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Original Research Article

Comparison of Effectiveness of Vilazodone with Sertraline in Major Depressive Disorder

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Abstract:

Depression is a major mental disorder in which feelings of sadness, hopelessness, loss of interest, anger, frustration, or other negative emotions like irritability last for weeks or years and interferes with daily life. It is a common illness affecting people of all ages, genders, different socioeconomic groups and religions in India and all over the world. Globally, an estimated 322 million people were affected by depression in 2015. India is home to an estimated 57 million people (18% of the global estimate) affected by depression. We find limited literature regarding comparison of the newer drug Vilazodone with Sertraline. The results of the previous studies, most of which were conducted in the western countries, may not be completely applicable to the patients in our set up in with different genetic and environmental patterns. Hence this study is planned to compare efficacy of Vilazodone with Sertraline in patients suffering from depression in north Indian population.

Keywords: Major depressive disorder, Psychiatric disorder, Antidepressants, Vilazodone and Sertraline.

Introduction

Depression is a major mental disorder in which feelings of sadness, hopelessness, loss of interest, anger, frustration or other negative emotions like irritability last for weeks or years and interferes with daily life. It is a common illness affecting people of all ages, genders, different socioeconomic groups and religions in India and all over the world. Globally, an estimated 322 million people were affected by depression in 2015. India is home to an estimated 57 million people (18% of the global estimate) affected by depression [1]. Depression causes mental anguish and can impact people's ability to carry out even the simplest everyday tasks, with sometimes devastating consequences for relationships with family and friends. Untreated depression can prevent people from working and participating in family and community life. At worst, depression can lead to suicide. It is one of the leading causes of death among adolescents and adults globally. People with depression are more likely to die from suicide as well as from other illnesses, such as heart disease [2]. Depression is likely to be due to a complex combination of factors that

include various factors like genetics, biological (changes in neurotransmitter levels), environmental, psychological and social. There are numerous factors that can trigger the onset of depression, including bereavement, illness (such as cancer or chronic pain), social isolation or loneliness and stressful life events (such as divorce or money difficulties). Depression can also occur spontaneously, without any obvious cause [3].

Depression even the most severe cases, is treatable and if the treatment is started earlier, it is more effective. Once diagnosed, depression can be treated with medications, psychotherapy or a combination of the two. Depression is a treatable mental illness. There are various components to the management of Depression which include support, ranging from discussing practical solutions and identifying the contributing stressors, to educating family members regarding it. Psychotherapy, also known as talking therapies, such as cognitive behavioral therapy (CBT) and drug treatment, specifically antidepressants are commonly used. If these treatments do not reduce symptoms electroconvulsive therapy is given [4]. Other methods include Transcranial magnetic stimulation (TMS) which is a noninvasive method used to stimulate small regions of the brain [5].

Antidepressants are classified as 1) Tricyclic antidepressants (TCAs) 2) Selective serotonin re-uptake inhibitors (SSRIs) 3) Serotonin and norepinephrine reuptake inhibitors (SNRIs) 4) Serotonin receptor modulators (SRMs) or atypical antidepressants 5) Monoamine oxidase inhibitors (MAOIs). Currently available antidepressants work on the monoamine-based mechanism of action and enhance either singly or in combination, serotonergic, noradrenergic, and to a lesser extent dopaminergic neurotransmission. TCAs have heterogeneous effects on neurotransmitter systems. Though they are very effective, but tend to cause more-severe side effects than newer antidepressants [6].

Antidepressants usually take 2 to 4 weeks to work [7]. Often symptoms such as sleep, appetite and concentration problems improve before mood lifts, so it is important to give medication a chance before reaching a conclusion about its effectiveness. Most clinically useful antidepressant drugs potentiate, either directly or indirectly the actions of norepinephrine and serotonin in the brain.

Vilazodone was approved in 2011 by the FDA for use in the United States to treat major depressive disorder. 8 It enhances the release of serotonin across the brain's serotonergic pathways by inhibiting the serotonin transporter (like SSRIs) and by simultaneously stimulating serotonin 5-HT1A receptors via partial agonism (similar to the anxiolytic drug Buspirone). Because of this dual activity, Vilazodone is a serotonin partial agonist–reuptake inhibitor (SPARI). The dual mechanism of action is attributed to faster onset of antidepressant action and more rapid improvement of symptoms.

Vilazodone was found to be superior to placebo in improving depressive symptoms, asmeasured by MADRS scores. During these clinical trials, commonly observed adverse reactions included diarrhea, nausea, insomnia, and vomiting [9]. Vilazodone may have a small adverse impact on sexual function in adults with MDD relative to the high prevalence of sexual dysfunction at baseline [10]. In contrast to other SSRIs, Vilazodone did not cause significant weight gain or decreased sexual desire or function as with many other antidepressants [11].

It causes less somnolence and it's a weight neutral drug and is generally very well tolerated. Despite the theoretical superiority and the claim of Vilazodone having novel dual mechanism of action, faster onset of action, more appropriate pharmacologically complete action and fewer side effects, in

clinical trials and practice this has not been established as yet.

Sertraline is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class. Inhibits neuronal uptake of serotonin in the CNS, thus potentiating the activity of serotonin, has little effect on norepinephrine or dopamine.

Sertraline is primarily prescribed for major depressive disorder in adult outpatients as well as obsessive-compulsive disorder, panic disorder and social anxiety disorder, in both adults and children.

Sertraline had much lower rates of adverse effects than these TCAs, with the exception of nausea, which occurred more frequently with Sertraline. Most common adverse reactions (>5% and twice placebo) in pooled placebo controlled clinical trials were nausea, diarrhea/loose stool, tremor, dyspepsia, decreased appetite, hyperhidrosis, ejaculation failure and decreased libido [12].

Significant numbers of patients show inadequate response or discontinue medication due to intolerable side effects. Residual symptoms and poor treatment adherence are two of the main risk factors for relapse with current therapies. Hence, there is a need for an antidepressant that is relatively more efficacious, has an earlier onset of action and is better tolerated. This will help to decrease patient suffering, risk of suicide and economic burden of depression. However we find limited literature regarding comparison of the newer drug Vilazodone with Sertraline. The results of the previous studies, most of which were conducted in the western countries may not be completely applicable to the patients in our set up in with different genetic and environmental patterns. Hence this study is planned to compare efficacy of Vilazodone with Sertraline in patients suffering from depression in north Indian population.

The aim of this study was to compare the effectiveness of Vilazodone with Sertraline in the treatment of Major Depressive Disorder.

Objectives

1. The primary efficacy outcome was measured by comparing the reduction in the score of Hamilton Depression Rating Scale (HDRS) or HAM– D, Montgomery– Asberg Depression Rating Scale (MADRS), Arizona Sexual Experience Scale (ASEX) in the two study groups.
2. The secondary efficacy outcome was measured by comparing the reduction in the score of Clinical Global Impression - Severity (CGI- S), Clinical Global Impression- Improvement (CGI-I), Clinical Global Impression– Efficacy Index scales and the comparison of safety profile of the two study drugs by comparing the adverse effect reports in the two study groups.

Methods:

Study Design: An eight-week randomized, prospective and comparative study. The study was conducted at Indira Gandhi Medical College, Shimla, (H.P.) which is a tertiary care center of Himachal Pradesh, and caters a large number of population of this state.

Methodology: Newly diagnosed patients of Major Depressive Disorders (MDD) attending Psychiatry out- patient department (OPD) of I.G.M.C. Shimla were screened for enrollment in the study by the Psychiatrist from 25th September 2017 to 1st September 2018 on his respective OPD days. The eligible patients fulfilling following inclusion and exclusion criteria and consenting to participate after signing the informed consent were enrolled in the study.

Participants in Group– A received Vilazodone 10 mg of the drug once a day at bedtime with meals for one week, then increased to 20 mg/ day upto 8 weeks (and a maximum dose of upto 40 mg/ day as decided by the Psychiatrist). The

participants in Group – B received Sertraline 50 mg of the drug once a day in the morning with meals (which was increased maximum upto 200 mg as per need as decided by the Psychiatrist) for 8 weeks.

These drugs were advised to be taken under supervision of a responsible attendant or a legal guardian to avoid serious complications and were told to report immediately in case of any serious side effect or sudden fluctuation in the mood.

First follow up was done at after 2 weeks to compare the onset of treatment response between the two groups and then after 8-weeks. It included history, examination, application of HDRS, MADRS, ASEX, CGI scales and side effects if any reported by the participants or noticed by the Psychiatrist. Doses of the drugs were 16 adjusted depending upon the patient's condition during the follow up or on the basis of side effects as per the need as felt by the Psychiatrist. Telephonic interview was also done to remind the participants to ensure follow up and avoid loss to follow up. Final assessment was done at the end of 8-weeks. Blood investigations like Hb, TLC, DLC, ESR, Blood sugar, Thyroid Function Tests etc. and other investigation like CT scan of head were to be carried out as advised by the Psychiatrist. The participants were monitored throughout the study period for adverse effects.

Inclusion criteria:

1. Patients within the age group of 18-65 Years.
2. Diagnosis of MDD according to ICD-10 criteria with Hamilton Depression Rating Score> 17.
3. Patient consenting himself or through his or her legal guardian when patient is unable to give their consent.

