAs administered



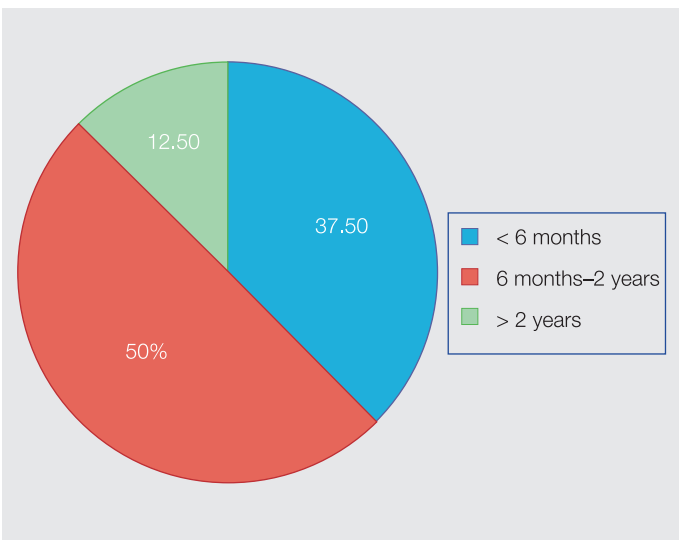
[Table/Fig-4]: Drugs administered



[[Table/Fig-7]: Other drugs



[Table/Fig-5]: Selective norepinephrine reuptake inhibitor



[Table/Fig-8]: Duration of treatment

CONCLUSION

Most of the patients in this study were females and the most susceptible age group was the 41-60 years age group. By and large, the newer group of drugs namely the SSRIs and SNRIs seem to have replaced the older group, namely the TCAs. This seems to be in accordance with other research findings [14], especially considering the fewer side effects of the newer group of drugs and the prolonged therapy which was needed to combat depression effectively.

DISCUSSION

Although pharmacological intervention is the primary treatment modality for relieving the depressive symptoms, the efficacy and suitability of other therapeutic options should not be overlooked. Other therapeutic options include psychotherapy, somatic intervention and lifestyle adjustment. The most established psychotherapies that are thought to be useful in treating depressed patients are cognitive and interpersonal psychotherapy. The role of psychotherapy alone in the management of recurrent depression seems to be less promising than the role of the antidepressants alone [9]. The somatic intervention involves electroconvulsive therapy (ECT) which is recommended for patients with treatment resistant depression, severe vegetative depression, psychotic depression and depression in pregnancy. ECT, which is administered weekly for one month and less frequently thereafter, may be as effective as aggressive pharmacotherapy in preventing relapse [10]. Lifestyle adjustment involves a minimal use of alcohol, recreational drugs and caffeine and increased physical activity and sustained cardiovascular activities [11].

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 [12]. Antidepressant drug therapy is divided into three phases: the acute phase, the continuation phase and the maintenance phase. The acute phase starts from the initiation of the therapy until remission (usually 6–12 weeks).The continuation phase is from remission to 6–9 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 [9].

Antidepressants do not differ in their overall efficacy and in their speed of response or long-term effectiveness, however, they differ in their side effects, their likelihood for the discontinuation of the symptoms and their ease of dose adjustment. Approximately 45–60% of all the outpatients with uncomplicated depression respond to the antidepressants (i.e. achieve a 50% decrease in the baseline symptoms) but only 35–50% achieve remission (i.e., virtual absence of the depressive symptoms) [13].

In this study, the age group which was commonly affected was the middle age. Also, there has been a dramatic change in the prescribing trends since the advent of the newer group of drugs, namely the SSRIs, which are being prescribed more as also shown by some other studies [14]. Studies to evaluate the recognition and the management of the depressed patients also need to be done. The methods to recognize/evaluate patients differ in different settings and many times depressed patients go untreated in primary care settings [15].

This study has taken into account only a small number of subjects and it has been conducted at tertiary care centre so it does not reflect the prescribing trends which are prevalent in the general practitioners. Different people may take services/support from different places as shown by certain studies [16]. 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.

TCAs, by inhibiting H_1 receptors cause 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 don't cause cardiovascular, histamine blocking or alpha-1 receptor side effects. But insomnia, anxiety, irritability and decreased libido result from the excess stimulation of the $5HT_2$ receptors. The stimulation of the $5HT_3$ receptors in the CNS and the periphery contributes to the GI side effects like nausea, diarrhoea, emesis, etc. SNRIs have a similar side effect profile as the SSRIs (nausea, constipation, headache and sexual dysfunction). Immediate release Venlafaxine can induce sustained diastolic hypertension [17]. Adverse events such as mania, hostile behaviour and suicide have been reported in teenagers who had been treated with SSRIs [18]. Suicidal tendencies however, have shown variation with respect to one SSRI to the other and fluoxetine has been shown to cause less suicidal tendencies [19]. A similar study in Sweden has shown a decrease in suicides as the effect of a primary care educational programme [20].

Depression may be commonly associated with chronic diseases in which case drug interactions with antihypertensives, hypoglycemics, etc. which are given for prolonged periods need to be studied. Such interactions may cause the physicians to prescribe drugs which may not be generally recommended for that group of population. Though it is seen that TCAs are less popular, they are more effective than SSRIs in treating severe depression [21]. Other studies which are related to depression in specific situations like post-natal depression etc., should be done as the drugs which are used for treating them may differ from the ones which are given in cases of normal depression. Similarly, studies can be conducted in vulnerable groups such as students, especially those who have recently faced a transition from school to hostel/university life.

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 [22].

Long term studies favour SSRIs over TCAs and the results indicate that the effect of SSRIs is mainly due to the prevention of relapse [23]. The popularity of SSRIs is mainly due to the ease in their use, their safety in overdose, their relative tolerability, and the broad spectrum of their uses.

ACKNOWLEDGEMENTS

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No financial or material support was received. No paid support from JCDR was taken.

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DECLARATION ON COMPETING INTERESTS:

No competing Interests.

Date of Submission: **Jan 15, 2011**
Date of per review: **Mar 16, 2011**
Date of acceptance: **Mar 29, 2011**
Date of Publishing: **Jun 13, 2011**