A prospective randomized comparative study of safety and efficacy of vilazodone and fluoxetine in depression

Usha Rani H. Patted¹, Hema, N. G.² and Anil Kumar Mysore Nagaraj³,*

¹Medical Affairs Department, Novo Nordisk Global Business Services, Bengaluru, 560066, India;
²Department of Pharmacology, Mysore Medical College and Research Institute, Mysuru, 570001, India;
³Department of Psychiatry, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, 576104, India.

ABSTRACT

Depression is one of the leading causes of disease burden globally. Over the past 6 decades we have seen a multitude of antidepressants from different classes. Vilazodone is a novel antidepressant with the combination of serotonin reuptake inhibition and 5HT1A partial agonism. We wished to study its efficacy and safety in comparison to fluoxetine, in the Indian population. This is a 6-week prospective randomized open label comparative study of efficacy and safety of vilazodone and fluoxetine in patients with major depressive disorder. We recruited 72 subjects and 66 completed the study. We rated the overall severity and improvement in psychopathology by using CGI-S and CGI-I, respectively on three occasions, i.e. day 1, week 3 and week 6. We also recorded and compared the side effects of study medication with the checklist from the vilazodone prescribing information, during week 3 and 6. We compared the efficacy data using independent t test and repeated measures analysis of variance (ANOVA), and side effects using Pearson Chi-Square test. The socio-demographic data was evenly distributed except for literacy, which was significantly better in the vilazodone group. There was no significant difference in the efficacy of fluoxetine and vilazodone both at week 3 and week 6. However patients on vilazodone reported significantly higher gastrointestinal side effects. The efficacy of vilazodone is comparable to fluoxetine in the Indian population in the short-term treatment of depression, though associated with frequent gastrointestinal side effects. We need further blinded studies on long term efficacy and safety, with a larger sample size to generalize the results.

KEYWORDS: vilazodone, fluoxetine, efficacy, safety, major depression.

INTRODUCTION

Depression is a common mental disorder, though it is one of the leading causes of disability worldwide. WHO has predicted that by 2030 depression will be the leading cause of disease burden globally. More concerning fact is that about 15% of depressive patients commit suicide [1]. Effective treatment of depression is all the more important. After the availability of Imipramine in 1958, we have seen a multitude of antidepressants from different classes. Each new class and each new medication of a particular class is supposedly an improvised molecule from the previous ones. After Tricyclic antidepressants (TCAs) and Mono Amino Oxidase inhibitors (MAOIs), the second-generation antidepressants, that include Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) and other newer drugs, were considered safer as well as efficacious. Fluoxetine is the first approved SSRI and one of the most studied drugs among second generation antidepressants. It binds less potently...
to muscarinic, histaminergic, and $\alpha_1$-adrenergic receptors and other membrane receptors from brain tissue in vitro, than do the tricyclic drugs [2]. However, it has the limitation of long therapeutic lag. Its common side effects include nausea, nervousness and insomnia; and also has sexual side effects, though least compared to other SSRIs [3, 4]. Efficacy, safety and novel mechanisms of action play a key role in medication compliance as antidepressants may be needed for years in many patients with major depression.

The combination of serotonin reuptake inhibition with 5HT1A partial agonism (dual mechanism) has long been known by clinicians to enhance the antidepressant properties and tolerability of SSRIs and SNRIs in some patients. So in pursuit of a better medication, in 2011 vilazodone was introduced in US. It is the first member of the serotonin partial agonist-reuptake inhibitor (SPARI) class of medications. Thus vilazodone has a unique dual action i.e. serotonin transporter (SERT) inhibition, which is nothing but the action of a SSRI; and serotonin (5HT 1A) partial agonism. For this reason, vilazodone is called a SPARI [5]. Vilazodone is reported to show its antidepressant action as early as 2 weeks [6], in studies on western population. It is also associated with some GI side effects and insomnia, similar to fluoxetine [7]. We wanted to study the safety and efficacy of vilazodone in Indian population, in a head to head trial with fluoxetine, the prototype SSRI. The authors could not find any head to head comparative studies of vilazodone and fluoxetine when our project was initiated in 2016.

