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A PROSPECTIVE STUDY ON EVALUATION OF EFFICACY AND SAFETY OF VILAZODONE IN DEPRESSION

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ABSTRACT

Background and Objectives: Vilazodone a novel Serotonin Reuptake Inhibitor and 5-HT_{1A}.Partial Agonist that is recently developed for the treatment of Major Depressive Disorder. The main objective of study to evaluate the efficacy and safety of vilazodone in depression. **Methods:** This is a prospective, observational, 9 month study conducted on department of psychiatry in a 500 bed tertiary care teaching hospital. The study population includes 30 subjects aged between 18-60 years with major depressive disorder (DSM-IV criteria). Vilazodone was titrated from 10 mg to 20 mg and efficacy assessed by mean change from baseline to week 4 on Hamilton Depression Rating Scale (HAMD), Montgomery-Asberg Depression Rating Scale (MADRS), Clinical Global Impression-Severity scale (CGI-S) and Improvement scale (CGI-I). Data were analysed using statistical package for social science version 20.**Results and Discussion**: The mean changes in HAMD-17 total scores, MADRS total score, CGI-S score and CGI-I score from baseline to week 4 were significantly greater in Vilazodone treated patients. Improvement in Hamilton Depression Rating Score, Montgomery-Asberg Depression Rating Score, Clinical Global Impression- Severity score and Improvement score were noted in 1 week, the earliest time point measured and persist till week 4 indicating reduction in depression symptomatology. Higher response and remission rate were shown by vilazodone treated patient on HAMD-17 and MADRS. Most common adverse events noted include diarrhea .**Conclusion**: Vilazodone is effective for treatment of Major Depressive Disorder in adults with symptom relief starting at 1 week and is well tolerated at dose of 20 mg/day.

KEYWORDS: Vilazodone; Safety; Efficacy; Major Depressive Disorder.

INTRODUCTION

Major Depressive Disorder is a disorder of mood in which the individual experiences one or more major depressive episodes without a history of manic, mixed, or hypomanic episodes. Depression is a serious chronic and recurrent psychiatric illness and is most common ailment among all psychiatric disorder. Depression is considered as third major cause of disability and premature death across the world. According to WHO depressive disorder will be second most important cause of Disability across the world by the year 2020. The prevalance of depression in India is 15.1% and is higher in female than male.

The underlying reason of depressive disorder is not yet fully understood; although psychiatric, social and biological factors play an major role. The catecholamine and serotonin deficiency hypothesis postulate that deficiency of monamine (norepinephrine and serotonin) within the synaptic cleft play an major role in depression. There are multiple variations of depression that a person can suffer from, with the most general distinction being depression in people who have or do not have a history of manic episodes.

Depressive episode involves symptoms such as depressed mood, loss of interest and enjoyment, and increased fatigability. Depending on the number and severity of symptoms, a depressive episode can be categorized as mild, moderate, or severe. An individual with a mild depressive episode will have some difficulty in continuing with ordinary work and social activities, but will probably not cease to function completely. During a severe depressive episode, it is very unlikely that the sufferer will be able to continue with social, work, or domestic activities, except to a very limited extent. Bipolar affective disorder typically consists of both manic and depressive episodes separated by periods of normal mood. Manic episodes involve elevated mood

and increased energy, resulting in over-activity, pressure of speech and decreased need for sleep.

The treatment of depressive disorders consists of a complex multimodel therapy that is determined by the current state of the illness. The treatment of depression includes pharmacotherapy, psychotherapy and sociotherapy, whereas pharmacotherapy is not always mandatory for less severe forms of depression, severe depression usually requires pharmacotherapy or electroconvulsive therapy. In addition, a variety of other biologic intervention, such as sleep deprivation and bright light therapy, may be of use in certain patient subgroups.

In the 1950s, the discovery of the therapeutic effects of medications now classified as tricyclic antidepressants (TCAs) (Imipramine, Amitriptyline, Desipramine, Nortriptyline) and monoamine oxidase inhibitors (MAOIs) (Moclobemide, Clorgyline) led to more widespread treatment of depression.[11] Although the antidepressant actions of the TCAs and MAOIs are likely to be initiated by different mechanisms, they ultimately have a similar effect of increasing neurotransmitter availability in the synaptic cleft. The TCAs inhibit reuptake of certain neurotransmitters, particularly norepinephrine and, for some TCAs, serotonin. The MAOIs, inhibit the metabolism of serotonin, dopamine, and norepinephrine. One major limiting factor in the use of these 2 drug classes is their side effect profiles. TCAs can produce adverse cholinergic and adrenergic effects, and, in excessive doses or overdoses, can cause seizures and potentially lethal arrhythmias. The MAOIs can produce orthostatic hypotension and edema. Moreover, because levels of the A form of the enzyme MAO are high in the gut and liver, inhibition of MAO requires dietary restrictions to reduce the risk of a serious and potentially fatal adverse event, hypertensive crisis. There was thus a clear motivation to develop newer, more selective antidepressant medications, and, by the late 1980s, research led to the introduction of a new class of antidepressants, the selective serotonin reuptake inhibitors (SSRIs) (Fluoxetine, Sertraline, Citalopram, Escitalopram). As compared with the first-generation antidepressants, SSRIs were found to be generally similar in efficacy for the treatment of depressed outpatients, with a better tolerability profile. Moreover, the SSRIs were profoundly safer in overdose than the TCAs. As a result of these differences, the SSRIs rapidly supplanted the TCAs and MAOIs as the antidepressant class of first choice for both psychiatrists and primary care providers. Indeed, by the end of the first decade of the "SSRI first" era, primary care physicians were prescribing more antidepressants than psychiatrists.

Shortly after the introduction of the SSRIs, another class of antidepressants known as the serotonin-norepinephrine reuptake inhibitors (SNRIs) (Duloxetine, Venlafaxine) was introduced. These medications inhibit the reuptake of norepinephrine in addition to serotonin and, as such, directly affect both serotonergic and noradrenergic neurotransmission. However, it should be noted that most of these compounds show much greater inhibition of serotonin reuptake than norepinephrine reuptake, such that at normal therapeutic doses, most of their activity very likely results from their serotonergic effects. Although not as widely prescribed as the SSRIs, several SNRIs are also now considered to be first-line treatment options for MDD. It was proposed that the property of dual reuptake inhibition might convey an efficacy advantage for the SNRIs over SSRIs.

Although newer antidepressant are better tolerated and caused fewer side effect, their specific side-effect profile has to be taken into account during the treatment of depression. In addition, the latency of several weeks until the onset of sufficient therapeutic effects remains a serious and clinically relevant problems. This principle holds true for each antidepressant and each class of antidepressant mechanisms. A further general problem in pharmacotherapy of depression is the possible non response to the first antidepressant treatment. Approxmately 30% of depressed patients do not show sufficient improvement after the first course of an adequate antidepressant treatment and a further 20% discontinue due to tolerability problems. Adequacy of treatment include the use of a treatment with proven efficacy during a time interval of at least 4-6 weeks in a sufficient therapeutic dose range including reliable patient adherence to therapy. Half of patients who do not respond adequately to a first course also fail to respond to a second antidepressant treatment trial. Hence there is a need for alternative antidepressant with more rapid onset of action, better response and remission and better tolerability.

