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The influence of antipsychotic drugs on fertility hormones in male patients – Khartoum state

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Abstract

Background: Psychiatric disorders are severe, depilating conditions with unknown a etiology and are commonly misdiagnosed when based solely on clinical interview. Antipsychotic drugs provide effective treatment of psychotic symptoms but might lead to neuroendocrine abnormalities. The study aim to assess fertility hormones Luteinizing and Testosterone among psychotic male patients at Khartoum State.

Materials and Methods: A cross-sectional study was conducted during the period from July to August 2021, with fifty known diagnostic psychiatric patients as cases and fifty healthy people as case controls. The levels of serum testosterone and luteinizing hormones were measured by enzyme linked immune sorbent assay (ELISA).

Results: The mean level of serum luteinizing hormone in psychiatric patients showed a significant decrease (3.8 0.54; P.value = 0.000) and the level of serum testosterone showed a significant increase (8.3 ± 0.92; P.value = 0.000) in psychiatric patients when compared to healthy individuals. There was a significant decrease in LH hormone in patients taking Olanzapine drugs compared to those taking Risperidone drugs (p value = 0.03).

Conclusion: There were significant sexual dysfunctions in psychiatric patients due to antipsychotic drugs, which led to a decrease in luteinizing hormone and an increase in testosterone hormone.

Keywords: Psychiatric disorders; Olanzapine; Risperidone; Luteinizing; Testosterone

1. Introduction

Mental disorder or mental illness or psychiatric disorder refers to conditions that affect cognition, emotion, and behaviour. It's the most common disease affecting the populations and can be categorized into three broad groups according to causes: idiopathic, psychoses due to medical conditions (including neurodegenerative disorders), and toxic psychoses (due to substances of abuse, prescribed medications, or toxins). Psychotic symptoms caused by drug abuse or prescribed medications and symptoms caused by medical disorders such as SLE, seizures, or fevers can occur at any age (1-2). Hormones are widely considered to cause powerful psychological effects. (3). Sexual dysfunction is common in people with psychiatric disorders, it's Known to affect all domains of sexual functions. Reductions in the free Androgen index, a measure of biologically active testosterone, were recently found in a study of first episode antipsychotic-naive men with psychosis (4,5).

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Antipsychotic drugs are used to treat schizophrenia, a chronic severe disease affecting 21 million people worldwide, and treat a manic episode of bipolar disorder [6,7]. Generally, typical antipsychotics have more adverse effects, while the second generation of these drugs, known as atypical ones, have a more favorable adverse effect profile. Sedation, orthostatic hypotension, anticholinergic effects, extrapyramidal symptoms, agranulocytosis, cardiac arrhythmias, hyperprolactinemia, and sexual dysfunction, are the known adverse effects of these drugs[8-10] An atypical antipsychotic drug, olanzapine (OLZ), is one of the most prescribed for acute phase and maintenance of schizophrenia, acute treatment of manic, mixed episodes of bipolar disorder and, also maintenance of bipolar I disorder[7,11].

Antipsychotics are a group of medicines that are mainly used to treat mental health illnesses such as schizophrenia, or mania caused by bipolar disorder, they can also be used to treat severe depression and severe anxiety (12).The exact mechanism of atypical antipsychotics is unknown. They are thought to block certain chemical receptors in the brain and hence relieve the symptoms of psychotic disorders. Risperdal Oral (risperidone) works by blocking the receptors of chemical messengers called dopamine and serotonin, although the principal brain target that all antipsychotic drugs attach to is the dopamine D2 receptor, traditional or typical antipsy chotics ,by attaching to it, induce extra pyramidal signs and symptoms (EPS), They also, by binding to the D2 receptor, elevate serum prolactin(13). Common side effects of antipsychotics include: Drowsiness, Dizziness, Restlessness, Weight gain (the risk is higher with some atypical antipsychotic medicines), Dry mouth, Constipation, Nausea, Vomiting [14].

Individuals with psychoses may have significant impairment in fertility and fecundity, placing them at a reproductive disadvantage **[14-15]**. Patients with schizophrenia have been extensively investigated in this regard **[16-17]**. Early studies attributed the apparent impairment to prolonged institutionalization **[15-16]**, but recent studies have showed similar decreased fertility despite decreased duration of hospital stays **[17-18]**

2. Material and methods

This was a cross-sectional hospital-based study. The study was conducted at Taha Baasher Hospital during the period from August to September 2021.

2.1. Study population

Fifty psychiatric patients aged 27–59 years as cases and fifty healthy individuals as controls were enrolled in the study.

2.2. Inclusion criteria

Psychotic male patients aged over 18 years who provided verbal informed consent were included in this study.

2.3. Exclusion criteria

Females, newly diagnosed psychotic patients, and undifferentiated psychotic patients without treatment were excluded.

2.4. Data collection

Attending clinical refers to filling out a questionnaire with pertinent questions such as age, disease duration, differential diagnosis, and treatment.

2.5. Ethical consideration

This study will be app roved by the ethical committee of Alzaeim Alazhary University-graduate Studies and local authorities in the area of the study. Informed consent was obtained from each participant in the study after explaining the objectives of the study. An interview and a questionnaire were used to collect data.

2.6. Sample collection

Under sterile conditions, 5 ml of venous blood was collected from each participant using a sterile disposable syringe. Serum was separated directly from the plain container by centrifugation at 300 rpm for 5 minutes.

2.7. Principles of measurement fertility hormones

Both testosterone and luteinizing hormones will be assessed with an enzyme linked immune sorbent assay (ELISA). The LH ELISA is based on the principle of a solid-phase enzyme-linked immunosorbent assay (ELISA). The assay system utilizes mouse monoclonal anti--LH for solid phase (microtiter wells) immobilization and a mouse monoclonal anti--LH antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample is allowed to react

simultaneously with the antibodies, resulting in the LH molecules being sandwiched between the solid phase and enzyme-linked antibodies. The Testosterone ELISA is based on the principle of competitive binding between testosterone in the test specimen and testosterone-horseradish peroxidase (HRP) conjugate for a constant amount of rabbit anti-testosterone. In the incubation, goat anti-rabbit IgG-coated wells are incubated with testosterone standards, controls, patient samples, testosterone-HRP conjugate reagent, and rabbitanti-testosterone reagent. The intensity of the color formed is proportional to the amount of enzyme present and is inversely related to the amount of unlabeled testosterone in the sample. A standard curve is obtained by plotting the concentration of the standard versus the absorbance. The testosterone concentration of the specimens and controls run concurrently with the standards can be calculated from the standard curve.

2.8. Data analysis

Statistical analysis was performed using the statistical package for Windows (SPSS v25). For categorical variables, the Student's exact test was used, and for continuous variables, the Kruskal-Wallis test was used. The data is presented as the mean standard deviation (SD). P value less than 0.05 was considered statistically significant.

3. Results

Fifty samples from known psychiatric patients and fifty samples from healthy people as controls were enrolled in the study. As shown in (Table 4.1), there was a significant decrease in luteinizing hormone mean level in psychiatric patients when compared with healthy individuals (P. value = 0.000). