

Effects of fluoxetine on sex hormonal levels in depressed male patients

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ABSTRACT

Objective: This study was conducted to assess the effect of fixed dose fluoxetine monotherapy in depressed male patients on serum levels of testosterone, prolactin, follicular stimulating hormone (FSH), luteinizing hormone (LH) and estradiol.

Subjects and methods: Twenty male patients with depression on 20 mg/day fluoxetine monotherapy and 20 apparently healthy male taken as a control group, were included in this study. Serum hormonal levels of testosterone, prolactin, FSH, LH, and estradiol were assessed in both patients on fluoxetine therapy and the control group, using special kits for each hormonal assay with the aid of Gamma Counter.

Results: There were no significant differences in levels of testosterone, prolactin, FSH, LH, and estradiol between depressed male patients on fluoxetine therapy and controls.

Conclusion: Fluoxetine therapy in a dose of 20 mg/day can be considered as a safe antidepressant drug on serum levels of testosterone, prolactin, FSH, LH and estradiol.

الخلاصة

أهداف الدراسة: أجريت هذه الدراسة لتحديد تأثير جرعة ثابتة من عقار الفلوكستين كعلاج أحادي في مرضى الاكتئاب من الذكور على مستوى هرمونات التستوستيرون، البرولاكتين، هرمون الحافز للحويصلات، هرمون المحفز للخلايا البينية وهرمون الاستراديول.

المشاركون وطرق العمل: عشرون مريض من الذكور يعانون من الاكتئاب وتحت عقار الفلوكستين كعلاج أحادي بجرعة 20 ملغ يوميا وعشرون من الأصحاء الذكور من أعمار متقاربة أخذت كمجموعة ضبط. تم في المجموعتين قياس مستوى هرمونات التستوستيرون، البرولاكتين، الحافز للحويصلات، المحفز للخلايا البينية، وهرمون الاستراديول باستخدام عدة عمل خاصة بكل هرمون وبمساعدة جهاز عداد كاما.

النتائج: أظهرت نتائج هذه الدراسة عدم وجود فرق معنوي في مستوى الهرمونات عند مرضى الاكتئاب المثبتين على علاج الفلوكستين بالمقارنة مع مجموعة الضبط.

الاستنتاج: يمكن اعتبار عقار الفلوكستين المضاد للاكتئاب امينا في مرضى الاكتئاب من الذكور في مستوى جرعة 20 ملغ/يوم قدر تعلق الأمر بمستوى هرمون التستوستيرون، البرولاكتين، هرمون الحافز للحويصلات، هرمون المحفز للخلايا البينية وهرمون الاستراديول.

Many drugs have been claimed to affect male sex hormonal levels, especially testosterone and prolactin.¹ Of these drugs, carbamazepine which is structurally related to imipramine, was shown to increase metabolic clearance of testosterone and reduce luteinizing hormone (LH).² In fact, sexual dysfunction induced by antidepressant drugs, is a well recognized complication of treatment for mood and anxiety disorders.³ There is a documentation of reduced free testosterone level during treatment with imipramine⁴

Fluoxetine is a widely prescribed antidepressant and acts physiologically as a selective serotonin reuptake inhibitor (SSRI).⁵ Several studies have been carried out to assess serum sex hormonal levels especially testosterone and prolactin in depressed patients on fluoxetine therapy.^{6,7} This study aimed to assess serum levels of testosterone, prolactin, follicular stimulating hormone (FSH), LH and estradiol (E₂) in male depressed patients on fluoxetine therapy at a fixed dose.

Table 1. Comparison of measured male sex hormones between patients on fluoxetine therapy and controls. Values are represented as mean \pm SD.

Parameters	Testosterone ng/ml	Prolactin ng/ml	FSH IU/L	LH IU/L	Estradiol pg/ml
Patients (n=20)	6.94 \pm 2.58	7.34 \pm 2.34	6.03 \pm 2.71	6.75 \pm 2.41	6.40 \pm 2.00
Control (n=20)	6.20 \pm 2.45	7.44 \pm 2.54	6.11 \pm 2.82	6.89 \pm 2.31	6.23 \pm 2.07
P value	NS	NS	NS	NS	NS

FSH=Follicular stimulating hormone, LH=Luteinizing hormone, NS= Not significant

Subjects and methods

Out of 34 patients referred to us, only 20 were included in this study based on the criteria of patient's selection as follow: male patient with depression (diagnosis made by specialist in the field of psychiatry), on fluoxetine therapy at a dose of 20 mg/day. Careful history made sure that no drug was added especially during the last 2 weeks of the study. Patients with duration of treatment less than 2 months were excluded, they were free from other organic diseases especially hepatic, renal, thyroid diseases or diabetes mellitus.

The mean age of the selected patients for the study was 29.5 \pm 6.9 years (ranged between 19 and 48 years) on fluoxetine therapy (20 mg/day) for a mean duration of 7.65 \pm 3.52 months (ranged between 2 and 15 months). Twenty apparently healthy males were also included, in this study, as a control group with a mean age of 30.15 \pm 6.31 years (ranged between 20 and 45 years).

Blood samples were taken from patients and controls nearly by afternoon for the assay of serum testosterone, prolactin, LH, FSH, and E₂. The concentration of serum parameters were measured by a radioimmunoassay kits (Immunotech Company-France), with the aid of Gamma counter set for ¹²⁵I. All assay procedures were performed according to instructions of reagent manufactures.

Values were represented as mean \pm SD. Unpaired t-test was used for comparison between treated patients and controls. Values were considered significant at p < 0.05.

Results

No significant difference was noticed between patients on fluoxetine therapy and controls in the serum levels of testosterone, prolactin, FSH, LH and estradiol, as shown in table 1.

Discussion

This study showed no significant difference in the levels of testosterone. However, Bell et al.⁶ did not find a significant relationship between fluoxetine therapy and

testosterone levels between treated patients and controls. Many drugs can play a role in modifying testosterone serum levels. Ketoconazole, megestrol, cimetidine, and spironolactone have all been reported to lower testosterone levels.^{1,8} Methadone and other opioids can also suppress testosterone by reducing LH levels centrally.¹ Studies investigating testosterone levels and mood disorders have shown conflicting results.^{9,10} Levels of testosterone in 12 depressed males were compared with controls, no significant differences were noted between the two groups.¹⁰

This study also showed insignificant differences in the levels of prolactin, FSH, LH and estradiol between patients on fluoxetine therapy and controls. Elevation of prolactin occurs with a number of medications used to treat psychiatric disorders. These include neuroleptics such as perphenazine, chlorpromazine and haloperidol and several antidepressants including imipramine, amitriptyline and paroxitin.¹¹ Fluoxetine is known to potentiate 5-hydroxytryptamine (5HT) induced elevation of prolactin in rats.¹² In addition, adolescent female has been reported with galactorrhoea and hyperlactinemia after treatment with fluoxetine.¹³ However karoussi⁷ reported no increase in prolactin response to difenfluramine following fluoxetine treatment in depressed patients. Peterson¹⁴ reported a case of 71 year old woman taking estrogen replacement therapy developing galactorrhoea after initiation of fluoxetine for depression and was found to have an elevated prolactin level, which can be explained by the fact that estrogen has positive effects on prolactin release by increasing the number of prolactin secreting cells in the pituitary as evidenced by autopsy studies.¹⁵

No published data has been found regarding the effect of fluoxetine therapy on serum levels of LH, FSH and estradiol in depressed patients. Roste¹⁶ did not find a significant difference between control rats and male rats receiving lamotrigine, regarding testosterone, FSH, and LH levels.

To our knowledge, this could be the first study conducted involving measurement of

testosterone, prolactin, FSH, LH and estradiol all together in patients with depression on fluoxetine monotherapy.

In **conclusion**, fluoxetine therapy at 20 mg/day can be regarded as a safe antidepressant in male patients concerning testosterone, prolactin, FSH, LH, and estradiol.

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