Vilazodone new option for depression

Vilazodone- a new antidepressant is selective and potent serotonin reuptake inhibitor and serotoin 1A receptor partial agonist approved by FDA in January 2011 for treatment of MDD. The combination of serotonin reuptake inhibition with 5-HT1A partial agonistic action leads to more rapid onset of mood elevation and enhanced therapeutic efficacy .Partial Agonist action at presynaptic somalodentric 5 HT level hence contribute to antidepressant action and partial agonist action at post synaptic 5HT1A receptor lead to less sexual Dysfunction. Mechanism of action include SERT inhibition with a serotonin (5HT) 1A partial agonism, hence called Serotonin Partial Agonist Reuptake Inhibitor (SPARI).

The recommended dosage is 40 mg once daily. Vilazodone should be titrated, starting with an initial dosage of 10 mg once daily for 7 days, followed by 20 mg once daily for an additional 7 days, and then an increase to 40 mg once daily. Vilazodone should be taken with food. If vilazodone is taken without food, in-adequate drug concentrations may result and the drug's effectiveness may be diminished.

Common ADR include diarrhea, nausea, insomnia and vomiting. Other adverse effects included dizziness, dry mouth, fatigue, abnormal dreams, decreased, libido, arthralgia, and palpitations.

Patients should be monitored for clinical worsening, suicidality, and unusual changes in behavior while they are taking vilazodone. Clinicians should dis-continue vilazodone and begin supportive treatment if serotonin syndrome or neuroleptic malignant syndrome occurs during vilazodone therapy. Like other antidepressants, vilazodone should be used with caution in patients with a history of a seizure disorder. Treatment with vilazodone may also increase the risk of bleeding if the drug is taken with NSAIDs, aspirin, and other agents that affect coagulation. Vilazodone should not be stopped abruptly; the dose should be reduced gradually. Although no cases of hyponatremia were associated with vilazodone therapy in clinical studies, hyponatremia has occurred as a result of treatment with other SSRIs and SNRIs. Activation of mania or hypomania can occur with vilazodone therapy. Therefore, patients should be screened for bipolar disorder.

MATERIALS AND METHODS

Study Type
Prospective observational study.

Study Duration
Total duration of the study was 9 months.

Study Site
Department of Psychiatry.

Study Population
Not less than 30 patients.

Ethical Approval
Ethical clearance was obtained from Institutional Ethics Committee.

Study Criteria
The study group consists of the patients who are diagnosed to have depression in Psychiatry departments during the study periods and who met the following criteria.

Inclusion Criteria
- Out patient ≥18 yrs of age
- Patients with DSM IV Major depressive episode
- 17-item HAM-D score, 18-24
- Patient prescribed with Vilazodone for the current depressive episode.

Exclusion Criteria
- Other antidepressant exposure for the current depressive episode.
- Pregnancy and lactation.
- Major cardiovascular comorbidity.
- Significant psychiatric comorbidity.
- Alcohol and substance abuse.

Source of data
Patient Case Records: It included following information:
- Patient Demographics
- Patient history notes
- Drug Treatment charts
- Laboratory investigation report

Interviewing the patients
Study materials
- Informed consent form and Patient information sheet.
- Patient data collection form
- HAM-D Rating Scale
- MADRS Rating Scale
- CGI-S
- CGI-I

Study Procedure
It is a prospective study in department of Psychiatry in a 500 bed tertiary care teaching hospital. The sample will comprise of not less than 30 patients with a DSM IV major depressive episode (unipolar or bipolar). Patients will be recruited only if they provide informed consent for participation. Patients will receive Vilazodone, ideally in monotherapy, in the dose of 10 mg/day for the first week and 20 mg/day thereafter. Patients will be assessed at baseline, at a 1-week follow up, and at the 4-week study endpoint. Safety profile of the drug is determined by describing adverse effect.

Statistics
Statistical analysis were done by using SPSS (Statistical Package for Social Science) statistical software package (Version 20).

Relevance
Selective serotonin reuptake inhibitors (SSRIs) are often recommended as first-line therapies in patients with major depressive disorder. It has been postulated, that the acute and long-term effects of these drugs may be limited due to autoregulatory feedback mechanisms involving the 5-HT1 class of serotonergic receptors. One approach to this drawback has been the investigation of augmentation therapies, such as the addition of 5-HT1A or 5-HT1B agonists to SSRIs in patients with MDD. Another approach has been the development of medications with additional mechanisms of action, such as Vilazodone, an SSRI and partial 5-HT1A receptor agonist that is currently approved for the treatment of Depression. Clinical trials related to vilazodone were not specifically designed to assess onset of action, side effects, or efficacy in patients, so future studies will be needed to confirm these proposed mechanism-based benefits. This prompted us to make a study to analyse efficacy and safety of vilazodone in in depressive patients.

RESULTS AND DISCUSSION

A total patient consulted in psychiatry department during the study period were analysed, among which 30 patients diagnosed as depression were included in study as per inclusion criteria

Age categorization

Table No. 1: Categorization of study population based on age

AGE RANGE	FREQUENCY	PERCENTAGE
20 – 30	5	16.7 %
31 – 40	9	30.0 %
41 – 50	11	36.6 %
51 – 60	5	16.7 %
TOTAL	**30**	**100 %**

The table No:1 shows the age wise categorization of the study population. They were divided into four groups, 20-30, 31-40, 41-50, 51-60 years. The maximum number of patients was in age group of 41-50 years 36.6% (n=11) and minimum number of patients were in an age group between 20-30 years 16.7% (n=5) and 51-60 years 16.7% (n=5). Minimum age of patient include in the study was 22 years and maximum was 56 years.

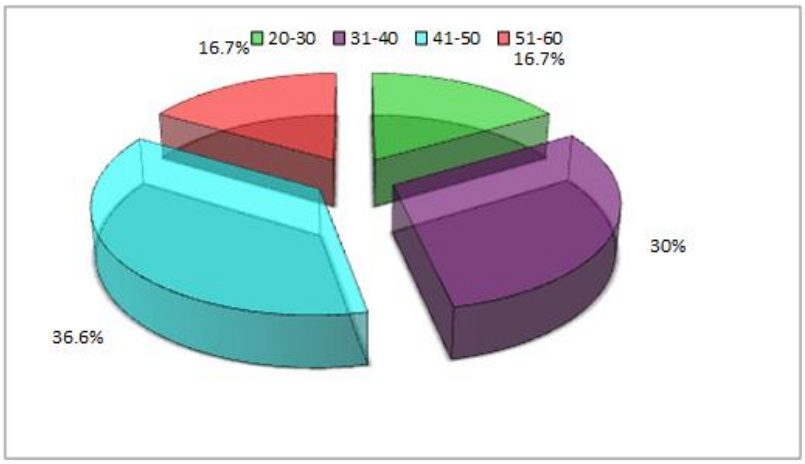

Figure No: 1 Categorization of study population based on age

Gender categorization

Table No. 2: Categorization of study population based on gender

GENDER	FREQUENCY	PERCENTAGE
Male	18	60.0 %
Female	12	40.0 %
TOTAL	**30**	**100 %**

The table No: 2 shows gender wise distribution of study population. Out of total population male patients were found to be more predominant than female patients, with a percentage of 60% (n=18) and 40% (n=12).