**MATERIALS AND METHODS**

This was a 6-week randomized, open-labelled, comparative, prospective, parallel group trial, conducted in a tertiary teaching hospital in the city of Mysuru in India, for 12 months, from January to December, 2016. The institutional ethics committee approval was obtained and the trial was registered in the Clinical Trials Registry of India (CTRI/2017/03/008202). The subjects were recruited through the computer-generated block randomization, with random number sequence table. Sample size (n) was calculated using the estimation technique with $\alpha$ error of 5%, effect size (d) 10%. According to the World Mental Health survey, the life time prevalence (p) of MDD in India is 11-14.6 % and 12-month prevalence is 5.5-6% [8].

We included all the consenting patients aged 18-60 yrs, male and female gender, diagnosed with Major Depressive Disorder according to DSM 5, [9] by the study psychiatrist. We included those who were diagnosed for the first time as well as those who had relapsed and were not on medication/ECT for at least 4 weeks at the time of screening for study. The exclusion criteria were the severe depressive episode that would interfere with insight to consent for the study, suicidal ideas, concurrent medical or psychiatric disorders and substance use disorders. Also, pregnant women and lactating mothers were not included.

This being a prospective study, we followed up the patients for 6 weeks. The first visit is the day of screening/enrolment (baseline visit), the second visit at the completion of 3 weeks, the third and last visit at the completion of 6 weeks. The patients seen and diagnosed as major depressive disorder according to DSM 5 [9] by the study Psychiatrist in the OPD or admitted to the inpatient by the psychiatrist, were screened. We recruited the consenting patients if found suitable for the study. We completed all study specific assessments on the same day in each visit.

To begin with, the socio-demographic data was obtained on the data sheet designed for the study. The modified BG Prasad’s socio-economic scale 2016 [10] was administered for assessing socio-economic status. Then the subjects’ severity of depression was rated on Clinical Global Impression-Severity scale (CGI-S) [11]. The CGI-S asks the clinician one question: “Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?” which is rated on the following seven-point scale: 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; 7 = among the most extremely ill patients. This rating is based upon observed and reported symptoms, behaviour, and function in the past seven days. Then a physical examination was done. In the end, according to the computer-generated randomization table, the medication was initiated.
Vilazodone was started as 10 mg, increased to 20 mg after a week and continued at same dose till the 2nd visit (week 3), if the score on CGI-S was 3 or 4 (mild to moderate). For the score 5 (severe) and above, it was further increased to 40 mg at the end of two weeks. Fluoxetine was started as 20 mg and continued at same dose for mild to moderate depression as above. For severe depression, it was increased to 40 mg after 1 week, till the 2nd visit.

In the second study visit after 3 weeks, re-assessment of severity of depression was done using CGI-S. Improvement in depression was assessed by Clinical Global Impression-Improvement (CGI-I) scale [11]. It is similarly simple in its format. The CGI-S score obtained at the baseline visit serves as a basis for making further assessment. For CGI-I, the following one query is rated on a seven-point scale: “Compared to the patient’s condition prior to medication initiation, his/her current condition is: 1 = very much improved since the initiation of treatment; 2 = much improved; 3 = minimally improved; 4 = no change from baseline (the initiation of treatment); 5 = minimally worse; 6 = much worse; 7 = very much worse since the initiation of treatment.” A routine physical examination was also carried out.

Then they were assessed on the adverse effects using an antidepressant side effect checklist adopted from vilazodone prescribing information 2011 [12]. The checklist consisted of symptoms from the domains of gastrointestinal (diarrhoea, nausea, dry mouth, vomiting, dyspepsia, flatulence, gastroenteritis), neurological (dizziness, somnolence, paraesthesia, tremor), psychiatric (insomnia, abnormal dreams, decreased libido, restlessness, abnormal orgasm), cardiac (palpitation), reproductive (erectile dysfunction, delayed ejaculation), musculoskeletal (arthralgia), metabolic and nutritional (decreased appetite), general (fatigue, feeling jittery), and others (if any). If there was any tolerance issue/adverse effect that could be harmful to patient, they were discontinued if they were on 20 mg dose; or dose reduced to 20 mg if they were on 40 mg, only if it was safe to continue in the study. Further, dose increase to 40 mg was done in the 2nd visit, in case of both the medication, if the patients on lower dose (20 mg) reported no improvement at all. No dose increase was done for those on higher dose (40 mg). If it needed further dose increase, then they would be excluded from study and referred to the psychiatrist for further treatment. The patients were also informed during the first visit that if they develop any clinical worsening or side effects, they can contact us and meet us in the hospital any time before the scheduled study visit.

The third study visit was done at the end of 6th week, consisting of re-assessment of severity of depression through the CGI-S. Improvement in depression was assessed by CGI-I scale. Treatment emergent adverse effects of fluoxetine and vilazodone were recorded on the check list. A routine physical examination was carried out. The subjects were prescribed the respective medication after the study ended, in discussion with them, if they were found to be responding to it and referred back to the psychiatry outpatient department.

After all the study subjects completed the study duration of 6 weeks, the data was analysed using the licenced version of the statistical software SPSS 20.0. Mean & SD was calculated for the demographic and clinical data of the sample. Cramer’s-V test was used to compare the demographic details. t test – independent samples was used to compare means between the two groups of subjects on the scores of CGI-S and CGI-I at all visits. Repeated measure ANOVA was used to measure the changes of CGI-S scores at Baseline, 3rd week and 6th week among the subjects within the same medication group. Adverse effects were compared using Pearson Chi-Square test. P value < 0.05 was considered statistically significant.

RESULTS

Seventy-six patients were assessed for eligibility and 72 of them were randomized to one of the two groups. Group I consisted of 36 patients on fluoxetine and Group II consisted of 36 patients on vilazodone. Between the first and second visits, one subject from the fluoxetine group discontinued due to gastric discomfort and two from the vilazodone group discontinued due to dizziness. Between the second and third visit, two were lost to follow up in the fluoxetine group and one subject from vilazodone group had started an alternate medication consulting a psychiatrist as he was not satisfied with the improvement. Thus 33 subjects from both groups completed the study. Data analysis included these 33 subjects.
Table 1. Comparison of scores on CGI-S across all study visits.

| Study visits | Fluoxetine group CGI-S scores (n=33) (Mean ± SD) | Vilazodone group CGI-S scores (n=33) (Mean ± SD) | P |
|--------------|--------------------------------------------------|-----------------------------------------------|---|
| Visit 1      | 3.37 ± 0.97                                      | 3.22 ± 0.95                                   | 0.517 |
| Visit 2      | 2.56 ± 0.67                                      | 2.4 ± 0.98                                    | 0.46 |
| Visit 3      | 1.97 ± 0.78                                      | 2.0 ± 0.92                                    | 0.884 |

Independent t test, p < 0.05 is significant.

Table 2. Comparison of scores on CGI-I across 2nd and 3rd study visits.

| Study visits | Fluoxetine group CGI-I scores (n=33) (Mean ± SD) | Vilazodone group CGI-I scores (n=33) (Mean ± SD) | P |
|--------------|--------------------------------------------------|-----------------------------------------------|---|
| Visit 2      | 2.56 ± 1.44                                      | 2.28 ± 1.3                                    | 0.42 |
| Visit 3      | 1.47 ± 0.72                                      | 1.75 ± 1.34                                   | 0.28 |

Independent t test, p < 0.05 is significant.
**Table 3.** Primary outcomes within the study groups.

| Rating Scales | Fluoxetine | Vilazodone |
|---------------|------------|------------|
|               | Mean ± SD  | P          | Mean ± SD  | P          |
| 3\textsuperscript{rd} week | 6\textsuperscript{th} week | 3\textsuperscript{rd} week | 6\textsuperscript{th} week |
| CGI – S       | 2.57 ± 0.67 | 1.97 ± 0.79 | <0.001   | 2.41 ± 0.98 | 2.00 ± 0.92 | 0.001 |
| CGI – I       | 2.56 ± 1.44 | 1.47 ± 0.72 | <0.001   | 2.29 ± 1.3 | 1.75 ± 1.34 | 0.067 |

p < 0.05 is statistically significant (using repeated measure ANOVA).

