Prashar L, Paul R. (September 2015). A comparative study for the efficacy and tolerability of Fluvoxamine and Venlafaxine in patients with obsessive compulsive disorder. Jour of Med Sc & Tech; 4(3); Page No: 235 – 241.

Journal of Medical Science & Technology

Original Article Open Access

A Comparative Study for the Efficacy and Tolerability of Fluvoxamine and Venlafaxine in Patients with Obsessive Compulsive Disorder

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Abstract

Objective of our study is to compare the efficacy and tolerability of Fluvoxamine and Venlafaxine in patients with Obsessive Compulsive Disorder (OCD). A total of 50 newly diagnosed patients with OCD were randomly assigned 25 each to receive either fluvoxamine (Selective serotonin reuptake inhibitor) or venlafaxine (selective serotonin norepinephrine reuptake inhibitor). Primary efficacy was assessed by the change from baseline on the Yale Brown Obsessive Compulsive Scale (Y-BOCS). The Clinical Global Impression Improvement Scale (CGI-S) was used to measure symptom improvement. Each patient was followed as a single visit in a week wise manner following the order; Week0, Week 1, Week 2, Week 4, Week 6, Week 8, Week 12 and Week 16. At each visit if any adverse reaction to either of the drugs experienced by the patient were noted. Treatment group comparison of patients, demographic characteristics and baseline severity measurements were done using a Chi square test and the student t-test. Statistical significance was defined as a 2-sided p value ≤ 0.05. Both drugs showed significant reduction in the OCD symptoms as measured on the Y-BOC Scale over the 16-week follow up. When compared fluvoxamine showed statistically significant reduction in overall YBOC score and Obsessive mean score. The difference in compulsive mean score was not significant in the two treatment groups. Our study concludes that Fluvoxamine is more efficacious than Venlafaxine in the treatment of OCD.

Key words: Obsessive Compulsive Disorder, Fluvoxamine, Venlafaxine.

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Received: August 4, 2015 Accepted: August 27, 2015. Published: September 20, 2015.

Introduction

Obsessions are frequent upsetting thoughts, in the process of trying to control them; a person feels an overwhelming urge to repeat certain rituals or behaviors which are referred to as compulsions. People with obsessive Compulsive Disorder (OCD) fail to control their obsessions and compulsions and gradually the rituals end up controlling them [1]. OCD is a chronic illness that produces substantial impairment of normal, daily life activities.

OCD initially thought to be a rare disorder is now classified as the fourth most common psychiatric disorder worldwide after substance abuse, specific phobias and major depression [2]. In a study done in 5, USA communities with a population of 18500, life time prevalence rates ranged from 1.9% to 3.3 %. These rates were found to be 25 to 60 times greater than had been estimated on basis of previous studies of clinical populations [3]. Before the advent of selective serotonin reuptake inhibitors (SSRIs) in 1980s, clomipramine (CMI); the tricyclic serotonin reuptake inhibitor, had been the longest serving drug for OCD. The active metabolite of clomipramine; desmethylated metabolite, is a potent norepinephrine reuptake inhibitor. CMI was used exclusively as an antidepressant, the serendipitious finding of its beneficial effect on obsessions in depression patients

motivated its use for OCD [4]. Presently clomipramine because of its cumbersome adverse drug reaction profile and the toxicity associated with the tricyclic moiety is no longer recommended as first line medication [4]. Since late 1980s SSRIs; fluoxetine, fluvoxamine, paroxetine and sertraline, have been the mainstay of treatment along with cognitive behavioral therapy. It has however been seen that upto 40 – 60 % of patients do not have satisfactory outcome [5]. Till date no useful predictive factors exist to orient the choice of SSRI, and there is limited information available comparing SSRIs among each other [6]. In the present study the therapeutic outcome of Venlafaxine a; Selective Serotonin Norepinephrine reuptake Inhibitor (SNRI) was compared to Fluvoxamine a; SSRI in patients with OCD.