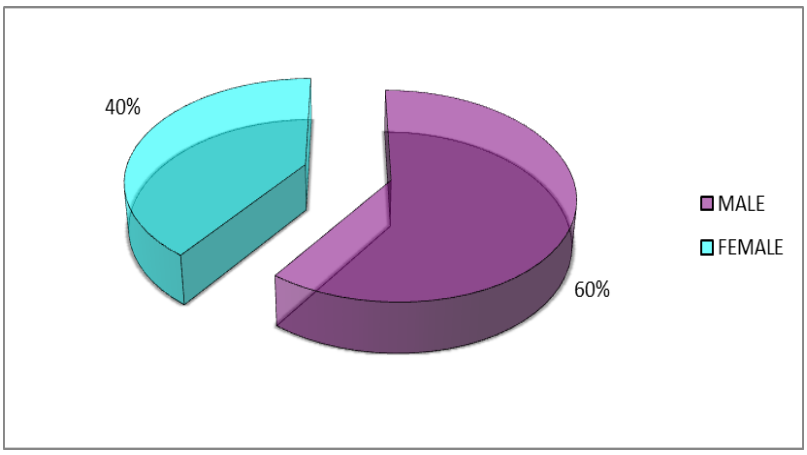

Figure No. 2: Categorization of study population based on gender

Categorization of Educational Qualification

Table No. 3: Categorization of study population based on educational qualification

EDUCATIONAL STATUS	FREQUENCY	PERCENTAGE
ILLITERATE	1	3.3 %
LITERATE	7	23.3 %
HSE	9	30 %
DEGREE	10	33.4 %
PG AND ADOVE	3	10 %
TOTAL	**30**	**100 %**

Table No.3 shows the Categorization of study population according to educational qualification. They were categorized into illiterate, literate, HSE, degree, PG and above. From this analysis it was found that majority of the population were qualified up to degree 33.4% (n=10) and 3.3% (n=1) are illiterate.

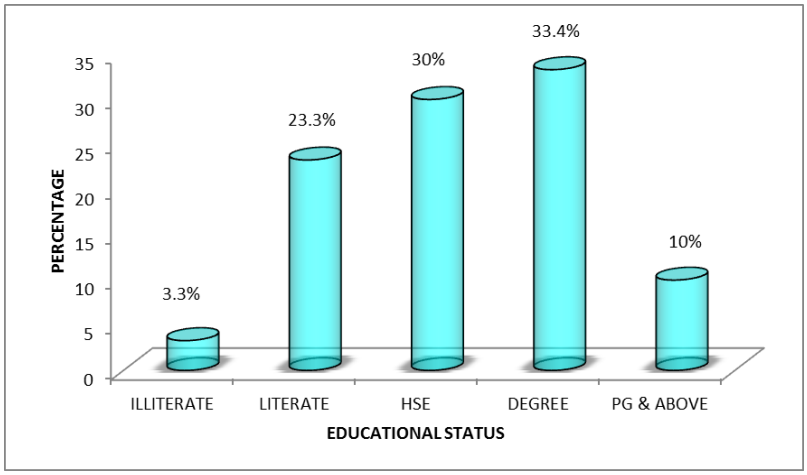

Figure No. 3: Categorization of study population based on educational qualification

Categorization of Occupational Status

Table No. 4: Categorization of study population based on occupational status

OCCUPATIONAL STATUS	FREQUENCY	PERCENTAGE
WORKING	22	73.3 %
NOT - WORKING	8	26.7 %
TOTAL	**30**	**100 %**

Table No.4 shows the Categorization of study population according to occupational status. From the table it was shown that 73.3% (n=22) of the population were working and 26.7% (n=8) were not working.

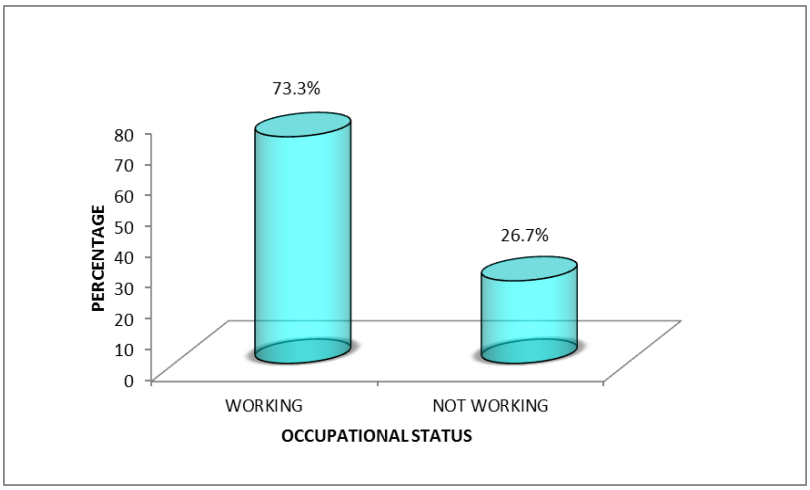

Figure No. 4: Categorization of study population based on occupational status

Categorization Based on Marital Status

Table No. 5: Categorization of study population based on marital status

MARITAL STATUS	FREQUENCY	PERCENTAGE
UNMARRIED	8	26.6 %
MARRIED	22	73.4 %
TOTAL	**30**	**100 %**

Table No.5 shows the Categorization of study population according to marital status. From the table it was shown that 73.4% (n=22) of the population were married and 26.6% (n=8) were not married.

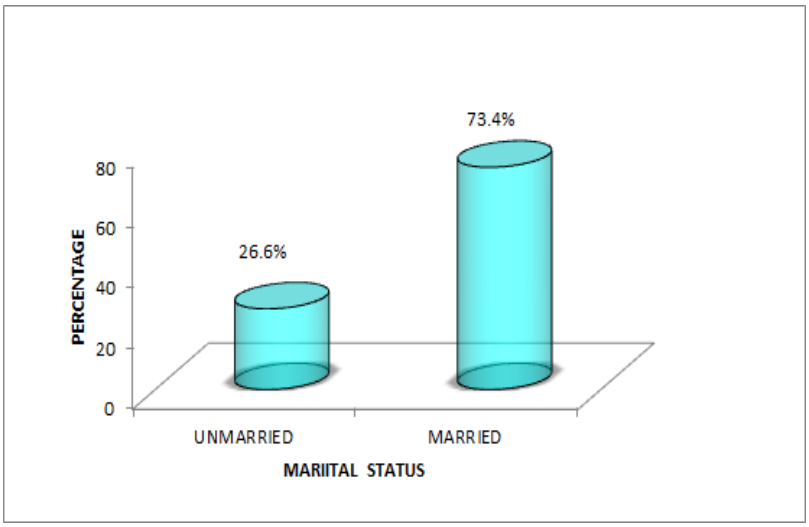

Figure No. 5: Categorization of study population based on marital status

Categorization Based on Family History of Psychiatric Disease

Table No. 6: Categorization of study population based on family history of psychiatric disease

FAMILY HISTORY OF PSYCHIATRIC DISEASE	FREQUENCY	PERCENTAGE
ABSENT	12	40 %
PRESENT	18	60 %
TOTAL	**30**	**100 %**

Table No.6 shows the Categorization of study population according to family history of psychiatric disease. From the table it was shown that 60% (n=18) of the population have history of psychiatric disease and 40% (n=12) have no history of psychiatric disease.

