Efficacy of combination of fluoxetine and cognitive behavioral therapy and fluoxetine alone for the treatment of obsessive compulsive disorder

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Abstract: A number of pharmacological approaches as well as psychological interventions are effective in the treatment of obsessive-compulsive disorder (OCD). The present study was conducted to see the relative efficacy of treatment approaches. 30 diagnosed cases of OCD were taken and divided into two groups. Each group consisted of 15 patients. Group A (N=15) received Capsule Fluoxetine and Group B (N=15) received Capsule Fluoxetine and CBT (13 weekly sessions). Twenty six participants completed the study (13 in each group). Dhaka University Obsessive-compulsive Scale (DUOCS) was used to measure the symptom severity. Symptom scores were measured at weeks 1, 5, 9 and 13. After 13 weeks, analysis of the data was done and the means of initial DUOCS score and 13th week score were compared. In both the groups the mean score changes were highly significant (p=0.000). Intra group analysis revealed that both the treatment approaches were highly efficacious. Inter-group analysis revealed that the response in combination group was significantly higher starting from 9th week, continuing up to 13th week. Mean symptom reduction and mean percentage reduction of symptoms were also higher in the case of combination group.

Keywords: Obsessive compulsive disorder, cognitive behavioral therapy, Dhaka university obsessive compulsive scale, Fluoxetine, efficacy study.

INTRODUCTION

Obsessive compulsive disorder (OCD) is characterized by obsessions, compulsions, or by a combination of both. According to some, OCD is the fourth most common mental disorder (Hollander and Stein, 1997). Both medication and psychological therapy are used to treat OCD. CBT is well documented intervention for children, adolescents, and adults with OCD (Barbara *et al*. 1998). CBT combines behavior therapy with an emphasis on changing patients' thought patterns. It aims to reduce the catastrophic thinking that leads to a heightened, unreasonable sense of responsibility. Open trials of CBT have yielded treatment response rates of 60 percent to 80 percent with mean symptom reductions of up to 60 percent. The development of serotonin specific reuptake inhibitors (SSRIs) was an important step in OCD management as these agents have proven to be effective in the disorder (Greist *et al*., 1995, Piccinelli *et al*., 1995). But the response to SSRI medication is limited as evidenced from empirical finding and literature review.

In a number of studies it was observed that there was an additive effect when medications were added to exposure therapy. Foa and colleagues conducted a double-blind, randomized, placebo-controlled study to test the relative and combined efficacy of clomipramine and exposure and ritual prevention in the treatment of OCD. They found that all the treatment approaches were efficacious for OCD, intensive exposure and ritual prevention may be superior to Clomipramine and, by implication, to monotherapy with other SSRI (Foa *et al*., 2005). Marks *et al*. (1980) were able to show that Clomipramine improved the response to exposure therapy for patients with chronic ritualistic behavior. The medication also improved compliance with the therapy.

Fluoxetine is an important proto type SSRI. It is assumed that the combined treatment of CBT and Fluoxetine is more efficacious than Fluoxetine alone. In this study we attempted to find out the actual response of patients to Fluoxetine alone or in combination with CBT. Drug trials and efficacy studies are rare in resource limited settings, and this study represents an approach to fulfill this gap.

METHODOLOGY

An open label, controlled, prospective and comparative study was conducted in the Department of Psychiatry, Bangabandhu Sheikh Mujib Medical University (BSMMU) for a period of one year starting from January 2006 to June 2007. The objective of the study was to assess the efficacy of Fluoxetine and combined Fluoxetine & CBT in the treatment of OCD. Thirty two consecutive patients, who were diagnosed with OCD using the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (American Psychiatric Association, 2000) by a psychiatrist, were asked to participate in the study. OCD patients with

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psychiatric co-morbidity or co-occurring neurological condition or mental retardation requiring treatment outside this study were excluded from the study to elicit the actual response on OCD. Patients getting concurrent treatment with psychotropic medication or psychotherapy outside the study were also excluded. Thirty of them gave informed written consent to enter the study and the protocol was approved by the ethical approval committee of BSMMU. The participants were randomly divided into two groups, Group A and Group B, each consisting of 15 patients. At the start of the study demographic data were obtained by using a semi-structured socio-demographic questionnaire.

To assess the baseline level of OCD symptoms, Dhaka University Obsessive Compulsive Scale (DUOCS) (Mozumder and Begum 2005) was used in both the groups. DUOCS is a 20-item scale with 5 answer points which can be used for diagnosis and measurement of severity of OCD. The ideal cut-off score for screening OCD was 17 with sensitivity of 87% and specificity of 90%. Four equal interval percentile ranges were set to indicate four levels of severity namely mild (up to 23), moderate (24 to 40), severe (41 to 49) and profound (50 to 80). It can measure obsessions and compulsions separately.

In a multi centre study, it was found that steady state plasma levels of fluoxetine and norfluoxetine are not related to clinical outcome in patients with OCD. The optimum dose of fluoxetine for a patient will be the dose that produces the largest therapeutic effect with the smallest side effect burden (Koran *et al*., 1996).