Methods

Our sample consisted of 50 patients diagnosed with primary OCD according to DSM-IV-TR criteria. They were seen from Psychiatry outpatients' clinic at a teaching hospital. The patients were randomly assigned; 25 each; to receive either Venlafaxine or Fluvoxamine and followed for 16 weeks, after providing voluntary written informed consent.

Only patients with obsessive-compulsive symptoms of at least 6- months' duration with no prior history of intake of drugs for relief of OCD symptoms were included in the study. Patients diagnosed with concurrent depression; based on Beck Depressive Inventory score of >21 or previous history of hypertension, myocardial infarction, seizures, hepatic or renal insufficiency, history of chronic alcohol intake; pregnant and lactating mothers were not included in the study.

Drug treatment and allocation:

Patients upon required psychiatric evaluation and diagnosis were randomly assigned to take fluvoxamine or venlafaxine on a open label basis.. The initial dose of venlafaxine was 75mg/day and of fluvoxamine 50mg/day. The dose was thereafter regulated individually (by weekly examination) until therapeutic effects or serious adverse reactions were observed. The maximum dose used was 375mg/day for venlafaxine and 300mg/day for fluvoxamine.

Clinical Assessments

Primary efficacy was assessed by the change from baseline on the Yale Brown obsessive compulsive Scale (Y-BOCS). The Clinical Global Impression Improvement scale (CGI-S) was used to measure symptom improvement. Patients in both groups were followed weekly till week 2 and thereafter once every two weeks till week 12 with a last visit a month thereafter i.e. week 16. Adverse drug reactions during the study period were noted.

Statistical Analyses

Treatment group comparisons of patients, demographic characteristics, and baseline severity measurements were done using a Chi square test and the student t test. Statistical significance was defined as a 2-sided p value ≤ 0.05. Mean YBOCS total score changes by time (week 16-baseline) were analyzed within each group using the paired t test; mean changes within from baseline were compared across the 2 groups using the independent samples t test. We used 2 different statistical methods to evaluate responders:

- A visit-wise statistical analysis and
- A last observation-carried-forward (LOCF) analysis

Responder rates were compared across the 2 groups with the Chi square test.

Results

Characteristics of the patients: The study involved 50 participants, 25 were subjected to fluvoxamine and 25 were subjected to venlafaxine. There were 32 males (15 in the fluvoxamine group and 17 in the venlafaxine group) and 18 females (10 in the fluvoxamine group and 8 in the venlafaxine group). Twenty-seven patients were aged 15-30 years, 18 were aged 40-45 years, and 5 were aged 46 years and above.

A comparative efficacy of fluvoxamine and venlafaxine in patients with obsessive compulsive disorder

Table 1 shows the visit-wise analysis of the mean YBOCS scores at baseline and during the study period. The results show consistent significant improvement throughout the study period in both groups, with an exception in week 2 for the Venlafaxine group. These results have revealed that treatment with either Fluvoxamine or Venlafaxine produces statistically significant reductions in YBOCS total scores. Furthermore, the response profiles of the two drugs were similar from week 3 onwards vs. baseline YBOCS scores.

Figure 1 below shows that mean scores of Fluvoxamine and Venlafaxine in patients with obsessive compulsive disorders (OCD) over a period of 16 weeks. Both Fluvoxamine and Venlafaxine show a downward trend in mean scores of OCDs

among patients. The most significant drop was observed in OCD mean scores of patients treated with Fluvoxamine; from 26.32 in week 1 to 13.32 in week 8 (this was approximately 50% drop). The largest drop was observed in week 3 from 25.2 in week 2 to 19.04 in week 3, a difference of 6.16. Another significant drop was observed in week 6 from 19.2 in week 5 to 14.6, a difference of 4.6. On the other hand, means scores in patients treated with Venlafaxine dropped from 24.0 to 20.4, a difference of about 3.6. There was a general gentle downward trend throughout the whole period in the Venlafaxine group.

