

## Comparing the Effects of Clomipramine and Fluoxetine on Fasting Blood Glucose in Children With Obsessive-Compulsive Disorder

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**Objective:** This study was conducted to compare the effects of clomipramine and fluoxetine on fasting blood glucose (FBS) in children with obsessive-compulsive disorder (OCD).

**Method:** Thirty nondiabetic children with OCD entered this randomized trial. Subjects were between 7 to 17 years of age and had not received any medication that could affect blood glucose level for at least 2 weeks prior to the initiation of the study. Patients were assigned to receive 20 to 60 mg/d of fluoxetine or 75 to 200 mg/d of clomipramine for 8 weeks. The exclusion criteria were pregnancy and lactation, history of diabetes mellitus, any liver and thyroid disorder, epilepsy and major heart disease. Additionally, none of the patients should have received electroconvulsive therapy within 6 months prior to the initiation of the study. FBS levels were measured at baseline, 4 and 8 weeks after the initiation of the trial.

**Results:** In the fluoxetine group, FBS level was decreased from 82.93 mg/dL (baseline) to 79.73 mg/dL at week 4 ( $P<0.001$ ) and to 72.53 mg/dL at week 8 ( $P<0.001$ ). On the other hand, in the clomipramine group, FBS level was increased from 84.93 mg/dL (baseline) to 87.00 mg/dL at week 4 ( $P<0.05$ ) and to 95.33 mg/dL at week 8 ( $P<0.001$ ).

**Conclusion:** This 8-week study demonstrated that FBS levels may decrease in children with OCD who received fluoxetine, and may increase in those treated with clomipramine. Therefore, it is suggested that FBS levels should be monitored and taken into consideration when choosing between fluoxetine and clomipramine in the treatment of OCD.

### Keywords:

Blood glucose, Child, Clomipramine, Fluoxetine, Obsessive-Compulsive disorder.

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Obsessive-compulsive disorder (OCD) is characterized by severe recurrent obsessions or compulsions that are distressing and may significantly affect some aspects of functioning. Fluoxetine, a specific serotonin reuptake inhibitor (SSRI), and clomipramine, a tricyclic antidepressant (TCA) with more potent inhibitory effect on serotonin reuptake as compared with other TCAs, are two antidepressants that have been successfully used in the treatment of OCD for many years. Clomipramine was once considered to be superior to SSRIs in the treatment of OCD; however, recent comparisons between these groups have noted comparable efficacies (1). Patients on clomipramine are more likely to discontinue treatment due to its side effects. When compared with SSRIs, clomipramine has a higher risk of toxicity and is less tolerated; therefore, it is currently regarded as a second-line agent for the treatment of OCD (2).

There are some reports on the alteration of fasting blood glucose (FBS) level in diabetic and non diabetic patients receiving TCAs or SSRIs. Goodnick et al. noted that due to the predominant noradrenergic effects of TCAs, these agents may increase gluconeogenesis and glycogenesis.

As a result, they may interfere with the control of diabetes.

The mentioned study reported that TCA use in diabetic patients could result in hyperglycemia and an increase in carbohydrate craving from 86% to 200%. On the other hand, SSRIs could decrease FBS levels by as much as 30% (3). Daubresse et al. evaluated 82 obese, non-insulin dependent diabetic mellitus patients who were receiving oral medications to control their blood glucose.

Thirty-nine of these patients received fluoxetine, while 43 received placebo. Patients' FBS levels were compared 3 and 8 weeks after the initiation of the study. FBS levels were decreased by 1.5 mmol/L in the fluoxetine group and by 0.4 mmol/L in the placebo group at the third week. Similarly, FBS levels were decreased by 1.7 mmol/L and 0.2 mmol/L in the fluoxetine and placebo groups, respectively, at week 8 (4).

In another study by Okane et al., 19 patients with noninsulin-dependent diabetes mellitus who had received either fluoxetine 60 mg/day or placebo for 12 months were studied. FBS levels significantly decreased by 0.9 mmol/L at month 3 and by 1.8 mmol/L at month

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6 in the fluoxetine group; however, changes were not significant at months 9 and 12 (5). One study noted that mean glycosylated hemoglobin improved to a greater extent, although not significantly, with fluoxetine when compared with placebo (6).

Ghaeli et al. conducted a double blind study that compared the effects of fluoxetine and imipramine on FBS in 43 depressed patients who did not suffer from diabetes mellitus or hypercholesterolemia. Serum FBS levels were measured at baseline and at weeks 4 and 8 of the study. This study noted that fluoxetine significantly decreased the FBS level from 88.5 mg/dL to 85.0 mg/dL at week 4, and to 79.8 mg/dL at week 8. On the other hand, imipramine increased the FBS level from 86.96 mg/dL to 89.71 mg/dL (not significant) at week 4 and to 96.90 mg/dL (significant) at week 8(7).