Group A received capsuled Fluoxetine (20 mg) in the morning after breakfast. After one month the dose was increased to 40 mg per day (20 mg in the morning and 20 mg after lunch). At the end of 2nd month the dose was increased to 60 mg per day (40 mg in the morning and 20 mg after lunch). In the first month follow up was done weekly by a psychiatrist to monitor clinical status and medication effects. During the third and fourth month, the follow up was done at least fortnightly. General support and information were given during the follow ups. The first visit took on an average 30-40 minutes and the follow up visits took 20-25 minutes for each patient. Dosage increase was delayed or dosages reduced for clinically significant side effects, e.g., those producing distress and dysfunction for which the clinician and the patient believed dosage reduction was indicated.

Group B was given capsuled Fluoxetine in the same manner and also received CBT. A detailed CBT treatment manual, prepared by the psychotherapy wing of BSMMU which involved the work of a number of psychiatrists and clinical psychologists, was used for the purpose. The CBT regimen consisted of 13 visits over 13 weeks' time and involved (1) Psychoeducation (2) Cognitive training (3) Mapping of OCD target symptoms and (4) Exposure and response (ritual) prevention. Visits were conducted weekly and lasted approximately one hour. Each session included a statement of goals, review of the previous week, provision of new information, therapist assisted practice, homework for the coming week, and monitoring procedures. The CBT manual provided sufficient flexibility to accommodate individual patient need and ensured uniformity of CBT delivery. CBT and medication visits were done in the same day to reduce any inconveniences for the patients. CBT was conducted by the clinical psychologists working at the Department of Psychiatry, BSMMU.

All patients were assessed at baseline and at weeks 5, 9 and 13 using the Dhaka University Obsessive Compulsive Scale (DUOCS) which is a self rating scale. The scale is in the native language of the participants (Bengali). Participants, who did not understand any part of the questionnaire, had it explained to them by the researchers. Twenty six patients completed the 13-week long study.

RESULTS

The mean age of the study population was 30.23±8.67 years, ranging from 20 to 52 years. The mean age of the Group A was 31.27±9.03 years and that for the Group B was 29.20±8.48 years. However, analysis did not find any statistically significant mean age difference between the two groups of patients (p=0.524). The mean initial DUOCS score in the study participants was 41.63±15.15. The mean initial score for Group A was 46.6±16.04 and for Group B it was 36.67±12.85 and it was not significant (p=0.072). The mean duration of illness at the time of interview was 8.50±6.87 years. The mean duration of OCD in Group A was 7.53±8.11 years and in Group B it was 9.47±5.47 years and the difference was not significant (p=0.451).

In 13 completed participants of Group A the DUOCS scores in the initial week ranged from 18 to 72 and mean score was 46.08±16.78, during 5th week the scores ranged from 12 to 65 with mean score of 39.21±15.21. During 9th week the score ranged from 8 to 62 with mean score 34.46±16.21. In the 13th week the score range was 10 to 50, and the mean score was 28.23±12.96.

It was observed that in 13 completed participants of Group B the DUOCS score in the initial week ranged from 21 to 59 and the mean score was 38.08±13.29, during 5th week the DUOCS score range was 16 to 47 with mean score of 30.64±10.98. During 9th week the score range was 10 to 35 with mean score 23.92±8.43, and in the 13th week score range was 8 to 29 and mean score was 18.77±6.3.

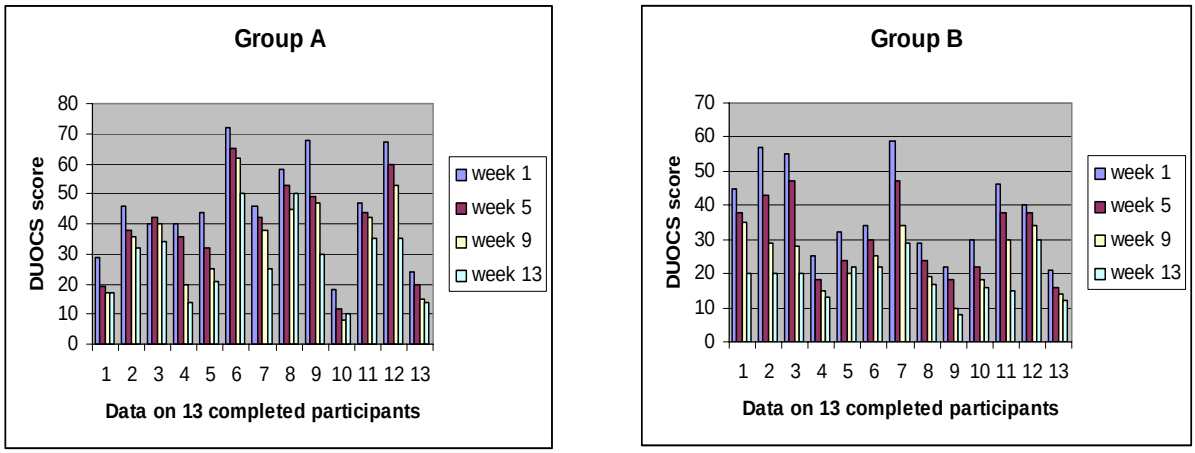

Fig. 1: DUOCS score in 13 completed patients in each group.