**Table 4.** Mean change in CGI-S scores within study groups.

| Visits | CGI-S scores (Mean ± SD) | Mean difference from baseline | P | CGI-S scores (Mean ± SD) | Mean difference from baseline | P |
|--------|--------------------------|-------------------------------|---|--------------------------|-------------------------------|---|
| Baseline | 3.37 ± 0.98               | 3.22 ± 1.01                   |   | 2.41 ± 0.98               | 0.81 ± 0.82                   | <0.001 |
| Week 3  | 2.57 ± 0.67               | 0.81 ± 0.74                   | <0.001 | 2.41 ± 0.98               | 0.81 ± 0.82                   | <0.001 |
| Week 6  | 1.97 ± 0.79               | 1.41 ± 0.98                   | <0.001 | 2.00 ± 0.92               | 1.22 ± 1.04                   | <0.001 |

Paired t test (The change in CGI-S mean scores from baseline to week 3 and week 6 visits was statistically significant within both study groups (p < 0.001))

**Figure 1.** Change in CGI-S scores at specific visits.

Visit, were no more differing significantly in 3\textsuperscript{rd} visit. Side effects from other systems/domains were uncommonly reported and were not significantly different across the groups. The specific side effect of dizziness was significantly higher in the vilazodone group at 2\textsuperscript{nd} visit, but at 3\textsuperscript{rd} visit it matched evenly with fluoxetine. Dry mouth was significantly high with fluoxetine during 2\textsuperscript{nd} visit; however it
However, doses could not be compared due to the different classes of drugs and lack of a standard equivalence comparator.

**DISCUSSION**

With the ongoing introduction of newer classes of antidepressants into market, transforming the pharmacological treatment of depression, the purpose of this study was to compare the efficacy and safety of vilazodone, an antidepressant having a novel mechanism of action (SPARI), with the traditional and time-tested fluoxetine (SSRI). This was an open label, prospective, randomized study of patients with major depression diagnosed according to DSM 5. Total subjects recruited were 72 and total completing the study was 66. We compared 33 subjects each receiving fluoxetine and vilazodone for efficacy and safety, as 3 subjects in both groups discontinued at different stages of the study.

### Table 5. Comparison of side effect domains across the groups.

| Side effects       | 3<sup>rd</sup> week (Visit 2) | 6<sup>th</sup> week (Visit 3) |
|--------------------|-------------------------------|-------------------------------|
|                    | Fluoxetine | Vilazodone | Chi Sq Value | P   | Fluoxetine | Vilazodone | Chi Sq Value | P   |
| Gastrointestinal   | 24(75%)    | 21(65.5%)  | 0.629        | 0.154 | 15(46.9%)  | 15(46.9%)  | 0.000        | 0.195 |
| Neurological       | 7(21.9%)   | 18(56.3%)  | 7.791        | 0.004 | 3(9.4%)    | 7(21.9%)   | 1.186        | 0.110 |
| Psychiatric        | 4(12.5%)   | 10(31.3%)  | 3.264        | 0.049 | 3(9.4%)    | 7(21.9%)   | 1.186        | 0.110 |
| Fatigue (general)  | 13(40.6%)  | 14(43.8%)  | 0.063        | 0.191 | 7(21.9%)   | 11(34.4%)  | 1.222        | 1.121 |
| Palpitation (cardiac) | 1(3.1%)   | 3(9.4%)    | 1.065        | 0.250 | 1(3.1%)    | 1(3.1%)    | 0.000        | 0.508 |
| Arthralgia         | 1(3.1%)    | 3(9.4%)    | 1.065        | 0.250 | 1(3.1%)    | 1(3.1%)    | 0.000        | 0.508 |