Week	Drug	Mean	Mean Score	df*	p*** value
0	Fluvoxamine Venlafaxine	26.32 24.00	2.320 1.332	48	.189
1	Fluvoxamine Venlafaxine	25.20 23.80	1.400 .783	48	.437
2	Fluvoxamine Venlafaxine	19.04 23.60	-4.560 -2.155	48	.036
4	Fluvoxamine Venlafaxine	19.04 22.24	-3.200 -1.470	48	.148
6	Fluvoxamine Venlafaxine	19.04 21.40	-2.200 0.941	48	.351
8	Fluvoxamine Venlafaxine	14.60 20.60	-6.000 -2.511	48	.015
12	Fluvoxamine Venlafaxine	14.48 20.40	-5.920 -2.443	48	.018
16	Fluvoxamine Venlafaxine	13.32 20.40	-7.080 -2.940	48	.005

Table 1: Independent Samples Test results YBOCS

Week Difference	t*	df**	Sig. (2-tailed)	Mean
0	-.506	48	.615	-.44
1	-.454	48	.652	-.36
2	-2.414	48	.020	-2.48
4	-1.777	48	.082	-1.92
6	-2.198	48	.033	-2.48
8	-2.590	48	.013	-3.20
12	-2.766	48	.008	-3.52
16	-2.766	48	.008	-3.52

t*- Unpaired t- test df**- Degree of Freedom

Table 2: Independent Samples Test Results Obsession Mean Score

Independent samples t tests were conducted to determine whether there were any significant differences in the mean scores of patients treated with Fluvoxamine and mean scores of patients treated with Venlafaxine. The tests were conducted at a significance level of 0.05. Table 3 presents a summary of the results. The results were not significant in Week 0 (t=1.332; p=.189), week 1 (t=1.400; p=.437), week 4 (t=-3.200, p=.148), and week 6 (t = -2.200; p=.351). The results were, however, significant in week 2 (t= -2.155; p=.036), week 8 (t= -6.000; p=.015), week 12 (t=-2.443;

p=.018), and week 16 (t= -7.080; p=.005). It was observed that in the weeks where the results were significant the OCD mean scores of patients treated with Fluvoxamine were smaller than those of patients treated with Venlafaxine. These results therefore show that Fluvoxamine is more effective that Venlafaxine in reducing OCDs.

Table 3; Independent Samples Test Results Compulsions Mean Score

Week Difference	t*	df**	Sig. (2-tailed)	Mean
0	1.981	48	.051	2.760
1	1.200	48	.236	1.760
2	-1.288	48	.204	-2.080
4	-.786	48	.435	-1.280
6	-.192	48	.849	.280
8	-1.764	48	.084	-2.800
12	-1.477	48	.146	-2.400
16	-1.764	48	.084	-2.800

t*- Unpaired t- test df**- Degree of Freedom

Adverse Drug Reactions	Fluvoxamine n+	Fluvoxamine %	Venlafaxine n+	Venlafaxine %
Somnolence	6	24	3	12
Dry Mouth	6	24	5	20
Constipation	6	24	2	8
Asthenia	6	24	3	12
Irritability	5	20	0	0
Gastritis	5	20	6	24
Nausea	3	12	6	24
Weight Gain	3	12	2	8
Loss of Appetite	2	12	5	20
Loss of Libido	2	8	0	0
Insomnia	2	8	2	8
Headache	1	4	0	0
Tremors	1	4	0	0
Hesitancy	0	0	1	4
Delayed Orgasm	0	0	2	8
Craving for Sweets	0	0	2	8
Total	50		44	

Table 4: Comparison of Adverse Drug Reactions among Patients Treated with Fluvoxamine and Venlafaxine.

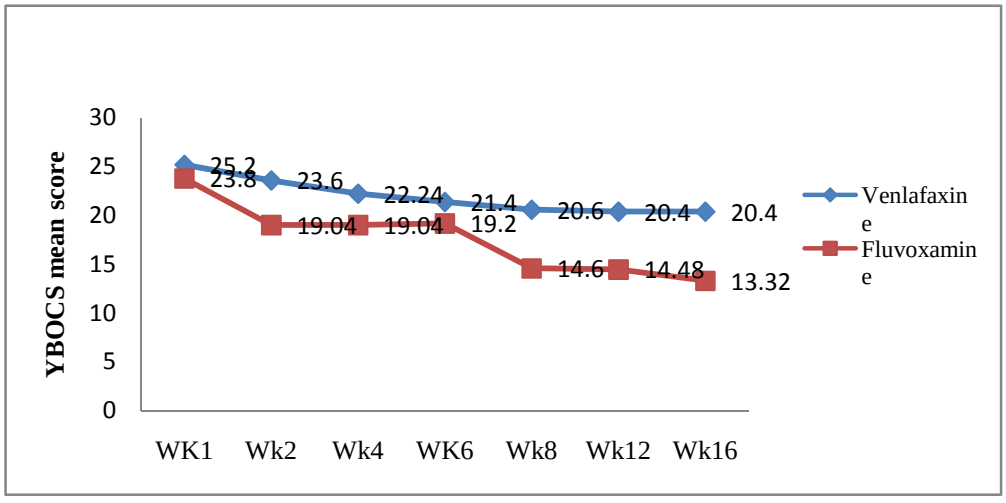

Figure 1: Comparison of YBOCS Mean scores of patients treated with Fluvoxamine and Venlafaxine.