Exclusion criteria:

1. Current diagnosis other than MDD as per ICD-10 criteria.
2. Substance dependence/ abuse.
3. Clinically significant/ unstable medical illness.
4. Women who were pregnant/ nursing or planning conception.
5. Patients judged to be at suicidal risk or too serious to be included in the study.
6. Had received Electro Convulsive Therapy (ECT) within one month before being enrolled into the study. 15
7. Required treatment with anticonvulsants, other antidepressants, psychostimulants or other antipsychotic drugs concurrently with study medications (except treatment for insomnia).
8. Schizoaffective disorder or bipolar disorder.
9. Concurrent major illness or systemic dysfunction involving hepatic and renal system.

Statistical analysis: The data was entered into MS Excel spreadsheet, cleaned and analysed using Epi info version 7.2.2.6 software. Categorical variables were presented as frequencies, percentages and proportions of each. Continuous variables were presented as Means ± Standard Deviation (S.D.) respectively. The normality of data was assessed using Shapiro Wilk test. The dichotomous categorical variables were analysed using Pearson's Chi Square test or Fischer Exact test. The mean of two groups was compared using Student t- test. The pre and post mean scores in one group were compared by using Paired t- test. Two tailed p-Value < 0.05 was considered statistically significant for all analysis.

Results: The present study was conducted on an outpatient basis in the Department of Psychiatry at Indira Gandhi Medical College, Shimla, H. P. in 2017-2018. The study was randomized, prospective and comparative. A total of eighty patients of MDD attending psychiatric outpatient department, who fulfilled the inclusion and exclusion criteria and who agreed to participate in the study by giving written informed consent were included as cases.

Total of eighty participants were enrolled. After a baseline assessment, patients were randomized to either of the two treatment groups through block randomization technique. Forty participants received Vilazodone (Group- A) and forty participants received sertraline (Group- B). There were two follow ups done one after 2 weeks and other after 8 weeks respectively.

A) Socio demographic Distribution:

I) Age and Sex distribution:

Demographic variables of age and gender were well controlled and matched in both the groups, having mean values for age 41.60 ± 11.16 years versus 38.70 ± 11.78 years, (p = 0.262) in the Vilazodone and Sertraline group, respectively. The mean values for gender (females) came out to be 47.90% (n=23) versus 52.10% (n=25), respectively, (p = 0.820). Majority of the patients were in the age group of 36- 55 years 53.80% (n = 21) and 46.20% (n = 18) in groups-A & B, respectively.

II. Locality: The participants in Vilazodone group from rural area and urban area were 45.0% (18) and 55.0% (22) respectively. In Sertraline group 50.0% (20) from rural area and 50.0% (20) from urban area.

III. Marital Status: Majority of participants were married in two study groups. 24 out of 40 (60.0%) in Group- A and 25 out of 40 (62.50%) in Group- B respectively.

IV. Education: Most of the patients in the two study groups were matriculate or graduate in the two study groups. Only two participants were illiterate which were in Vilazodone group (Group- A).

V. Occupation: Majority of the study participants were employed in the two study groups.

VI. Socio Economic Status: Majority of participants were of lower middaye socio-economic class (Modified Kuppuswamy's Socioeconomic Scale) 18 out of 40 in Vilazodone group (Group – A) and 17 out of 40 in Sertraline group (Group – B).

VII. Baseline profile: It included Systolic blood pressure, Diastolic blood pressure, weight at start and Mini Mental State Examination (MMSE) which was comparable between the two study groups. The p – value showed no statistically significant difference in these parameters [Table 1].

Table 1: Baseline Profile

BaselineProfile	Vilazodone(Group – A) Mean ± S.D.	Sertraline (Group – B) Mean ± S.D.	P-Value
Systolic B.P.	123.95 ± 13.43	125 ± 9.81	0.609
Diastolic B.P.	77.30 ± 7.87	78.05 ± 6.71	0.648
Weight At Start	60.53 ± 7.37	50.97 ± 6.92	0.474
MMSE	28.05 ± 1.43	28.15 ± 1.35	0.749

B) Hamilton Depression Rating Score (HDRS) or HAM- D, Montgomery–Asberg Depression Rating Scale (MADRS), Clinical Global Impression - Severity (CGI- S), Clinical Global Impression- Improvement (CGI- I), Clinical Global Impression -Efficacy Index Scales, Arizona Sexual Experience Scale (ASEX).

I. Baseline HAM-D, MADRS, ASEX, CGI-S Scores. The mean values of HAM- D score was 23.35± 3.22 in Vilazodone group (Group- A) and 23.50 ±2.98 in Sertraline group (Group- B) respectively at baseline. The difference in the baseline score between the two groups exhibited a p-value of0.829 which was statistically non – significant. The mean values of MADRS scorewas28.65 ± 3.65 in Vilazodone group

(Group- A) and 28.90 ± 3.76 in Sertraline group (GroupB) at baseline. The difference in the baseline score between the two groups exhibited a p-value of0.764 which was statistically non – significant [Table 2].