Pearson’s Chi Square Test
P < 0.05 is statistically significant

| Side effects       | 3<sup>rd</sup> week (Visit 2) | 6<sup>th</sup> week (Visit 3) |
|--------------------|-------------------------------|-------------------------------|
|                    | Fluoxetine | Vilazodone | Chi Sq Value | P   | Fluoxetine | Vilazodone | Chi Sq Value | P   |
| Dry mouth          | 20(62.5%)  | 12(37.5%)  | 3.882        | 0.029 | 1(3.1%)    | 12(37.5%)  | 11.591       | 0.001 |
| Nausea             | 0(0)       | 14(43.8%)  | 17.769       | 0.000 | 0(0)       | 8(25%)     | 9.103        | 0.002 |
| Dizziness          | 7(27.9%)   | 15(46.9%)  | 4.364        | 0.024 | 3(9.4%)    | 6(18.8%)   | 1.158        | 0.163 |
| Fatigue            | 13(40.6%)  | 14(43.8%)  | 0.063        | 0.191 | 7(21.9%)   | 11(34.4%)  | 1.222        | 1.121 |

p < 0.05 is statistically significant.

Mean doses of study drugs were calculated at visit 2 and 3. At visit 2, mean dose of fluoxetine was 25.8 ± 9.17 mg, and that of vilazodone was 25.0 ± 8.78. At visit 3, mean dose of fluoxetine and vilazodone were 25.9 ± 9.09 and 28.75 ± 10.08, respectively. The overall results indicate that the subjects responded to both medications in the clinically effective dose range of 20 to 40 mg. However, doses could not be compared due to the different classes of drugs and lack of a standard equivalence comparator.
Our study showed that both at 3 weeks and 6 weeks, the study medications did not differ significantly in efficacy. The scores on CGI-S and CGI-I showed steady decline throughout the study period for both medications. Ever since vilazodone has been launched for the first time in US in 2011, there have been several initial placebo-controlled studies favouring the efficacy of vilazodone. A meta-analysis involving 1200 patients of depression on vilazodone and 1193 patients on placebo inferred that vilazodone is superior to placebo in efficacy and safety [13]. The authors did not come across any head to head comparison with fluoxetine; however over the past couple of years, there are published head to head comparison studies with amitriptyline, citalopram, escitalopram and sertraline. Most of these are 12-week, multiple visit, prospective, open label, randomized studies. Studies have shown that vilazodone is superior to amitriptyline in efficacy and is as efficacious as the other comparator SSRIs. Also, these studies have used HAM-D and MADRS as efficacy measuring tools, unlike CGI-S and CGI-I as the main efficacy tools in our study, which is our limitation. Nevertheless, the main short coming in the above studies is the low sample size and hence the difficulty in generalization of results [14-16].

Another study has compared low dose (20 mg) and high dose (40 mg) of vilazodone with citalopram 40 mg and placebo, in a randomized double blind 10-week prospective trial involving 1138 patients with depression, divided into 4 groups. The study showed that vilazodone is superior to placebo and equi-efficacious to citalopram. It also inferred that both 20 mg and 40 mg vilazodone are equally effective [17]. The authors came across preclinical studies in rats that have compared vilazodone to fluoxetine and found to be comparable in efficacy [18]. Our study, with a similar methodology to the other head to head comparative studies infers a similar result that vilazodone is comparable to fluoxetine in efficacy. However, one study based on Bayesian meta-analysis of FDA reviews studied 16 second-generation antidepressants, including fluoxetine and vilazodone. Based on the Bayesian concept of evidence load rather than effect size, the study reported vilazodone (and Bupropion) as inferior in efficacy compared to other drugs. However, the authors point out their study limitation that not all the published studies were included, as they did not meet the criteria of their study design [19].