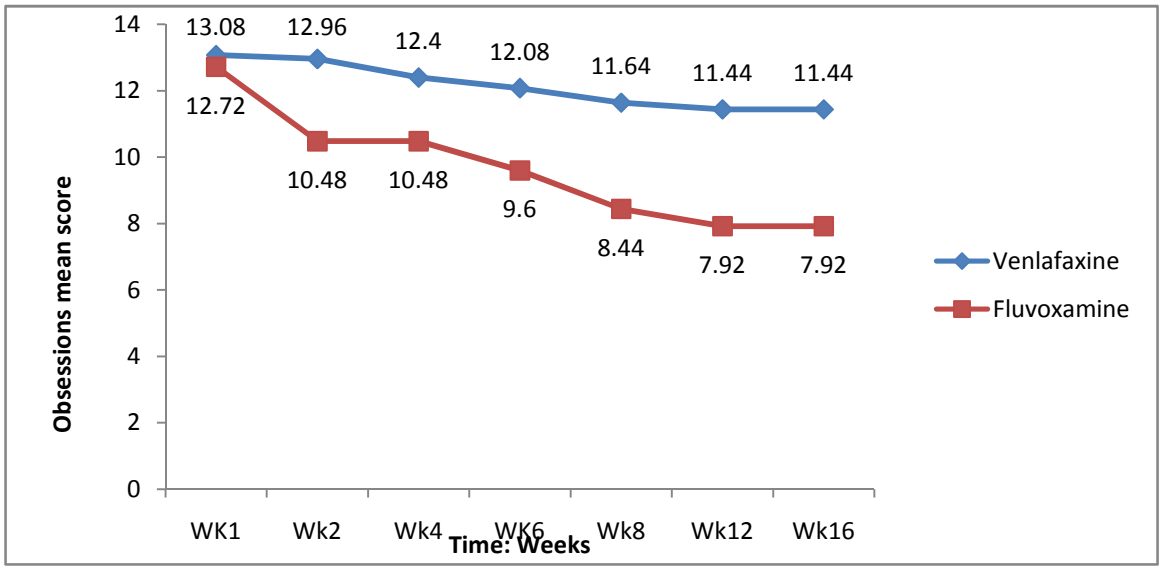

Figure 2: Comparison of obsessive disorder mean scores

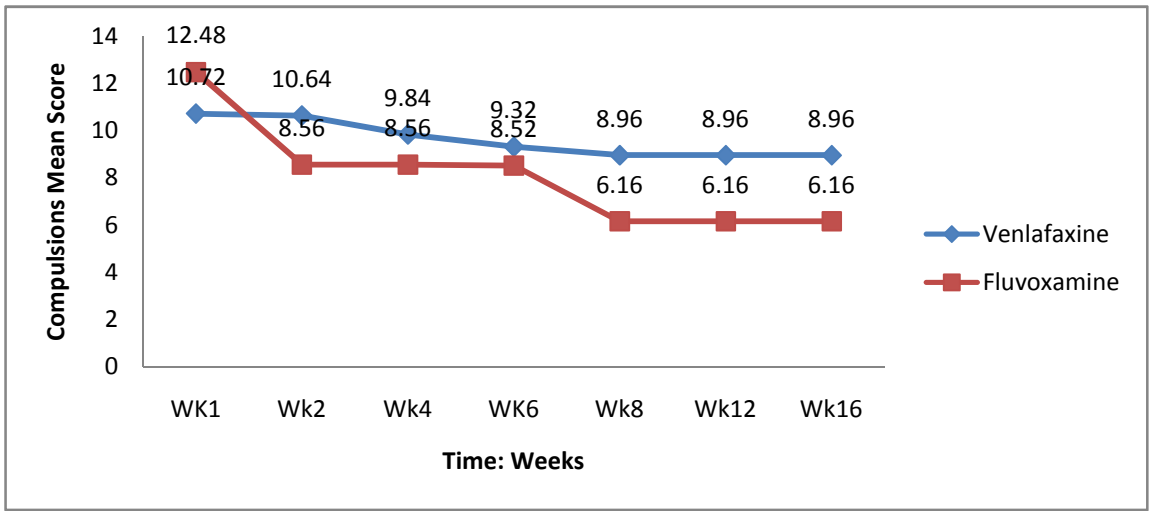

Figure 3: Comparison of compulsive disorder mean scores

A comparative efficacy of fluvoxamine and venlafaxine in management of obsessions:

Figure 2 reveals that patients in both the Fluvoxamine and Venlafaxine groups showed a marked and significant improvement over the 16 week study period with regard to compulsive disorders (paired t test for mean obsessions total score at 16 week vs. baseline: t=4.214; df=24; p=0.000 for the Fluvoxamine group and t=3.115; df=24; p=0.005 for the Venlafaxine group). A week-wise analysis of the mean obsessive disorder scores at baseline and during the study period shows consistent significant improvement throughout the study period in both groups. In the Venlafaxine group, obsessive disorder mean scores dropped from 13.28 at baseline to 11.44 in week 16 while in the Fluvoxamine group, obsessive disorder mean scores dropped from 12.84 to 7.92. The results from independent samples t tests showed statistical significant differences in the obsessive disorder mean scores of patients treated with Fluvoxamine and Venlafaxine, in week 2 through week 16 (Table 2). The results show that Fluvoxamine is a more effective drug in the treatment of obsessive disorders.

A comparative efficacy of fluvoxamine and venlafaxine in management of compulsions

Figure 3 shows that patients in both the Fluvoxamine and Venlafaxine groups showed a marked and significant improvement over the 16 week study period with regard to compulsive disorders (paired t test for mean compulsive total score at 16 week vs. baseline: t=7.080; df=24; p=0.000 for the Fluvoxamine group and t=3.173; df=24; p=0.004 for the Venlafaxine group). A week-wise analysis of the mean compulsive disorder scores at baseline and during the study period. The results show consistent significant improvement throughout the study period in both groups, with an exception in week 2 for the Venlafaxine group. In the Venlafaxine group, disorder mean scores dropped from 10.72 at baseline to 8.96 in week 16 while in the Fluvoxamine group, disorder mean scores dropped from 13.48 to 6.16. However, the results from independent samples t tests showed no statistical significant difference in the compulsive disorder mean scores of patients treated with either Fluvoxamine or Venlafaxine, throughout the study period (Table 3).