Table 2: Baseline scores of HAM-D, MADRS, ASEX, CGI-S scales

BaselineProfile	Vilazodone (Group – A) Mean ± S.D.	Sertraline (Group – B) Mean ± S.D.	P-Value
Systolic B.P.	123.95 ± 13.43	125 ± 9.81	0.609
Diastolic B.P.	77.30 ± 7.87	78.05 ± 6.71	0.648
Weight at start	60.53 ± 7.37	50.97 ± 6.92	0.474
MMSE	28.05 ± 1.43	28.15 ± 1.35	0.749

The mean values of ASEX score was 17.85 ± 5.83 in Vilazodone group (GroupA) and 17.10 ±5.36 in Sertraline group (Group- B) at baseline. The difference in the baseline score between the two groups exhibited a p-value of0.551 which was statistically non – significant.

The mean values of CGI-S score was 4.32± 0.89 in Vilazodone group (Group- A) and 4.38 ± 0.74 in Sertraline group (Group- B) at baseline. The difference in the baseline score between the two groups exhibited a pvalue of 0.785 which was statistically non-significant.

II. HAM- D, MADRS, ASEX, CGI- I Scores after 2 weeks

The mean values of HAM-D score after 2 weeks in Vilazodone group was 18.83 ± 3.52 (Group – A) and 19.68 ± 3.11 in Sertraline group (Group-B) respectively.

The difference in the baseline score between the two groups exhibited a p-value of 0.255 which was statistically non – significant.

The mean values of MADRS score was 23.20 ± 4.01 in Vilazodone group (Group – A) and 24.28 ± 3.90 in Sertraline group (GroupB). The difference in the baseline score between the two groups exhibited a p-value of 0.228 which was statistically non – significant [Table 3].

Table 3: Baseline scores of HAM-D, MADRS, ASEX, CGI-S scales

Scales	Vilazodone (Group - A) Mean ± S.D.	Sertraline(Group – B) Mean ± S.D.	P-Value
HAM-D	18.83 ± 3.52	19.68 ± 3.11	0.255
MADRS	23.20 ± 4.01	24.28 ± 3.90	0.228
ASEX	16.82 ± 4.89	16.58 ± 4.72	0.817
CGI-I	2.88 ± 0.52	2.90 ± 0.63	0.847

III. HAM-D, MADRS, ASEX, CGI-S, CGI-I, CGI – Efficacy Index scores at 8 weeks At the end of eight weeks, the mean HAM- D score was 10.85± 3.68 in Vilazodone Group (Group - A) and 10.53 ± 3.76 in Sertraline group (Group - B).

The p-value came out to be 0.69 which was statistically non-significant. The MADRS score 13.17 ± 4.40 in Vilazodone group, 13.85 ± 5.31 in Sertraline group (p = 0.538).The ASEX score was 14.43 ± 4.03 and 15.67 ± 4.08 in Vilazodone group and Sertraline group respectively at the end of eight weeks.

III. HAM-D, MADRS, ASEX, CGI-S, CGI-I, CGI Efficacy Index scores at 8 weeks

At the end of eight weeks, the mean HAM-D score was 10.85± 3.68 in Vilazodone Group (Group - A) and 10.53 ± 3.76 in Sertraline group (Group - B).The p-value came out to be 0.69 which was statistically non-significant. The MADRS score 13.17 ± 4.40 in Vilazodone group, 13.85 ± 5.31 in

Sertraline group (p = 0.538).The ASEX score was 14.43 ± 4.03 and 15.67 ± 4.08 in Vilazodone group and Sertraline group respectively at the end of eight weeks [Table 4].

Table 4: Scores of HAM- D, MADRS, ASEX, CGI-S, CGI- I, CGI- Efficacy Index at 8 weeks

Scales	Vilazodone Group (Mean ± S.D.)	Sertraline Group (Mean ± S.D.)	P - Value
HAM- D	10.85 ± 3.68	10.53 ± 3.76	0.697
MADRS	13.17 ± 4.40	13.85 ± 5.31	0.538
ASEX	14.43 ± 4.03	15.67 ± 4.08	0.172
CGI- S	2.20 ± 0.85	2.18 ± 0.90	0.899
CGI- I	1.82 ± 0.68	1.72 ± 0.64	0.499
CGI - EfficacyIndex	2.60 ± 2.20	2.46 ± 1.60	0.751

The CGI- S score at the end of eight weeks was 2.20 ± 0.85 and 2.18 ± 0.90 in Vilazodone and Sertraline group respectively.

The CGI- I score was 1.82 ± 0.68 and 1.72 ± 0.64 in Vilazodone and Sertraline group respectively (p= 0.499).The CGIEfficacy Index in Vilazodone group was 2.60 ± 2.20 and 2.46 ± 1.60 in the Sertraline group. The difference in the scores had a p– value of 0.751 which was statistically non – significant.

C) Side effects profile in the two study groups:

Table 5 states the side effects profile in both the group.

Table 5: Comparison of side effects in both groups

Side Effects	Vilazodone (Group-A)	Sertraline (Group-B)	P-Value
Diarrhoea	9 (47.4%)	10(52.6%)	0.793
GI upset	4 (21.1%)	15(78.9%)	**0.004**
Headache	10(62.5%)	6 (37.5%)	0.264
Nausea	14(56%)	11(44%)	0.469
Vomiting	4 (57.1%)	3 (42.95)	0.692
Dizziness	7 (46.7%)	8 (53.3%)	0.775
Insomnia	7 (50%)	7 (50%)	1.00
Sweating	1 (14.3%)	6 (85.7%)	**0.048**
Tiredness	2 (20.0%)	8 (80%)	**0.043**
Abnormal dreams	4 (66.7%)	2 (33.33%)	0.396
Reduced sexual drive	6 (37.5%)	10(62.5%)	0.533
Abnormal orgasm	4 (36.4%)	7 (63.6%)	0.330
Interference in arousal	1 (33.3%)	2 (66.7%)	0.556

Discussion: Major depressive disorder (MDD) is a widespread, debilitating illness. According to the World Health Organization (WHO), unipolar depressive disorders rank third among leading causes of global disease burden [13]. Depression is often recurrent, and leads to medical and psychiatric morbidity, functional disability and steep health care costs.89While long-term treatment decreases the odds of relapse by as much as 70%, only 25%– 50% of patients comply with their prescribed regimen. Lack of efficacy, in addition to tolerability issues like sexual dysfunction, is often behind cases of noncompliance [14].

The efficacy of existing antidepressant medications is limited. Response rates in major depression are generally in the 50%–70% range, and remission averages 30% (for instance, 28% remission to Citalopram as rated by Hamilton Depression Rating Scale (HDRS) or HAM-D and 33% rated by Quick Inventory of Depressive Symptomatology – self-related [QIDS-SR] in the STAR*D study. Whether antidepressants have any efficacy at all was questioned in a meta- analysis [14].

Emerging data from Vilazodone clinical trials and secondary data analyses have now begun to address possible benefits of quicker onset, greater efficacy, and better tolerability [15]. However, like a faster onset of action, this property has not yet been shown in head-to-head trials of Vilazodone versus an SSRI either. There is limited data of comparison of Vilazodone with Sertraline (SSRI) regarding safety and efficacy. Thus the present study was designed to compare the effectiveness of Vilazodone with Sertraline in the treatment of major depressive disorders. In this study the following results were obtained.

In the present study, mean age of the participants was 41.60 ± 11.16 years in Vilazodone group (Group-A) while in the Sertraline group (Group- B) it was 38.70 ± 11.78 years showing anon-significant difference as the p-value was 0.262. In this study, majority of the patients (52.5%) and (45%) in the groups-A & B were in the age group of 35-55 years, respectively followed by 18 – 34 years in both the groups. The most common time of onset is in a person's 20s and 30s [16]. Adults aging 30 to 60 tend to have a lot going on that can trigger depression: caring for children as well as aging parents, financial stress, isolation, work and relationship issues, menopause and peri- menopause, dealing with major illnesses, and lots of responsibilities. In the World Mental Health surveys, the median reported age of onset of MDD is in the mid - 20s, with the inter quartile range indicating that across all countries the peak risk period for onset of MDE ranged from mid to late adolescence to the early 40s [17].

In this study, the mean values for gender (females) came out to be 47.9% (23) in Vilazodone group (Group-A) while it was 52.1% (25) in the Sertraline group (GroupB) with p - value of 0.820 which shows the difference in the two group was nonsignificant. Females are affected about twice as often as males.83, 84 Other biological and hormonal factors are also likely to increase the chances of suffering from depression. Issues with pregnancy, fertility, peri- menopause, menopause, and menstrual cycles increase women's risk factors of developing depression as documented in a report [18]. Female preponderance to depression is also depicted in this study.