We documented all the adverse effects reported with both medications using the checklist adopted from vilazodone prescribing information 2011 [12]. Domain-wise, gastrointestinal side effects were most common, followed by the neurological and psychiatric adverse effects, in both groups. This is in line with a meta-analysis comparing vilazodone to placebo that reported gastrointestinal side effects as the most commonly reported side effects and were significantly higher than placebo [13]. Dry mouth, dizziness, decreased appetite and fatigue are the most common individual side effects reported by subjects from both groups in our study. In addition, nausea was a commonly reported side effect of vilazodone. Though some side effects disappeared or became minimal by the end of the study, dry mouth and nausea were significantly common with vilazodone. Nausea has been reported as one of the frequent side effects in other previous studies which also report diarrhoea as another common side effect [13, 17, 20, 21]. Some studies have also reported dizziness, dry mouth and fatigue as other common side effects of vilazodone [7, 21]. Thus, we find a similar side effect profile in our study subjects, like the previous studies. Most studies have reported either no sexual side effects or minimal sexual dysfunction with vilazodone [14, 15, 20, 21]. No sexual side effects were reported with both drugs in our study. Headache, vomiting and insomnia are the other commonly reported side effects of vilazodone [7, 21]. Thus, we find a similar side effect profile in our study subjects, like the previous studies. Vilazodone-associated side effects are seen to be somewhat higher than fluoxetine overall, and some GI side effects are significantly higher than fluoxetine. All in all, dry mouth, dizziness, nausea and fatigue are some of the major side effects that our study subjects on vilazodone reported.
Our methodology to study the short-term efficacy and safety is similar to other studies, in being prospective and randomized, having a standard comparator. However, our study was not blinded, but there was no placebo arm. Some studies that have used HAM-D and MADRS have reported that clinician rating scales are one of their limitations as it may result in bias [13, 14]. Our limitation, as mentioned earlier, is that we did not use a comprehensive rating scale like HAM-D or MADRS to assess depressive symptoms. However, the CGI severity and improvement scales offer a readily understood, practical measurement tool that can easily be administered by a clinician in a busy clinical practice setting [22]. This scale does not need a mental health professional, which is relevant to some investigators of this study that are not from the mental health background. They performed the study assessments following a clinical diagnosis from the psychiatrist. Further, studies have shown that CGI scale is a core metric in psychiatric research and a valid clinical outcome measure for routine use [23].

Also, our sample size, though less (n = 66), is comparable to other studies that have compared vilazodone to sertraline (n = 60), to escitalopram (n = 36), and to escitalopram as well as amitriptyline (n = 50) [13-15]. The rate of literacy significantly differed across the groups; however all the patients were able to understand the study procedures and were able to comply with them. Thus, it was not a limiting factor as far as this study is concerned.

Also, as mentioned earlier, there is a possibility of type I error here due to smaller sample. On the whole, our study supports the existing evidence that vilazodone has a comparable efficacy to fluoxetine, a time-tested SSRI. However, our study differs from others with respect to the short-term adverse effect profile. Thus, our study infers that the short-term efficacy of vilazodone is comparable to fluoxetine though adverse effects are more frequent with vilazodone and hence caution is advised before starting it as a first-line medication for depression.

CONCLUSION

We infer that vilazodone can be considered to have a comparable efficacy to fluoxetine in Indian population, in the acute phase of treatment of depression. However, its dual mechanism of action doesn’t appear to play any significant or unique role as its efficacy doesn’t appear to be superior to the time-tested fluoxetine. Also, the adverse effects, especially GI side effects are significantly more frequent with vilazodone, suggesting caution. We recommend a longer duration of blinded studies with a larger sample size and psychopathology measurements on concurrent self-rated and clinician-rated rating scales, for generalization of the results.