Comparison on CGI-I Scale

A comparative analysis of responders among the treatment groups was undertaken using CGI-I Scale. The number of responders in the Fluvoxamine group progressively increased from week 4 to week 16 from 12 to 18. On the other hand, the number of responders increased marginally in the Venlafaxine group from 4 in week 4 to 7 in week 16. While there was no significant increase in the number of responders in the Venlafaxine group (χ^2=7.000; df=3; p=0.072) across the study period, there there was a significant increase in the number responders within the Fluvoxamine group (χ^2=74.095; df=3; p=0.000).

Comparative tolerability of Fluvoxamine and Venlafaxine in patients with obsessive compulsive disorder

Table 4 reveals that the most prominent adverse effects of drug treatment among patients treated with Fluvoxamine were somnolence, dry mouth, constipation, asthenia, and irritability while the most prominent adverse effects of drug treatment among patients treated with Venlafaxine were gastritis, nausea, dry mouth, loss of appetite, and headache. Dry mouth and gastritis were prominent in both Fluvoxamine and Venlafaxine groups. Hesitancy, delayed orgasm, and craving for sweets were only experienced by patients treated with Venlafaxine while irritability, loss of libido and tremors were only experienced by patients treated with Fluvoxamine.

Discussion

Anti-obsession effects of drugs were first demonstrated about 35 years ago [4]. The tertiary amine tricyclic anti-depressant; Clomipramine (CMI) was found to be more effective than secondary amine compounds such as desipramine[4].Clomipramine as compared to desipramine is a more potent serotonin reuptake inhibitor. In this study a selective serotonin reuptake inhibitor; fluvoxamine, was compared to venlafaxine; a selective serotonin and nor-epinephrine reuptake inhibitor, in the management of OCD.

Goodman and colleagues found a highly significant drop in YBOCS scores from week 3 onwards in the fluvoxamine group when compared to placebo [7]. This study similarly demonstrated a significant fall in YBOCS score from week 2 onwards with fluvoxamine while in the venlafaxine group it was seen only week 4 onwards. In another study by Goodman et al., fluvoxamine was found to be superior to desiparmine in treatment of OCD from week 7 onwards [8]. In our study a statistically significant difference between the two treatment groups was observed in favor of fluvoxamine from week 8 onwards. In a switch over design Denys D et al, demonstrated a significant drop in total YBOCS score from baseline in both paroxetine, a SSRI, and venlafaxine group followed for 12 + 12 weeks. When the two groups were compared paroxetine was clearly superior to venlafaxine, a finding similar to this study.

The decrease from baseline in the obsessions subtotal of YBOCS seemed to precede improvement in compulsive symptoms in the study done by Goodman et al. [7], in our study when compared both fluvoxamine and venlafaxine were found to be equally effective in the treatment of compulsions with fluvoxamine proving to be more efficacious in the treatment of obsessions.

There were significantly more responders (as defined by a score of much improved or very much improved on the CGI-I scale), among the

patients treated with fluvoxamine than those who received venlafaxine. A similar result was seen with other studies done using fluvoxamine [7, 8].

Hesitancy, delayed orgasm and craving for sweets were more prevalent side effects in the venlafaxine group whereas irritability, loss of libido, and tremors were more commonly seen with fluvoxamine. Sexual dysfunction was significantly more prevalent with citalopram; a SSRI, in a similar comparison study done by Pallanti and colleagues [10].

Conclusion

In brief our data demonstrates that both fluvoxamine and venlafaxine are effective in treating OCD. However response to fluvoxamine is more efficacious when compared to venlafaxine. This finding substantiates the response seen with SSRIs in other similar studies [6, 7, 8, 9]. OCD is considered to be an anxiety disorder and venlafaxine is considered to be efficacious in a number of anxiety disorders. The results of our study however indicate that norepinephrine reuptake-blocking effects of venlafaxine do not result in a higher response rate in OCD. This finding further supports the notion that serotonin is the major transmitter involved in the pathophysiology of OCD.

Acknowledgements: Dr Akakandelwa; Senior Lecturer, Department of Library and information studies. University of Zambia.

Conflict of interest: We declare that we have no conflicts of interest.

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