In this study 55.0% (22) in Vilazodone group and 50.0% (20) in the Sertraline group lived in urban area and 45.0% (18) and 50.0% (20) in the Sertraline group lived in rural area of Himachal Pradesh, respectively. There was a non-significant difference in locality distribution in both the groups (p -value = 0.823). Lifetime rates are higher in the developed world (15%) compared to the developing world (11%) [19]. The European Study of the Epidemiology of Mental Disorders (ESEMeD 2000 study) in 2005 is a cross-sectional, in-person, household interview survey which confirmed previous findings on the variation in mood disorders between rural and urban areas. Overall, urbanization seemed to be linked to a higher risk of mental health disorders, particularly depressive disorders [20]. In our study, 49.0% (24) in Vilazodone group and 51.0% in the Sertraline group were married. The number of participants who were unmarried, widow or separated were comparatively less in both the groups. The p-value of 0.182 signified that there was non-significant difference in both the groups. Marital dissatisfaction and discord are strongly related to depressive symptoms

as documented by National Comorbidity Survey [21], With an average correlation between marital dissatisfaction and depressive symptoms across studies and very similar patterns for men and women. This is seen in this study also [21].

In our study 39.4% (13) were graduate and 15(65.2%) were matriculate in the Vilazodone group. In the Sertraline group 60.6% (20) were graduate and 34.8% (8) were matriculate. The p-value of 0.122 showed statistically non-significant difference education wise. Only 2 participants out of 80 were illiterate. Lifetime rates are higher in the developed world (15%) compared to the developing world (11%). Several studies show that early-onset mental disorders are associated with termination of education [22].

In the present study 25.0% (10) participants were employed, 15.0% (6) were agriculturist, 7.50% (3) were students, 25.0% (10) were homemaker,20.0% (8) were unemployed, 0.5% (1) retired and 5.0% (2) were doing business in Vilazodone group. In the Sertraline group 37.5% (15) participants were employed, 25.0% (10) were agriculturist, 12.5% (5) were students, 15.0% (6) were homemaker, none were unemployed, 7.50% (3) retired and 2.50% (1) were doing business. There was statistically non-significant difference between the two groups as suggested by the pvalue of 0.412. Lifetime rates are higher in the developed world (15%) compared to the developing world (11%). Although depression is known to be associated with unemployment, most research on this association has emphasized the impact of job loss on depression rather than depression as a risk factor for job loss [23].

In a study the Vilazodone group, no participant belonged toupper socio-economic class, 20.0% (8) belonged to upper middle class, 45.0% (18) to lower middle class, 32.5% (13) to upper lower class, 2.5% (1) belonged to low socio-economic class. In the Sertraline group 2.50% (1) one participant belonged to uppersocio- economic class, 12.5% (5) belonged to upper middle class, 42.5% (17) to lower middle class, 40.0% (16) to upper lower class, 2.5% (1) belonged to low socio-economic class [24].

There was no statistically significant difference between the two groups in this regard (p= 0.212). There was a COURAGE survey conducted in Finland, Poland and Spain between 2011 and 2012 [25]. It was a crosssectional, general population survey of non-institutionalized adults (aged ≥ 18 years), 35 (n= 10,800 individuals: Finland 1976; Poland 4071; and Spain 4753). It illustrated that for each country, higher education and a higher socio-economic status index score act as protective factors against depression. A higher income was associated with lower odds of having depression in Finland and Poland, but not in Spain [25]. However, it is unclear whether depression is a cause, consequence, or both in these associations owing to the possibility of reciprocal causation between income earnings and MDD.

The baseline HAM- D score was 23.35 ± 3.22, MADRS score 28.65 ± 3.65, ASEX score 17.85 ± 5.83, CGI- S score 4.32 ± 0.89 in the Vilazod one group (GroupA).While in the Sertraline group (Group- B) the baseline HAM-D score was 23.50 ± 2.98, MADRS score 28.90 ± 3.76, ASEX score 17.10 ± 5.36, CGI- S score 4.38 ± 0.74. The p- value of 0.829 suggests that the difference in the baseline scores of the scales used was statistically non-significant. The baseline score of CGI-I scale was done after 2 weeks.

The change in the HAM- D score with Vilazodone (Group – A) at the start of treatment and at the first follow up after two weeks was 4.525 ± 2.050 with a p-value of < 0.001 which is highly significant. This shows that the response started after one week of treatment. This is also observed in a pooled analysis [26]. which aimed to assess the efficacy of Vilazodone across a

range of symptoms and severities of depression. The study, by including 431 Vilazodone treated and 432 placebo treated patients compared the efficacy of Vilazodone and a placebo. Vilazodone showed statistically significant differences that were apparent from week 1 ($p< 0.01$, all weeks). Similar results were also noted for HDS, CGI-S, and CGI-I scores [26].