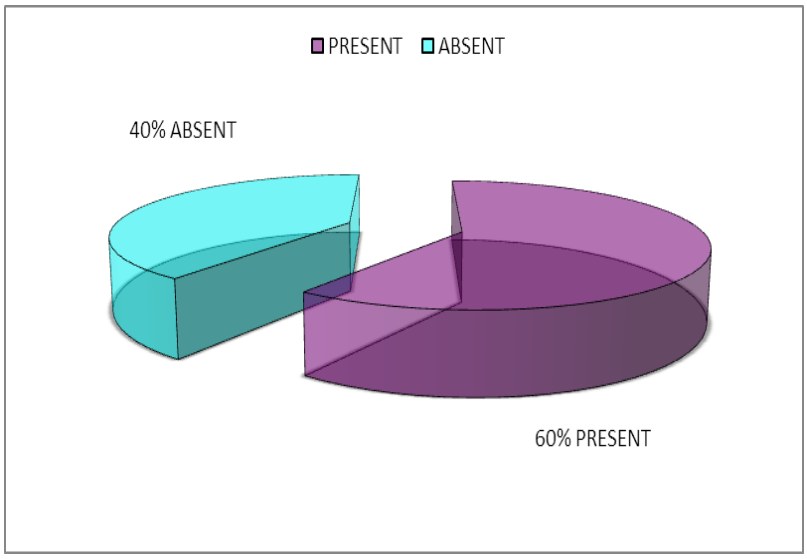

Figure No. 6: Categorization of study population based on family history of psychiatric disease

Categorization Based on Type of Psychiatric Disease in Family

Table No. 7: Categorization of study population based on type of psychiatric disease in family

TYPES	FREQUENCY	PERCENTAGE
NO DISEASE	12	40.0 %
DEPRESSION	6	20.0 %
MANIA	3	10.0 %
PSYCHOSIS	3	10.0 %
ALCOHOLISM	2	6.7 %
OTHERS	4	13.3 %
TOTAL	**30**	**100 %**

Table No.7 shows the Categorization of study population according to type of psychiatric disease history in family. From the table it was shown that 40% (n=12) of total patients with no family history psychiatric disease, 20%(n=6) with family history of depression, 10% (n=3)with family history of mania, other 10% (n=2)with family history of psychosis, 7% (n=2)with family history of alcoholism and 13%(n=4) with other psychiatric diseases.

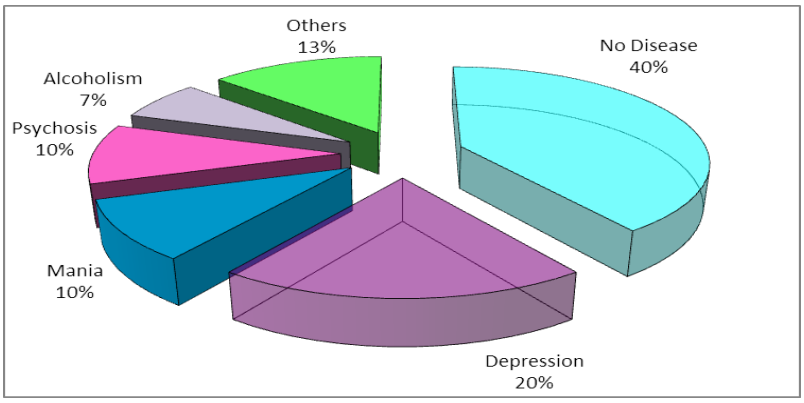

Figure No. 7: Categorization of study population based on type of psychiatric disease in family

Categorization based on class of depression

Table No. 8: Categorization of study population based on class of depression

TYPEOF DEPRESSION	FREQUENCY	PERCENTAGE
MILD	0	0
MODERATE	9	30 %
SEVERE	10	33.4 %
VERY SEVERE	11	36.6 %
TOTAL	**30**	**100 %**

Table No. 8 shows the Categorization of study population based on class of depression. From the table it was shown that 36.6% (n=11) of the population are in very severe depression, followed by 33.4% (n=10) in severe depression and 30% (n=9) in moderate depression respectively.

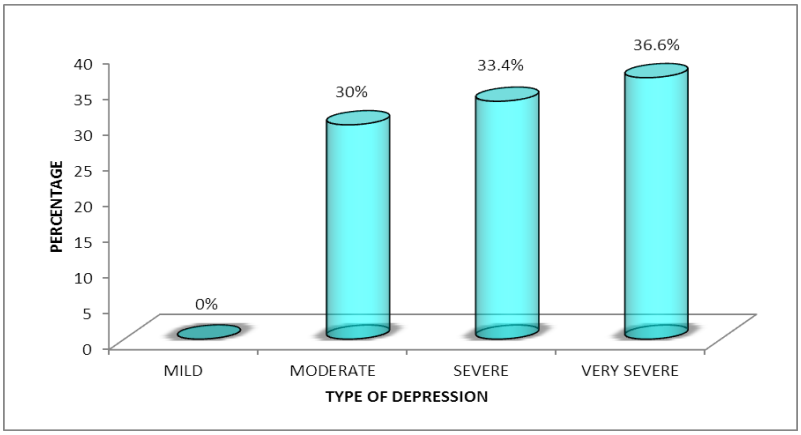

Figure No. 8: Categorization of study population based on class of depression

Categorization based on duration of depression

Table No. 9: Categorization of study population based on duration of depression

DURATION OF DEPRESSION	FREQUENCY	PERCENTAGE
<1 YEAR	10	33.4 %
1-5 YEARS	15	50 %
6-10 YEARS	5	16.6 %
TOTAL	**30**	**100 %**

Among the study population, 33.4% (n=10) of patients were with depression history of <1 year, 50% (n=15) between 1-5 years, 16.6% (n=5) between 6-10 years.

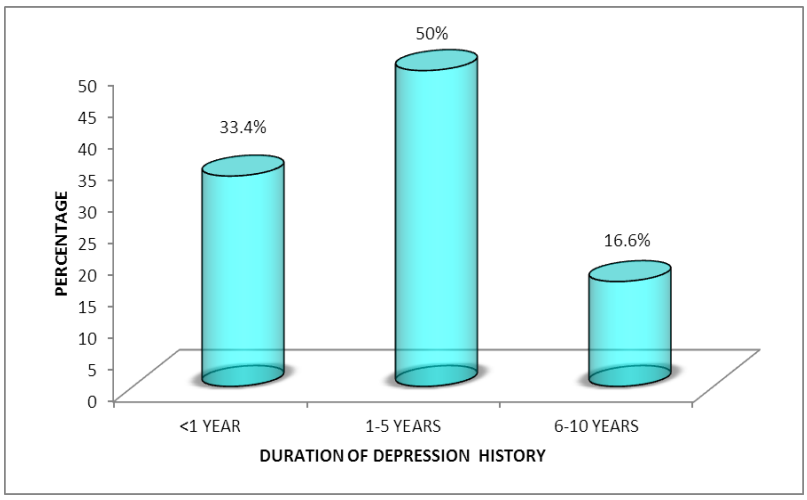

Figure No. 9: Categorization of study population based on duration of depression

MEAN SCORE CHANGES FROM BASELINE TO 4 WEEK IN EFFICACY MEASURES

MEAN CHANGE IN HAMD 17 ITEM TOTAL SCORE

Table No. 10: Mean change in HAMD 17 item total score from baseline to 4 week end of the treatment

HAMD	BASE LINE	1 WEEK	4 WEEK
	Mean(Std dev)	Mean(Std dev)	Mean(Std dev)
	21.43(3.82)	13.26(6.36)	8.83(8.10)

Table No.10 shows the. mean change in HAMD 17 item total score from baseline to 4 week end of the treatment. From the table it was shown that mean change from baseline to week 4 on total HAMD score shows dramatically greater reduction and thereby greater response towards the treatment. Here the study patients have shifted from severe depressive state to mild depression.