ACKNOWLEDGEMENT

The authors sincerely thank Dr. R. Rajagopal and Dr. Narendra Kumar M. S., the faculty in the department of Psychiatry at MMC&RI, Mysuru for referral of subjects to screen for the study. The authors also thank Dr. B. M. Parashivamurthy, Professor and HOD, Dept. of Pharmacology for his encouragement and support. We are grateful to Dr. Lancy D. Souza, Professor of Psychology at the University of Mysore, for statistical analysis, Dr. Samir Kumar Praharaj, Professor of Psychiatry, MAHE, Manipal, Dr. Mamatha and Dr. Bharadwaja for their assistance.

FUNDING SOURCE

None.

CONFLICT OF INTEREST STATEMENT

None.

REFERENCES

1. Barbier, D. 2001, Presse. Med., 30, 1719.
2. [Internet]. 2017 [cited 5 October 2017]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/018936s075s077lbl.pdf
3. Benfield, P., Heal, R. C. and Lewis, S. P. 1986, Drugs., 32, 481. doi: 10.2165/00003495-198632060-00002.
4. Montejo, A. L., Liorca, G., Izquierdo, J. A. and Rico-Villademoros, F. 2001, J. Clin. Psychiatry., 62, 10.
5. Stahl, S. M. 2014, CNS. Spectr., 19, 105.
6. Croft, H. A., Pomara, N., Gommoll, C., Chen, D., Nunez, R. and Mathews, M. 2014, J. Clin. Psychiatry., 75, 1291.
7. Cruz, M. P. 2012, Drug. Forecast., 37, 28.
8. Lim, G. Y., Tam, W. W., Lu, Y., Ho, C. S., Zhang, M. W. and Ho, R. C. 2018, Sci. Rep., 8, 2861.
9. Diagnostic and statistical manual of mental disorders. 5th ed. Washington: American Psychiatric Publishing; 2014.
10. Vasudevan, J., Mishra, A. K. and Singh, Z. 2016, Int. J. Res. Med. Sci., 4, 4183.
11. Busner, J. and Targum, S. D. 2007, Psychiatry., 4, 28.
12. Viibryd® (vilazodone HCl) Tablets, prescribing information. St. Louis: Forest Laboratories; April 2011. Available at: https://media.allergan.com/actavis/actavis/media/allergan-pdf-documents/product-prescribing/2018-05-8-Viibryd(vilazodone)-USPI-Clean.pdf. Retrieved January 13, 2022.
13. Zhang, X-F., Wu, L., Wan, D-J., Liu, R-Z., Dong, Z., Chen, M. and Yu, S-Y. 2015, Neuropsychiatric. Disease. and Treatment., 11, 1957.
14. Bathla, M. and Anjum, S. 2020, Indian. J. Pharmacol., 52, 10.
15. Bathla, M., Anjum, S., Singh, M., Panchal, S. and Singh, G. P. 2018, Indian. J. Psychol. Med., 40, 80.
16. Kadam, R. L., Sontakke, S. D., Tiple, P., Motghare, V. M., Bajait, C. S. and Kalikar, M. V. 2020, Indian. J. Pharmacol., 52, 79.
17. Mathews, M., Gommoll, C., Chen, D., Nunez, R. and Khan, A. 2015, International. Clinical. Psychopharmacology., 30, 67.
18. Paulis, T. 2007, I. Drugs., 10, 193.
19. Monden, R., Roest, A. M., Ravenzaaij, D., Wagenmakers, E-J., Morey, R., Wardenaar, K. J. and Jonge, P. 2018, Journal. of Affective. Disorders., 235, 393.
20. Hallerstein, D. J. and Flaxer, J. 2015, Core. Evidence., 10, 49.
21. Wang S-M., Han, C., Lee, S-J., Patkar, A. A. and Masand, P. S. 2016, Chonnam. Med. J., 52, 91.
22. Busner, J. and Targum, S. D. 2007, Psychiatry. (Edgmont)., 4, 28.
23. Berk, M., Ng, F., Dodd, S., Callaly, T., Campbell, S., Bernardo, M. and Trauer, T. 2008, J. Eval. Clin. Pract., 14, 979.