In a post hoc analysis [27], which contained pooled data from the two pivotal phase III trials, showed significant superiority of Vilazodone in cumulative response rates which was evident from week 1 ($p< 0.05$), and the time to cumulative response was quicker in the Vilazodone group than the placebo group ($p< 0.0001$). There was a significant reduction in MADRS score of 5.450 ± 2.207 after two weeks with Vilazodone (p-Value < 0.001). The ASEX score was also reduced by 1.025 ± 2.082 (p-value=0.003). This shows the response started early after two weeks of treatment with Vilazodone.

In a study [22]. in which data sources were three Phase III studies: two 8- week, placebo-controlled studies and a 52- week openlabel study. Sexual function was assessed by analyzing changes from baseline to end of treatment using validated measures. Population included 869 patients (Vilazodone, 36 436; placebo, 433) from placebo-controlled studies and 599 patients from the openlabel study. Sexual dysfunction prevalence was high (50%, men; 68%, women) before treatment and declined during treatment in Vilazodone and placebo groups, indicating improvement on average. At the end of treatment, stable/improved sexual function was observed in ≥ 91% of patients in placebo-controlled studies. Differences vs. placebo in changes from baseline of sexual function scores were small and were generally not statistically significant. Half of men and two thirds of women with MDD had sexual dysfunction at baseline; sexual function improved on average in both Vilazodone and placebo groups.

The change in the HAM-D score with Vilazodone (Group – A) from the start of treatment and at the second follow up after eight weeks was 12.50 ± 4.45 (p-value of < 0.001) which is highly significant. There was a significant reduction in MADRS score of 15.47 ± 4.972 after eight weeks with Vilazodone (p-Value< 0.001). The ASEX score was also reduced by 3.43 ± 4.840 (p-value=0.003). This shows a significant improvement with Vilazodone in treating depression and also not increasing sexual dysfunction [8]. The CGI-S score reduced by 2.50 ± 1.086 (p-value of < 0.001) and CGII score improved by 1.050 ± 0.714 (p-value< 0.001) [27]. This shows a significant improvement with Vilazodone in treating depression. The change in the HAM-D score with Sertraline (Group – B) from the start of treatment and at the first follow up after two weeks was 3.825 ± 1.534 (p-value of < 0.001) which is highly significant. This reduction is less compared to that shown by Vilazodone but the difference is statistically non-significant which is shown by a pvalue of 0.225. Thus in this study both Vilazodone and Sertraline led to a significant reduction in HAM-D score but there was not a significant difference between the response of the two drugs in reducing HAM-D score after two weeks of treatment.

There was a significant reduction in MADRS score of 4.625 ± 1.807 after two weeks with Sertraline (p-Value < 0.001). The ASEX score was also reduced by 0.525 ± 1.502 (p-value=0.03). But this reduction is less compared to Vilazodone which shows Sertraline causes less improvement in the sexual dysfunction in the patient suffering from major depressive disorder compared to Vilazodone but this difference was not statistically significant (p - value = 0.817).

The change in the HAM-D score at the start of treatment and at the second follow up after eight weeks was 12.975 ± 3.059 (p-value< 0.001) which is highly significant.

However the difference between Sertraline and Vilazodone was statistically non-significant (p-value of 0.697). This result shows comparable effectiveness of Vilazodone and Sertraline in reducing HAM-D score after eight weeks of treatment. There was a significant reduction in MADRS score of 15.050 ± 4.332. The CGI-S score reduced by 2.200 ± 0.966 (p-value < 0.001) and CGI-I reduced by 1.175 ± 0.844(pvalue < 0.001).

This showed a statistically significant response with Sertraline in group B in the treatment of depression. This is also shown in some studies [28]. The CGI-Efficacy Index in Vilazodone group was 2.60 ± 2.20 and 2.46 ± 1.60 in the Sertraline group also seen in other studies. The difference in the scores had a p – value of 0.751 which was stastically non – significant. The ASEX score reduced by 1.425 ± 4.601 (p value = 0.05).

In this study the side effects reported in the Vilazodone group (Group – A) were nausea 35% (14), headache 25%(4), diarrhea 22.5%(9), dizziness17.5%(7), insomnia 17.5%(7), reduced sexual drive 15%(6), vomiting 10%(4), abnormal dreams 10%(4), gastrointestinal upset 10%(4), abnormal orgasm 10%(4), tiredness 5%(2), interference 38 in arousal 2.5%(1) and sweating 2.5%(1).

In a systematic review [29], greater incidence in Vilazodone - treated versus placebo-treated patients were diarrhea (28.0% vs 9.2%, respectively), nausea (23.4% vs 5.1%, respectively), dizziness (8.5% vs 4.6%, respectively), insomnia (6.0% vs 2.1%, respectively), vomiting (4.6% vs 1.2%, respectively), and abnormal dreams (4.1% vs 1.2%, respectively) which is similar to this study. A study also showed similar results [29].