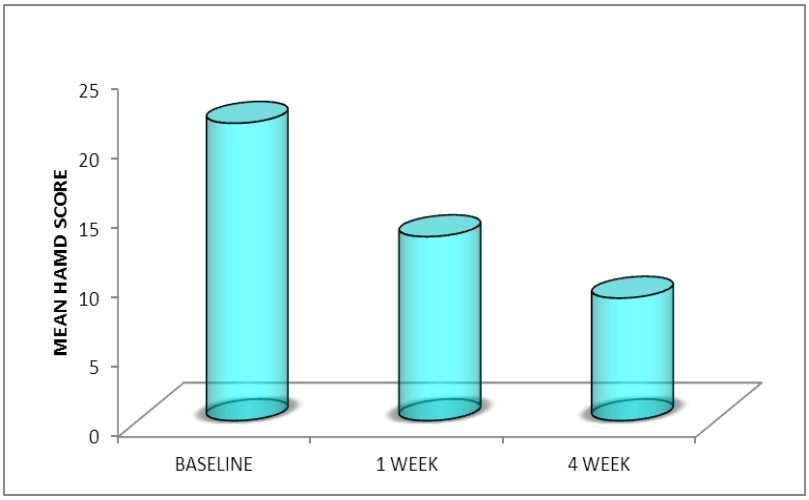

Figure No. 10: Mean change in HAMD 17 item total score from baseline to 4 week end of the treatment

MEAN CHANGE IN MADRS TOTAL SCORE

Table No. 11: Mean change in MADRS item total score from baseline to 4 week end of the treatment

	BASELINE	1 WEEK	4 WEEK
MADRS	Mean(Std dev)	Mean(Std dev)	Mean(Std dev)
	26.2(5.06)	19.8(7.29)	8.93(7.35)

Table No.11 shows the. mean change in MADRS item total score from baseline to 4 week end of the treatment. From the table it was shown that MADRS score from baseline to 4 week end point shows that there is a greater reduction in depression severity(severe depression to normal) and thereby greater response towards the treatment.

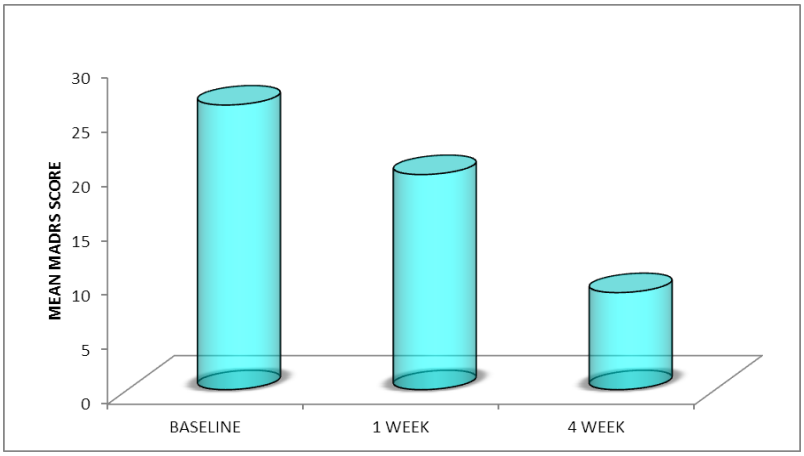

Figure No. 11: Mean change in MADRS item total score from baseline to 4 week end of the treatment

MEAN CHANGE IN CGI-S SCORE

Table No. 12: Mean change in CGI-S score from baseline to 4 week end of the treatment

	BASELINE	1 WEEK	4 WEEK
CGI S	Mean(Std dev)	Mean(Std dev)	Mean(Std dev)
	4.3(0.65)	3.3(0.98)	2.6(1.30)

Table No.12 shows the. mean change in CGI-S score from baseline to 4 week end of the treatment. From the table it was shown that CGI-S score from baseline to 4 week end point shows that in vilazodone treated patient severity of illness had shifted from moderate to borderline and more better respone.

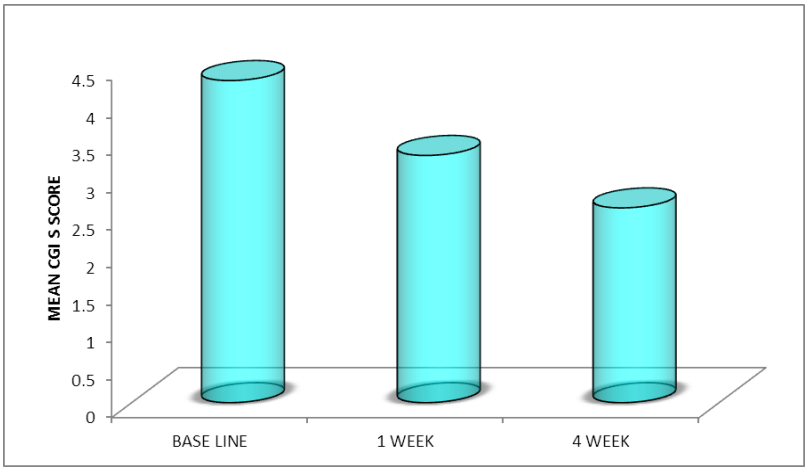

Figure No: 12 Mean change in CGI-S score from baseline to 4 week end of the treatment

MEAN CHANGE IN CGI-I SCORE

Table No. 13: Mean change in CGI-I score at 1 week and 4 week end of the treatment

	1 WEEK	4 WEEK
CGI- I	Mean(Std dev)	Mean(Std dev)
	2.8(0.71)	2.4(1.3)

Table No.13 shows the. mean change in CGI-I score at 1 week and 4 week end of the treatment. From the table it was shown that CGI-I score at 1 week and 4 week end point patient had showed minimal improvement from baseline after 1 week and much improvement from baseline after 4 week.

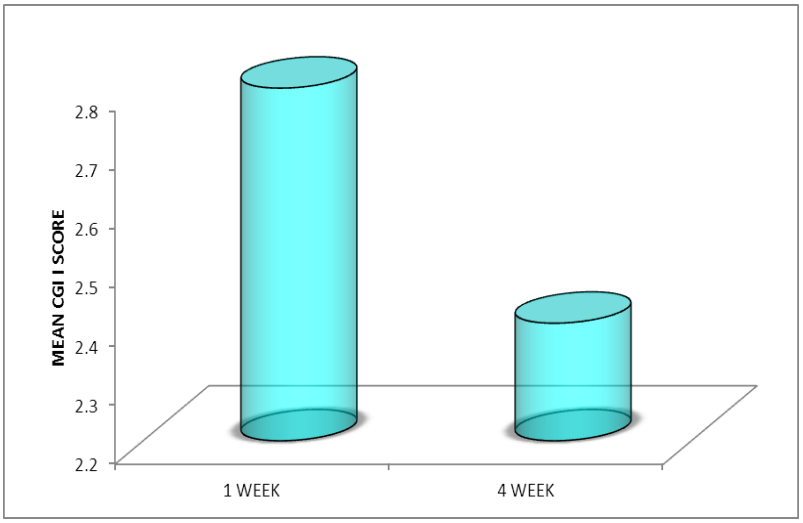

Figure No. 13: Mean change in CGI-I score at 1 week and 4 week end of the treatment

EFFICACY ASSESSMENTS BY BASELINE DEPRESSION SEVERITY SUBGROUP
MEAN CHANGE IN HAMD 17 ITEM TOTAL SCORE

Table No. 14: Mean change in HAMD score from baseline to 4 week end of the treatment by baseline depression severity subgroup

		MODERATE	SEVERE	VERY SEVERE
		Mean(Std Dev)	Mean(Std Dev)	Mean(Std Dev)
HAMD	BASE LINE	17.77(0.98)	20.2(1.31)	25.54(2.94)
	1 WEEK	11.55(4.19)	11.1(4.17)	16.6(8.94)
	4 WEEK	4.88(3.4)	8.4(6.50)	12.4(10.60)

Table No.14 shows the. Mean change in HAMD 17 item total score from baseline to 4 week end of the treatment by baseline depression severity subgroup. From the table it was shown that mean change from baseline to week 4 on total HAMD score shows dramatically greater reduction. In moderate sub group patients have shifted from moderate to mild condition within 1 week and to normal condition within 4 week. In severe sub group, patients have shifted from severe to mild condition within 1 week and persist in same condition till 4 week. In very severe sub group, patients have shifted from very severe to moderate condition within 1 week and mild condition within 4 week.

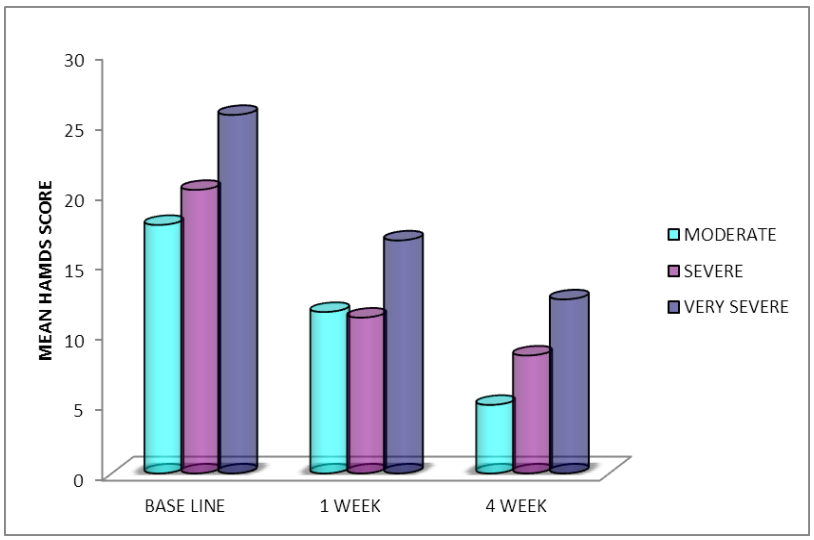

Figure No. 14: Mean change in HAMD score from baseline to 4 week end of the treatment by baseline depression severity subgroup

MEAN CHANGE IN MADRS TOTAL SCORE

Table No. 15: Mean change in MADRS score from baseline to 4 week end of the treatment by baseline depression severity subgroup

		MODERATE	SEVERE	VERY SEVERE
		Mean(Std Dev)	Mean(Std Dev)	Mean(Std Dev)
MADRS	BASE LINE	22.63(4.56)	30.72(1.27)	-
	1 WEEK	15.31(6.75)	23.81(5.70)	-
	4 WEEK	10.10(6.99)	6.90(7.8)	-

Table No.15 shows the. mean change in MADRS total score from baseline to 4 week end of the treatment by baseline depression severity subgroup. From the table it was shown that mean change from baseline to week 4 on total MADRS score shows greater reduction. In moderate sub group patients have shifted from moderate to mild condition within 1 week and persist the same condition till 4 week. In severe sub group, patients have shifted from severe to moderate condition within 1 week and to recovered state within 4 week.

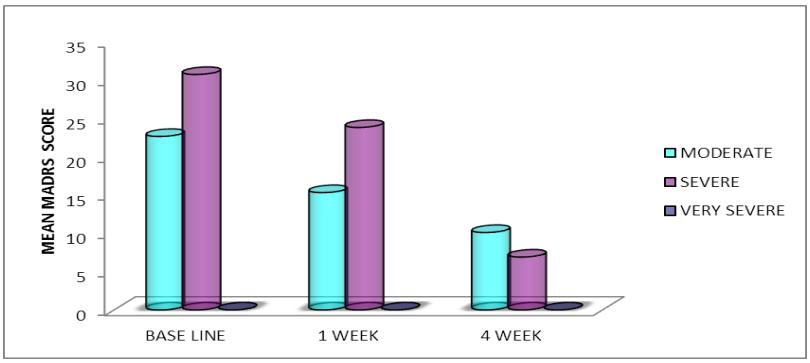

Figure No. 15: Mean change in MADRS score from baseline to 4 week end of the treatment by baseline depression severity subgroup

MEAN CHANGE IN CGI-S SCORE

Table No. 16: Mean change in CGI-S score from baseline to 4 week end of the treatment by baseline depression severity subgroup

		MODERATELY ILLNESS	MARKEDLY ILLNESS	SEVERELY ILLNESS
		Mean(Std Dev)	Mean(Std Dev)	Mean(Std Dev)
CGI-S	BASE LINE	4 (0.00)	5.0(0.00)	6.0(0.0)
	1 WEEK	2.9(0.23)	3.5(0.57)	6.0(0.0)
	4 WEEK	2.4(1.7)	3.0(2.0)	4.5(2.12)

Table No.16 shows the. mean change in CGI-S score from baseline to 4 week end of the treatment by baseline depression severity subgroup. From the table it was shown that mean change from baseline to week 4 on CGI-S score shows reduction. In moderate sub group patients have shifted from moderate to mild condition within 1 week and to borderline within 4 week. In markedly illness sub group, patients have shifted from markedly illness to moderately illness within 1 week and to mildly illness within 4 week. In severely illness sub group, patients have persisted in same condition till 1 week and shifted to moderately illness within 4 week.

