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Research Article

A COMPARATIVE STUDY OF EFFICACY AND TOLERABILITY OF FLUVOXAMINE AND SERTRALINE IN TREATMENT OF OBSESSIVE COMPULSIVE DISORDER

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ABSTRACT

Objective: The objectives of this study are to compare the efficacy and tolerability of Fluvoxamine with Sertraline in relieving symptoms in obsessive compulsive disorder and to compare the improvement in quality of life.

Methodology: The study was a randomized, open label, comparative study conducted from November 2009 to April 2011. The patients were randomized in 1:1 ratio into two treatment groups. Patients either received Fluvoxamine 50-200 mg or Sertraline 50-200 mg once daily orally for 12 weeks. Assessment was done by calculating Yale Brown obsessive - compulsive score (Y-BOCS) and WHO 5 well being score at baseline, 6 weeks and 12 weeks. Tolerability assessment was based on adverse events.

Results: There was a statistically significant reduction in the Yale Brown obsessive - compulsive scores and WHO 5 well being scores from base line to 6 weeks, baseline to 12 weeks and from 6 weeks to 12 weeks in both groups. Incidence of side effects was similar and there were no serious adverse effects in both the groups.

Discussion: In the present study, both the drugs decreased the Y-BOCS score form their respective baselines which was statistically significant ($P<0.01$). Regarding adverse events there was no statistically significant difference between the two groups, but sertraline group had lesser number of adverse events.

Conclusion: From the results of this study it can be concluded that both Fluvoxamine and Sertraline are effective in the treatment of obsessive - compulsive disorder and Sertraline has a slightly better tolerability profile than fluvoxamine.

Keywords: Obsessive - compulsive disorder, Anxiety Disorders, Fluvoxamine, Sertraline.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a chronic psychiatric disorder characterized by recurrent persistent thoughts (obsessions) and/or repetitive compulsory behaviors (compulsions) that cause anxiety or distress, are time-consuming, and cause significant socio occupational dysfunction [1]. OCD is associated with significant suffering, leads to a great deal of morbidity, and is associated with major economic costs. Many aspects of quality of life are negatively impacted by OCD, and there is an association between increased OCD severity and worse quality of life [2].

There is only one epidemiological study from India [3]. The study found lifetime prevalence of 0.6%. The neurotransmitter system of interest in both the etiology and pharmacological treatment of OCD is the serotonergic system [4]. It has been suggested that the brain dopaminergic system also plays an important role in the genesis of OCD [5].

OCD can now be alleviated with modern pharmacological and behavioral treatments. Treatment of OCD typically involves use of medication in combination with other modalities (such as CBT, psycho education, and support groups). First-line treatment options for OCD include both serotonin reuptake inhibitor (SRI) medication and CBT.

SRIs include selective serotonin reuptake inhibitors (SSRIs) and the tricyclic antidepressant (TCA) clomipramine. SSRIs and the SRI clomipramine are recommended as first-line agents for drug treatment of OCD due to the convincing database from numerous published randomized controlled trials (RCTs), according to several meta analysis [6].

According to NICE guidelines, the initial pharmacological treatment in adults with OCD should be one of the following SSRIs: fluoxetine, fluvoxamine, paroxetine, sertraline, or citalopram[7].There are very few studies which compare fluvoxamine and sertraline in OCD. Hence the present study is undertaken with an objective to compare the efficacy and tolerability of Fluvoxamine with Sertraline in relieving symptoms in OCD.

MATERIALS AND METHODS

Study design

This was a 12 week, randomized, open labeled, comparative study. The study was initiated after seeking the necessary approval institutional ethics committee. Good Clinical Practice guidelines were adhered. The patients were randomized into two treatment groups. Patients either received Fluvoxamine 50-200 mg or Sertraline 50-200 mg once daily. Both the treatments were administered orally for 12 weeks. No other SSRI's were allowed during the study period.

The study was conducted from Nov 2009 to April 2011. Written informed consent was obtained prior to initiation of the study. Work up of all patients who satisfy the inclusion and exclusion criteria were done before their enrolment into the study. Patient assessment was done at baseline, 6 weeks and 12 weeks.

Inclusion criteria

1) Males and females aged 18 to 65 years.

2) Patients with a DSM IV diagnosis of Obsessive Compulsive Disorder and Yale

Brown Obsessive Compulsive Score >/= 16.