No case of Serotonin syndrome was reported with Vilazodone (Group – A) in this group although Vilazodone has shown to cause it. A retrospective review [30] of two databases: the American Association of Poison Controls Centers' National Poison Data System (NPDS) and the American College of Medical Toxicology's Toxicology Investigators Consortium (ToxIC Registry) shows results during the 52-month study period, a total of 3192 Vilazodone human exposures were reported to NPDS. Of these, 1734 (54%) were isolated Vilazodone cases. Of these, 17 (74%) had Vilazodone listed as the first (primary) agent and 10 (43%) involved Vilazodone-only ingestions. Nine (39%) cases documented serotonin syndrome. reported one case report of a 28-year-old female with anxiety treated with Vilazodone. Prior to the initiation of Vilazodone, vital signs were normal and the patient exhibited no signs of excessive serotonin. The patient was prescribed Vilazodone with the appropriate 2-week titration per the FDA-approved prescribing information. During the first week, the patient reported excessive perspiration and gastrointestinal symptoms. On day 17 of Vilazodone therapy, the patient reported a major neurologic reaction and discontinued Vilazodone. The patient was diagnosed with possible serotonin syndrome.

The difference in the reports of diarrhea, headache, nausea, vomiting, dizziness, insomnia, abnormal 40 dreams, reduced sexual drive, abnormal orgasm and interference in arousal was comparable in the two study groups which was depicted by p-values which were statistically non-significant. However the incident of GI upset, sweating and tiredness was higher in the Sertraline group (Group-B) than in the Vilazodone group (Group-A). In Vilazodone group (Group-A) reports of GI upset were 21.1%(4) while in Sertraline group (Group-B) it was 78.9%(15) with a p-value 0.004 which was statistically significant. Increased gastrointestinal upset is seen with Sertaline [31]. Gastrointestinal (GI) disturbances are the most frequently reported side effects with SSRIs as documented [31].

In this study there has been a significant decrease in scores of HAM-D, MADRS, ASEX, CGI-S and CGI-I at the end of 8th week as compared to baseline Scores. The reduction in these scores showed a non-significant difference between the two groups. Results are indicating that the use of Vilazodone and Sertraline have resulted in significant improvement in symptoms of patients of MDD. Therefore, the findings reveal that both these agents are effective in the treatment of MDD. On comparing the efficacy, there was no statistically significant difference between the two groups i.e. Vilazodone and Sertraline in reducing the scores of HAMD, MADRS, ASEX, CGI-S and CGI-I after 8-weeks i.e. at the end of the study.

However, the reduction in ASEX score is in favour of Vilazodone group (Group – A) in our study though the difference is statistically non-significant. The literature suggesting significant early reduction in the scores of HAM-D, MADRS, ASEX, CGIS and CGI-I Scales with Vilazodone compared to SSRIs is however, not seen in this study as the reduction of the scores after 2 weeks was comparable in the two groups and the difference was statistically non-significant. One of the possible reasons for this difference in findings may be that the past studies were mostly from the West and the difference in genetic make-up of this study population from the western population could have been contributed to the difference in the result of this study.

Limitation:

The study was conducted at Indira Gandhi Medical College (I. G. M. C.) Shimla, H. P. which is one of the tertiary care hospitals of Himachal Pradesh. As the catchment area of the hospital includes both urban and rural areas, areas of different socioeconomic strata, a more representative sample of the population could be obtained. The study was conducted with a relatively sound methodology. However, the study had a few limitations.

This being a part of a time bound study, a large sample size could not be obtained. This study was of a duration of 8 weeks, so the comparison between the shortterm effectiveness of Vilazodone with Sertraline could be done in this study. The longterm comparison of safety and effectiveness between the two drugs could not be done in this study.

Conclusion:

In this study we found that Vilazodone and Sertraline are effective antidepressant drugs. Certain pharmacological characteristics of Vilazodone were observed, including fewer sexual side effect and minimal effect on weight gain, that may provide potential clinical advantages compared with currently available antidepressants. The mechanism of action of Vilazodone which suggested an earlier treatment response and to be more effective than Sertraline was however not found in this study. The reduction in HAM – D score was comparable in the two study groups which suggest almost equal effectiveness.

The side effect profile was comparable in the two study groups, but there was a significantly higher incidence of gastrointestinal upset, sweating and tiredness with Sertraline. The difference in the weight of the study participants at the beginning of the study and after eight weeks was statistically non-significant with Vilazodone and Sertraline, respectively. Vilazodone showed slightly less sexual dysfunction in the participants compared to Sertraline but the difference was statistically non-significant.

However, in order to generalize the results regarding comparison between Vilazodone and Sertraline regarding effectiveness and safety, more studies with a large sample size and longer duration are required in the near future.

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