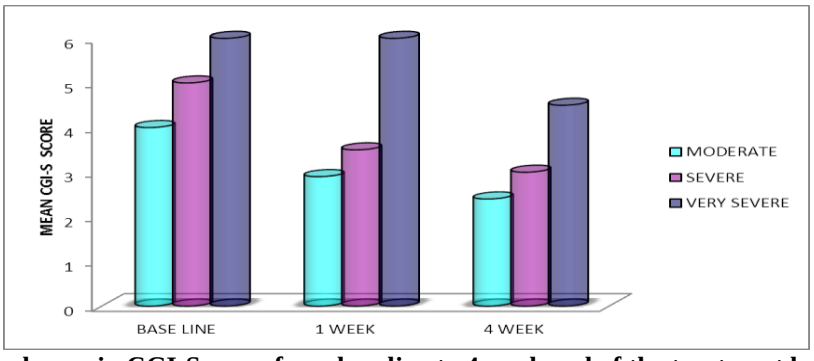

Figure No. 16: Mean change in CGI-S score from baseline to 4 week end of the treatment by baseline depression severity subgroup

EFFICACY ASSESSMENTS BY RESPONSE AND REMISSION RATES IN HAMD TOTAL SCORE AND MADRS TOTAL SCORE

7.17 RESPONSE RATES AT END OF 1 WEEK AND 4 WEEK IN HAMD TOTAL SCORE AND MADRS TOTAL SCORE

Table No. 17: Responders (≥50%improvement in HAMD total score/MADRS total score) at end of 1 week and 4 week

		FREQUENCY	PERCENTAGE
HAMD	1 WEEK	13/30	43.3 %
	4 WEEK	23/30	76.6 %
MADRS	1 WEEK	8/30	26.6 %
	4 WEEK	23/30	76.6 %

Table No.17 shows the. Percentage of responders at the end of 1 week and 4 week in HAMD and MADRS total score. From the table it is shown that in HAMD 43.3% of total patient shows response to the treatment at the end of 1 week and at the end of 4 week it has changed to 76.6%. In MADRS 26.6% of total patient shows response to the treatment at the end of 1 week and at the end of 4 week it has changed to 76.6%.

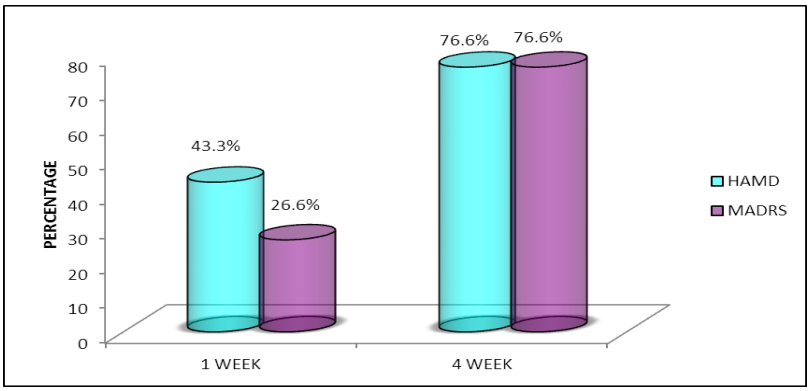

Figure No. 17: Responds (≥50%improvement in HAMD total score/MADRS total score) at end of 1 week and 4 week

REMISSION RATES AT END OF 1 WEEK AND 4 WEEK IN HAMD TOTAL SCORE AND MADRS TOTAL SCORE

Table No. 18: Remission (HAMD total score ≤ 7/MADRS total score ≤ 10) at end of 1 week and 4 week

		FREQUENCY	PERCENTAGE
HAMD	1 WEEK	3/30	10.0 %
	4 WEEK	17/30	56.6 %
MADRS	1 WEEK	6/30	20.0 %
	4 WEEK	23/30	76.6 %

Table No.18 shows the. Percentage of remission at the end of 1 week and 4 week in HAMD and MADRS total score. From the table it is shown that in HAMD 10% of total patient shows remission to the treatment at the end of 1 week and at the end of 4 week it has changed to 56.6%. In MADRS 20% of total patient shows remission to the treatment at the end of 1 week and at the end of 4 week it has changed to 76.6%.

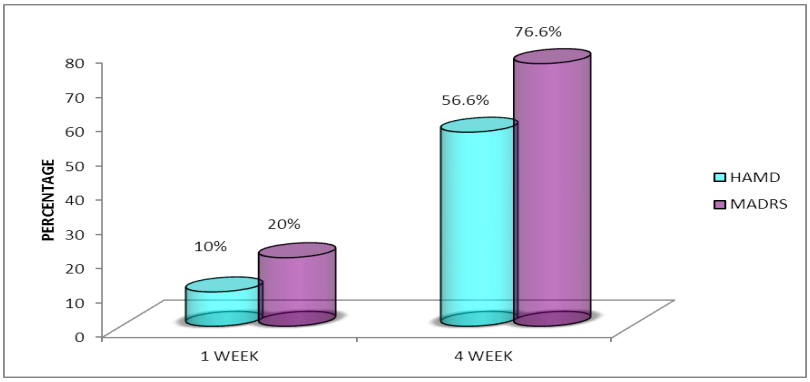

Figure No. 18: Remission (HAMD total score ≤ 7/MADRS total score ≤ 10) at end of 1 week and 4 week

DRUG RELATED SAFETY BY DESCRIBING ADVERSE EFFECT OF DRUG

Table No. 19: ADVERSE EFFECT OF VILAZODONE

ADR	FREQUENCY	PERCENTAGE
No ADR	9	30 %
Diarrhea	13	43.6 %
Manic Attack	2	6.6 %
Fatigue	1	3.3 %
Dry Mouth+Fatigue	1	3.3 %
Confusion+Fatigue	1	3.3 %
Decreased libido+Diarrhea	1	3.3 %
OCD+Tremor	1	3.3 %
Tremor+Diarrhea	1	3.3 %

Table No.19 shows the adverse drug reaction of the drug in the study population. 43.6% of the total patients shows diarrhea, 6.6% shows manic attack, 3.3% shows Fatigue, 3.3% shows dry mouth and fatigue, 3.3% shows confusion and fatigue, 3.3% shows decreased libido and diarrhea, 3.3% shows OCD and tremor, other 3.3% shows tremor and diarrhea. 30% of the total population shows no ADR.

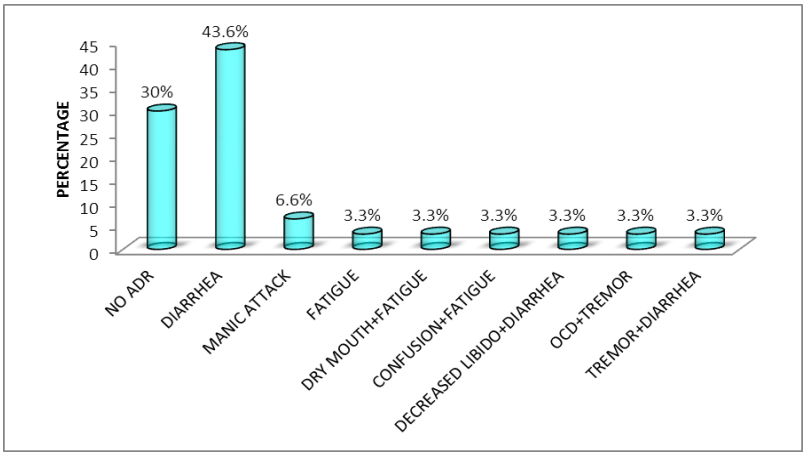

Figure No. 19: ADVERSE EFFECT OF VILAZODONE

DISCUSSION

The clinical course of depression is complicated by the strong correlation of depression to psychiatric and physical comorbidity. Though historically difficult to achieve owing to poor tolerability of available drugs, the goal of therapy for depression is remission and resolution of residual symptoms. A response to therapy, defined as a 50% reduction in the Hamilton Rating Scale for Depression (HAM-D) or a Montgomery-Asberg Depression Rating Scale (MADRS) score from baseline, was previously accepted as an appropriate therapeutic outcome. However, with the advent of newer and more tolerable drug therapies, the paradigm has shifted such that full remission is considered the only acceptable goal of therapy.

