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Original Research Article

Anti-Depressants & Sexual Dysfunction - Is Vilazodone A Better Choice Than SSRIS?

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Abstract:

Context: To compare the efficacy of new anti-depressant Vilazodone with SSRIs and associated sexual dysfunction.

Aims: To assess and compare the Sexual Dysfunction of escitalopram, fluoxetine, sertraline and paroxetine with vilazodone.

Methods and Material: One hundred and fifty patients diagnosed with Depression according to the DSM 5 criteria, seen in the Out-patient department of psychiatry at a tertiary care hospital, participated in the study after obtaining written and informed consent. Thirty patients were randomly assigned for treatment with either of the following drugs: escitalopram, fluoxetine, sertraline, paroxetine and vilazodone. Changes in Sexual Functioning Questionnaire (CSFQ) was applied on Day 1 to assess the baseline sexual functioning and again at week 1, week 2 and week 8 following initiation of treatment, to assess the extent of improvement, if any.

Statistical analysis used: SPSS v20 and independent sample t tests were used to tabulate and calculate the results.

Results: Vilazodone was associated with the fastest improvement in sexual functioning as compared to other drugs; however, the difference in Sexual Dysfunction associated with all five drugs was not statistically significant at the end of the 8 week follow up study.

Conclusions: Further studies are needed to verify or contradict the findings of this study.

Keywords: Anti-depressants, Vilazodone, CSFQ, Depression, Sexual Dysfunction.

Introduction

Despite being one of the most prevalent mental illness worldwide, a single, universally accepted and comprehensive definition of Depression does not exist. Many guidelines have been laid down since ancient times to try and encompass the complex pattern of illness that is seen in Depression and the trend still continues. Depression consists of mainly a pervasive feeling of sadness with the diminished ability to feel emotion and decreased interest in important aspects of life. Other features that are commonly seen in the disorder include sleep and appetite disturbances, decreased sense of energy and easy fatiguability and cognitive impairments.

The earliest treatment records available for Depression date back to 1813 when Samuel Tuke treated 30 patients suffering from melancholia with a combination of medical and moral treatment, with warm bath being the medical aspect of the treatment and bodily exercise the moral aspect. This methodology of treatment of depression is followed till date with the most success experienced with a combination of pharmacological treatment along with various psychotherapies.

Though initial class of antidepressants - MAOIs and TCAs - were associated with good antidepressant response their overall tolerability was low due to the high incidence of associated troublesome adverse effects. The advent of SSRIs revolutionised the treatment of Depression and till date is the greatest discovery in the treatment of Depression. SSRIs were initially thought to be the magic bullets against treating depression as they were free of the worrisome adverse effects that were associated with previous class of antidepressants. However, post marketing studies and meta-analysis have revealed that SSRI are also associated with their own range of adverse effects which are generally unacceptable to the patient in the long run and which lead to discontinuation of the treatment. These adverse effects include nausea, headache, sleep disturbances, appetite changes and sexual dysfunction. Current research in

pharmacotherapy of Depression is aimed towards reduction of these adverse effects in order to achieve better treatment compliance and results.

Depression and Sexual Dysfunction (SD) share a bidirectional relationship with each other. Major Depressive Disorder increases the risk for developing SD by 50-70% [1] and the presence of SD itself is an independent risk factor for developing depression [2]. However this equation is further complicated by the independent sexual adverse effects that have been seen with treatment with various SSRIs which increases the risk of treatment dropout. The mechanisms underlying SD caused by SSRIs are unclear, however a role for 5HT1a has been proposed. 5HT1a agonist - Buspirone - has been successfully used in adjunction with SSRIs in the management of depression to reduce sexual adverse effects [3]. Various animal behavioural models have also outlined down-regulation of 5HT1a receptors in the brain as one of the key mechanisms associated with SSRI induced SD [4,5].

Vilazodone differs from SSRIs as it combines Serotonin Transporter (SERT) inhibition (the principle mechanism of SSRIs) along with partial agonism at the 5HT1a receptors [6]. Thus it theoretically proposes a paradigm of robust antidepressant action (similar to that of SSRIs) without the burden of compliance reducing sexual dysfunction (as achieved by SSRI - Buspirone combination). The present study aims to compare the differences in the adverse effect profile of four popular SSRIs - Escitalopram, Paroxetine, Fluoxetine and Sertraline - with Vilazodone, with respect to SD.

Subjects and Methods:

This 8-week follow-up study was conducted at the Department of Psychiatry of a tertiary care hospital which primarily caters to a rural and suburban population of western Uttar Pradesh. One hundred and fifty patients who visited the outpatient department of psychiatry were selected for the study after obtaining due approval from the Institute's Ethics Committee.

Only patients who consented to participate in the study and fulfilled the diagnostic criteria laid down by DSM-5 for Major Depressive Disorder were included. The patient selection was done on the basis of a predetermined set of inclusion and exclusion criteria. Baseline levels of sexual functioning (Day 1) were measured using Changes in Sexual Functioning Questionnaire. Thirty patients each were then randomly assigned to five groups (Vilazodone, Fluoxetine, Paroxetine, Escitalopram and Sertraline) and antidepressant treatment was initiated. Randomisation was done using paper chit method.

Following doses of the drugs were used in this study:

- Vilazodone - 10mg/day titrated upto 20mg/day

- Escitalopram - 10mg/day titrated upto 20mg/day

- Paroxetine (Controlled Release Preparation) - 12.5mg/day titrated upto 25mg/day

- Fluoxetine - 20mg/day titrated upto 40mg/day

- Sertraline - 25mg/day titrated upto 100mg/day

Patients were called for follow ups at Week 1, Week 2 and Week 8 to assess sexual adverse effects associated with antidepressant treatment using CSFQ.

The data was collected and entered in MS Excel. Data was analysed using SPSS 20.0 and statistical differences in proportion were calculated using the chi square test, t-test and ANOVA.

The results were explained in the form of baseline identification and socioeconomic parameters of the subjects in all five drug groups (vilazodone, escitalopram, paroxetine, fluoxetine and sertraline) in terms of descriptive and inferential statistics.

Descriptive statistics were explained by frequencies, mean, standard deviation and range for numeric variables and by proportions and percentages for categorical variables in (vilazodone, escitalopram, paroxetine, fluoxetine and sertraline) groups. Inferential statistics were done by applying statistical test for significance testing by t test for continuous variables, univariate analysis wherever applicable and with 95% confidence intervals and Chi-square test for proportions and categorical variables. Post hoc analysis was done using Dunnett's Test following the derivation of initial results. In post hoc analysis, four drugs (I drug) were compared against vilazodone as the control (J drug). The difference in the score at different time intervals was estimated by applying t test for the difference of mean score at different time intervals.

Results:

91.3% of the patients included in the study had complaints of sexual dysfunction as per the CSFQ scores at the beginning of the study. At the end of 8 week treatment with various drugs, the total percentage of patients suffering from sexual dysfunction decreased to 87.3% (Figure 1 & 2).

The study included 55 males, 82.24% of which had sexual dysfunction prior to the initiation of antidepressant therapy (Figure 1). Of the rest 95 females, 96.64% had baseline sexual dysfunction (Figure 2). Participants in the Vilazodone group had the highest baseline sexual dysfunction (CSFQ = 36.4(8.9)).

The increase in CSFQ scores was seen in almost all treatment groups, which is in contrast to studies which have been previously conducted (Figure 3 & 4). The rate of sexual dysfunction was more in females as compared to males at both baseline and at the end of 8 weeks of treatment. Age showed no significant changes in sexual functioning of the patients with CSFQ scores being comparable for patients less than and more than 45 years of age. Post hoc analysis of Vilazodone with other four antidepressants revealed no significant findings (P>0.05). While in females improvement in sexual functioning was seen with all the study drugs, in males the results differed slightly. While all the drugs improved sexual functioning leading to increase in mean CSFQ scores, a slight decrease in week 8 CSFQ scores was observed with Paroxetine which was not statistically significant. The drugs associated with the most improvement in sexual functioning in both males and females were Escitalopram and Vilazodone, however the difference was not statistically significant (P>0.05).

However, the shows the difference in CSFQ score at 8th week, 2nd week and one week time interval with the CSFQ score at Day 1 for all the drugs.

The CSFQ score difference was found significant between 2nd week and Day 1 (P<0.05) as well as 1 week and Day 1 (P<0.05) for Vilazodone.

The CSFQ score difference was found significant between 8th week and Day 1 (P<0.05) as well as 2nd week and Day 1 (P<0.05) for Escitalopram. However, the said difference was not found significant at any time interval for other drugs.

For Escitalopram, the difference in CSFQ score was observed late in the 8th week whereas, Vilazodone has shown the difference in the CSFQ score right from the 1st week onwards lasting consistently upto 2nd week.

Discussion:

Sexual Dysfunction can be associated with depression in many ways. It could be a) causative factor for Depression, b) caused by Depression, or c) caused by drugs used in the treatment. The latter is responsible for a significant number of dropouts especially in the Indian society where both mental illness and sexual wellbeing are highly stigmatised topics. Due to Vilazodone being a relatively new molecule there is marked paucity of data on its pharmacological profile.

However a number of animal studies have suggested a significant role of 5HT1a receptors linked with sexual functioning [4,5]. Another newer antidepressant - Vortioxetine - has also been associated with lower rates of sexual dysfunctions on account of its varied receptor profile [6].

Few studies have shown similar results as the present study however they are placebo control trials and have not compared Vilazodone to a known molecule [3,7]. A study conducted to compare Escitaolpram and Vilazodone in patients suffering from Depression found no difference in the sexual adverse effect profile of both the drugs8. Head to head trials of Vilazodone with other antidepressants are rare. A study conducted in US comparing Vilazodone with Citalopram showed statistically significant lower rates of sexual dysfunction in the Vilazodone group [9]. Similarly an Indian study found similar findings when Vilazodone was compared with Escitalopram in patients suffering from Depressive Disorder [10]. These differences can be attributed to a long 12-week follow-up performed in both the above mentioned studies.

A number of placebo control trials have shown Vilazodone's superiority with respect to sexual functioning in patients with depression and anxiety [11,9,12]. This could be due to a number of reasons such as the placebo being an unknown substance, its effect on sexual functioning not being known. This study compares Vilazodone directly with a well-researched group of drugs with established sexual adverse effects profile.

Sexual functioning in an individual and is the result of interactions between a number of factors such as genetic polymorphisms associated with genes coding for SERT (Serotonin Transporter), feedback regulation of Dopamine in Dorsal Raphae Nucleus, 5HT1a receptors and their chronic down-regulation. Due to the complexity of these mechanisms it becomes very difficult to predict a binary outcome with respect to any drug acting on the above mentioned factors.

Conclusion

This is the first study to compare Vilazodone with a number of other popularly used SSRIs to our knowledge. Most other data that is available on Vilazodone is derived from placebo control trials. Our study has shown that there is no statistically significant difference between adverse effect caused by Vilazodone versus four popular SSRI group of drugs. However it shows that the onset of amelioration of sexual dysfuction associated with depression is fastest with Vilazodone followed by Escitalopram. As this is a relatively new molecule further and more long term follow up studies are required to enable better understanding of this drug.

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