3) Written informed consent

Exclusion criteria

1) Pregnant and lactating women

2) Dementia

3) Patients with medical diseases like uncontrolled hypertension, uncontrolled diabetes mellitus, congestive cardiac failure, hepatic disease, renal disease

4) Patients with a known history of allergy to Fluvoxamine or Sertraline.

Sample size calculation

The sample size was calculated with a power of 80% to detect a difference at the 95% confidence interval. Considering an alpha error of 5% and beta error of 20% (power of study 80%) sample size estimated was 50 (25 study subjects in each group). Assuming that around 20% of patients will be lost to the follow up, a total of 60 patients were recruited to ensure there were 50 evaluable patients

Assessments

Clinical assessment was done by calculating YBOCS and WHO 5 well being score at baseline, 6 weeks and 12 weeks. Tolerability assessment was based on adverse events. Adverse events were monitored and noted at every visit. To obtain a comprehensive assessment of the effect of study medications on the multiple clinical manifestation of Obsessive compulsive disorder, both patients and investigator assessed the following endpoints for efficacy.

Primary Outcome Measures

1) Patient's overall improvement in obsessive compulsive symptoms was recorded on YBOCS scale.

2) Quality of life was assessed on WHO 5 well being scale.

Secondary Outcome Measures

Secondary outcome measure was tolerability of the drug by the patient. Adverse events were monitored at each visit. For all adverse events, the investigator recorded the relation to the test drug. Certain adverse events such as somnolence, anxiety, dry mouth and rash were specifically asked at each visit for tolerability assessment. These were anticipated adverse events, which were prospectively identified and were sought with the intention to find the difference between the two drugs.

Method of Statistical Analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean ± SD and results on categorical measurements are presented as percentage. Significance is assessed at 5% level of significance.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups inter group analysis) on metric parameters, Mann Whitney U test has been used to find the significance between two groups for parameters on non-interval scale.

Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value: $0.01<P \leq 0.05$)

** Strongly significant (P value: $P \leq 0.01$)

Statistical software SPSS 15.0 and Stata 10.1, were used for the analysis

RESULTS

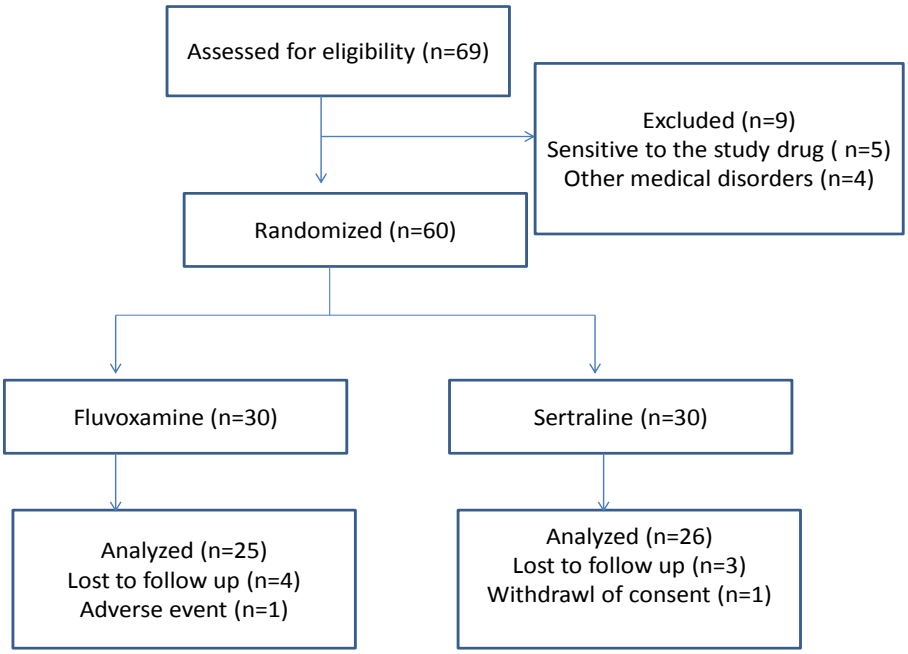

Fig. 1: Flow chart of study

Table 1: Demographic data in two groups (Mean±SD)

Variables	Fluvoxamine	Sertraline	P value
Number of patients	25	26	-
Male : Female	13:12	14:12	0.777
Age in years	32.60±9.17	33.12±8.36	0.835
Weight (kg)	61.96±6.69	64.36±7.38	0.234