Vilazodone is a new antidepressant, which is effective safe for MDD, with a low occurrence of side effects. It offers promise as an effective oral drug for the treatment of MDD, with a balance of efficacy and safety.

In this study, we aimed to assess the efficacy and safety of Vilazodone in depression with in 4 week. For this purpose 30 depression patients were recruited from the department of psychiatry as per the selection criteria. The patients where provided will Vilazodone, ideally in monotherapy in the dose of 10mg/day for the first week and 20mg/day there after. Patients are assessed at baseline, at a 1 week follow up and at the 4 week study endpoint. We also assessed the safety of drug in study population by noting the adverse effect. Patient demographic details were collected and assessed.

Higher incidence of Depresssion was seen in the age range of 41-50 years (36.6%) and is followed by 31-40 years (30.0%). According to study by *Kessler et al*. high incidence of depression is found in adults between 25-44 years of age and the reason is mainly unknown.

Male patients constituted the majority in total study population 60% and rest of them females 40%. The total number of patients were selected as per the same criteria. Thus the difference in number of male and female is not comparable.

Most of the patient in study population were qualified upto degree (33.4%) and is followed by patient with HSE qualification (30%). Study conducted by *Avanthi et al*. shows that depression seen more in educated one than others.

In total population 73.35% were working and 26.7% were not working. According to study by *Mausner et al*. occupation may have a clear connection with disease state, and reveals that depression are more prevalent among working due to job stresses.

Most of the patient in the study population were married 73.3% and 26.7% were not married. According to the study by *Bolloch et al.* there is a clinically significant interplay exists between depression and marital status. The high prevalence of depression in marital status is mainly due to separation/divorced.

While categorizing the total population according to family history of psychiatric disease, 60% of total population were having family history of psychiatric disease, of that 20% patient is having history of depression. Study conducted by *Weissman et al.* reveals that depressive disorders tends to occur with in families and first degree relatives of patients with depression are 1.5 to 3 times more likely to develop depression than normal patients.

When the total population were categorized as per HAM.D depression Rating Scale majority of the patient were having very severe depression followed by severe and moderate depression.

The main objective of this prospective observational study was to assess the efficacy and safety of vilazodone in depression. In the study population depression symptoms was measured by HAM.D, MADRS, CGI-S and CGI-I from baseline, 1 week and 4 week. The mean change in HAM.D score, MADRS score and CGI-S score shows that vilazodone treated patient have statistically significant improvement in depressive symptoms within 1 week of treatment even though patient did not attain full therapeutic dosage from baseline to 1 week. The rating shows that depression severity have changed from severe or moderate condition to mild condition. *Taylor et al.* reveals that early improvement may enhance treatment compliance and lessen relapse or recurrence. Mean CGI-I score from baseline to first week shows that there is a minimal improvement in patient within 1 week. The overall score change in HAM.D, MADRS, CGI-S and CGI-I within one week support that vilazodone has more rapid onset of action and there by enhanced therapeutic efficacy.

At 4 week end point the mean score for the HAMD, MADRS and CGI-S shows that depressive symptoms were decreased and patient have enhanced mild or recovered depression stage. The mean score for CGI-I suggest that patient have much improvement from baseline to 4 week. Hence it was found that patient who underwent 4 week of treatment with vilazodone 20mg/day were found to have significant mean reduction in HAMD total, MADRS total, CGI-S score and CGI-I score, indicating improvement in disease state and the study result is supported by research conducted by *Zhang et al.* and reveals that vilazodone treated patient were found to have significant mean reduction in HAMD total, MADRS total, CGI-S score and CGI-I score in 4 week.

In this study efficacy assessment by baseline depression severity subgroup. reveals that mean change from baseline to week 4 on total HAMD score shows dramatically greater reduction .In moderate sub group patients have shifted from moderate to mild condition within 1 week and to normal condition within 4 week. In severe sub group, patients have shifted from severe to mild condition within 1 week and persist in same condition till 4 week. In very severe sub group, patients have shifted from very severe to moderate condition within 1 week and mild condition within 4 week. In MADRS total score moderate sub group patients have shifted from moderate to mild condition within 1 week and persist the same condition till 4 week. In severe sub group, patients have shifted from severe to moderate condition within 1 week and to recovered state within 4 week. By CGI-S score moderate sub group patients have shifted from moderate to mild condition within 1 week and to borderline within 4 week. In markedly illness sub group, patients have shifted from markedly illness to moderately illness within 1 week and to mildly illness within 4 week. In severely illness sub group, patients have persisted in same condition till 1 week and shifted to moderately illness within 4 week. Hence vilazodone is a better treatment option for depression in adults .The efficacy of vilazodone in treatment of MDD was established by *Rickels et al. and Khan et al.* in two 8 week trial studies and shows that significant mean reduction in HAM D score and MADRS score of vilazodone treated patient,indicating improvement in depressive symptomatology.

In the study additional efficacy assessment is done through respone and remission rate in HAM-D and MADRS. In HAMD 43.3% of total patient shows response to the treatment at the end of 1 week and at the end of 4 week it has changed to 76.6%. In MADRS 26.6% of total patient shows response to the treatment at the end of 1 week and at the end of 4 week it has changed to 76.6%. In HAMD 10% of total patient shows remission to the treatment at the end of 1 week and at the end of 4 week it has changed to 56.6%. In MADRS 20% of total patient shows remission to the treatment at the end of 1 week and at the end of 4 week it has changed to 76.6%. *Citrome et al.* analysed that significant outcome were obtained with vilazodone for MADRS response, remission and complete remission. Patients receiving vilazodone. Also met remission criteria for HAMD and CGI-S and hence treatment with vilazodone 20 mg/day may help adult patients with MDD achieve remission of depression.

The safety aspects of vilazodone is assessed by describing the Adverse effect of Vilazodone. The most frequent adverse effect noted were diarrhea (43.3%,), Manic attack(6.6%), Fatigue (3.3%), dry mouth and

fatigue,(3.3%) confusion and fatigue, (3.3%) decreased libido and diarrhea(3.3%), obsessive-compulsive disorder and tremor(3.3%), tremor and diarrhea (3.3%).30% of the total population shows no ADR. According to study by *Robinson et al*. side effect such as diarrhea, nausea, gastrointestinal AE are common in Vilazodone treated patient.

CONCLUSION

A very exciting concept for the treatment of depression is the novel antidepressant Vilazodone, a compound that exhibit a selective and potent serotonin reuptake inhibition and serotonin receptor partial agonistic action. The study result shows that patient treated with Vilazodone shows significant improvement in depressive symptoms within 4 week of treatment. Better response and remission rate in 1 week and 4 week indicate clinically better treatment effect for depression thereby improving overall disease burden. Vilazodone treatment is most efficacious in patient with severe symptoms and thereby prove the therapeutic benefit of drug across a spectrum of depressive severities. Treatment related side effect is also less and hence conclude that Vilazodone may become a unique treatment option for depression with a rapid onset, minimal side effect and enhanced therapeutic efficacy.

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