This study was designed to compare the effects of fluoxetine and clomipramine on FBS in nondiabetic children suffering from OCD.

### Material and Methods

Twenty-nine nondiabetic children with OCD (based on DSM-IV criteria) entered this randomized, double blind study. Patients were between 7 to 17 years of age. Except for the medications under study, patients did not receive any psychotropic drugs or any other medication that could affect FBS levels (e.g. corticosteroids, sulfonyleureas, insulin, metformin, beta-blockers, etc) for at least two weeks before entering and throughout the study.

The exclusion criteria included diabetes mellitus, pregnancy and lactation, any liver and thyroid disorders, epilepsy and major heart diseases. Additionally none of the patients had received electroconvulsive therapy within 6 months prior to study.

Subjects were assigned to receive oral fluoxetine (20-60 mg/day) or clomipramine (75-200 mg/day) for a period of 8 weeks. FBS levels were measured at the initiation of therapy as well as 4 and 8 weeks after starting the medications. All patients/guardians gave informed consent. Repeated-measures analysis of variance with a 2-tailed post hoc Tuckey mean comparison test was utilized for the FBS changes from baseline. A paired Student t-test was used to compare the outcomes of the two groups. Differences were considered significant when  $P < 0.05$ .

### Results

Eleven males and four females received fluoxetine and 10 males and 5 females received clomipramine in this study. In the fluoxetine group, FBS level decreased from 82.93 mg/dL (baseline) to 79.73 mg/dL at week 4 ( $P < 0.001$ ) and to 72.53 mg/dL at week 8 ( $P < 0.001$ ) (Figure 1). On the other hand, FBS level increased from 84.93 mg/dL (baseline) to 87.00 mg/dL and to 95.33 mg/dL at weeks 4 ( $P < 0.05$ ) and 8 ( $P < 0.001$ ), respectively, in the clomipramine group (Figure 2).

It should be noted that in both groups, the FBS levels were significantly different at weeks 4 and 8 from the

baseline. In the fluoxetine group, FBS levels increased in 2 patients and decreased in the remaining 13 patients

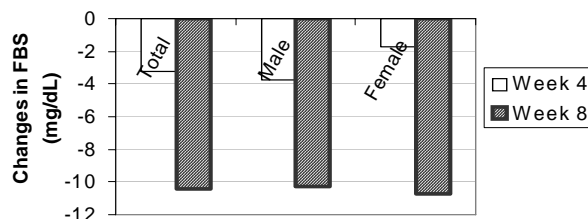


figure 1.  
FBS Changes (mg/dl) from Baseline  
in Patients on Fluoxetine

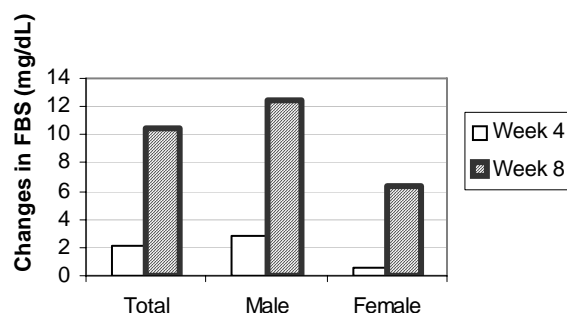


figure 2.  
FBS Changes (mg/dl) from Baseline  
in Patients on Clomipramine

during the study. In the clomipramine group, one patient showed a decrease in FBS level, this level did not change in one patient and the remaining 13 patients showed increased FBS levels.

### Discussion

Even though there are some reports on alteration of blood glucose levels in diabetic patients receiving TCAs or SSRIs(3-6), only one study compared FBS changes after initiation of a TCA (imipramine) and a SSRI (fluoxetine) in nondiabetic adults who suffered depression(7).

Similar to the latter study, the present study on nondiabetic children with OCD noted decreased FBS levels in patients treated with fluoxetine and increased FBS levels in patients treated with clomipramine (a TCA) after 4 and 8 weeks of the treatment with these agents. It is suggested that FBS levels of patients at high risk for developing diabetes and of those with high normal or low normal FBS should be taken into consideration before starting fluoxetine or clomipramine. Additionally, to prevent further complications, it may be necessary to regularly monitor FBS levels in patients on these medications. It is also very important to consider coexisting medical conditions and any drug interactions before initiating fluoxetine or clomipramine.

In general, fluoxetine may be preferred in OCD patients with high normal FBS or with a high risk of developing diabetes. It should be noted that the duration of the present study was not long enough to show the chronic effects of fluoxetine and clomipramine on FBS. Further studies are needed to assess the effects of long-term use of clomipramine and fluoxetine in nondiabetic, OCD patients.

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