Table 1: Differences between group A and B for the DUOCS scores

	df	Mean Difference	Std. Error Difference	Sig. (p value)	95% Confidence Interval of the Difference	
					Lower	Upper
Base line score	1	9.9	5.3	.072	-.9	20.8
Score at 5th week	1	8.6	5.0	.099	-1.7	18.9
Score at 9th week	1	10.5	5.0	.048*	.1	21.0
Score at 13th week	1	9.5	3.9	.026*	1.2	17.7

*p < 0.05; df= Degree of freedom

Table 2: Comparison of score between 1st week and 13th week

Characteristics	Group A: Fluoxetine (Mean ± S.D.)	Group B: Fluoxetine+ CBT (Mean ± S.D.)	*t* value, degrees of freedom	Significance (p value)
Mean of Difference between 1st and 13th week score	17.85±10.02	19.31±10.56	0.362*, 24	0.721
Mean % reduction of symptoms from 1st to 13th week	39.29±15.45	48.95±13.68	1.712*, 24	0.1

P<0.05 = significant, S.D.=Standard Deviation, *=equal variances assumed.

The in between group comparisons for the group A and group B for the DUOCS scores was carried out using the ANOVA with post hoc analysis using the Bonferroni correction and independent sample t-test. The mean difference for the score for DUOCS for the two groups at base line was 9.9 (SE±5.3; 95% CI -.94 to 20.8). It was not statistically significant. This means that the two groups did not differ significantly at base line for the scores on DUOCS and hence were comparable for the severity of illness. The mean difference at 5th week was 8.6 (SE ±5.0; 95% CI -1.7 to 18.9). This difference was also not statistically significant. However, the mean differences between the two groups were statistically significant at the 9th and 13th weeks. The mean difference for the DUOCS for the two groups at 9th week was 10.5 (SE ±5.0; 95% CI .1 to 21.0; p<.05) and at 13th week it was 9.5 (SE ±3.9; 95% CI 1.2 to 17.7; p<.05), with group B (both fluoxetine and CBT) having a higher reduction in scores as compared to group A (only flouxetine). This represents that combination of CBT and fluoxetine produces a greater improvement in severity of OCD as compared to fluoxetine alone (table 1).

To see the efficacy of different treatment groups we compared the means of initial DUOCS score and 13th week score using paired t test in both the treatment groups. The t-test score for Group A was 6.419 with df=12 and for Group B it was 6.591 with df=12. In both the groups the mean score changes were highly significant (p=0.000). This finding echoes the fact that both Fluoxetine, and combined CBT & Fluoxetine are standard proved treatment of OCD. This finding was similar to a number of previous studies conducted on similar topics Marks *et al*., 1980; Pigott *et al*., 1990 and Griest *et al*., 1995).

In analysis of means of differences between the initial score and 13th week score it was found that more reduction in symptom score occurred in Group B patients (19.31±10.56) than Group A patients (17.85±10.02) but it was not statistically significant (p=0.721). In case of means of percentage of reduction of symptom score from 1st week to 13th week more reduction was observed in Group B (48.95 ± 13.68) than Group A patients (39.29 ± 15.45) but it was not statistically significant (p=0.1) (table 2).

DISCUSSION

This was the first time that a study for measuring the efficacy of pharmacological and psychological treatments in a psychiatric disorder has been conducted in Bangladesh. The participants were comparable at baseline and 5th week after initiation of the treatments. But at the 9th week and 13th weeks follow up, the greater improvement in combination group becomes evident. Reduction of symptom score as well as percentage of reduction of symptom score were more in case of combination group. The findings of the current study support previous findings of Marks *et al.* (1980).

The participation rate of the current study was 93.75%, which is acceptable for a valid study. Out of an initial thirty patients, twenty six (88.66%) completed the study, which was consistent with the dropout rate of similar follow up studies. Nevertheless, as this was an open label study which may cause biases, the study results should be considered with caution. The CBT plus Fluoxetine group received more contact time with the therapist than the only Fluoxetine group which may cause bias. There were also several limitations of cognitive behavioral therapy. The patient may not comply with the therapeutic directions, including homework and may also substitute ritualistic thoughts in place of overt behaviors to diminish the anxiety. This result, therefore, may not be representative for the whole population. However, this can be used as a baseline for any future study in this subject or this type of efficacy study in any topic.

CONCLUSION

The challenges for professionals involved in the treatment of OCD are now to discover the biology of this disorder and to make pharmacological and psychological treatments available to patients from all resource settings. Worldwide trained CBT therapists are limited in number. To deal with the present need and future demand we need to increase the number of trained CBT therapists. To initiate treatment with medication we should keep in mind to use suitable drugs to minimize patients' financial burden and side effect profile. Also the established dose titration and drug combination should be followed with the same goal of patient benefit.

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