Demographic variables are matched with no statistically significant difference

Table 2: Comparative evaluation of Y-BOCS in two groups of study subjects (Mean±SD)

YB-OCS	Fluvoxamine	Sertraline	P value
Baseline	22.64±2.93	22.12±3.37	0.563
6th week	19.16±2.98	18.36±2.97	0.347
12th week	16.00±2.99	15.20±3.15	0.819
P value from baseline			
6th week	<0.001**	<0.001**	-
12th week	<0.001**	<0.001**	-

**Highly significant

Both the drugs reduced the Y-BOCS which was highly significant

Table 3: Comparative evaluation of WHO well being scale in two groups of study subjects (Mean±SD)

WHO well being	Fluvoxamine	Sertraline	P value
Baseline	14.76±1.48	13.92±1.35	0.041
6th week	17.36±1.75	16.80±1.32	0.208
12th week	19.72±1.86	18.96±3.05	0.293
P value from baseline			
6th week	<0.001**	<0.001**	-
12th week	<0.001**	<0.001**	-

**Highly significant

Both the drugs increased the WHO scale which was highly significant

Table 4: Comparison of adverse events in two groups of patients

Adverse events	Fluvoxamine N = 9	Sertraline N = 6
Somnolence	5(20.0%)	0
Headache	2(8.0%)	2(8.0%)
Nausea	1(4.0%)	2(8.0%)
Nervousness	1(4.0%)	0
Dry mouth	0	1(4.0%)
Anxiety	0	1(4.0%)

No statistically significant difference between the two groups

DISCUSSION

The present study is a head on trial that compares the Yale Brown scores and the quality of life in patients with OCD and an improvement in the WHO 5 well being scores over a period of 12 weeks.

The efficacy of fluvoxamine in the management of OCD has been confirmed by a number of randomized, double-blind, controlled studies, making it the first selective SSRI to be registered for this clinical indication [8]. Fluvoxamine showed a consistent earlier onset of therapeutic effects across different efficacy parameters when compared with the findings of previous studies involving other SSRI's.

Sertraline is effective in the treatment of obsessive-compulsive disorder. The ability of sertraline to maintain improvement was demonstrated in a double-blind, placebo-controlled study in which the patients were assigned to a double-blind, fixed-dose trial for 52 weeks.

At the 52- week end point, mean scores on four primary outcome measures—the YBOCS, the Clinical Global Impression (CGI) severity-of-illness and improvement scales, and the National Institute of Mental Health Global Obsessive Compulsive Scale— showed significantly greater improvement ($p<0.005$) in the sertraline group than in the placebo group[9].

A Cochrane review compared the SSRIs in term of their efficacy and tolerability in OCD [10]. The SSRIs compared were fluoxetine, fluvoxamine, sertraline, paroxetine, and citalopram. The SSRIs as a group were shown to be more effective for treating OCD symptoms compared with placebo, and individually all drugs showed effect sizes of reasonable magnitude

In the present study, both the drugs reduced the YB-OCS from the baseline significantly ($P<0.01$). Although sertraline reduced the YB-OCS more than that of fluvoxamine, but it was not significant ($P>0.05$).

The quality of life was compared with WHO scale, both the drugs increased the score form their respective baseline which was statistically significant ($P<0.01$). Sertraline improved the WHO scale more than fluvoxamine, but it was not significant ($P>0.05$).

Regarding adverse events there was no statistically significant difference between the two groups, but Sertraline group had less number of adverse events, both the groups had no serious adverse events.

Long term SSRI treatment is needed for OCD. Hence, an ideal agent should have good efficacy and low propensity to cause adverse effects.

Although many studies have confirmed the efficacy and tolerability of Fluvoxamine and Sertraline in OCD patients, due to some unknown reasons there have been very few head to head trails. This present study compares both drugs which are commonly used in treatment of OCD

Limitations of the Study

Limitation of the present study is the study design, it was an open labelled study and the study duration was only 12 weeks. More randomized, longer duration double blind studies with large sample size are needed to accurately determine the efficacy and tolerability of fluvoxamine and Sertraline in OCD.

CONCLUSION

From the results of this study it can be concluded that both Fluvoxamine and Sertraline are effective in the treatment of OCD for treatment of obsessive compulsive disorder, and Sertraline has a slightly better tolerability profile than fluvoxamine.

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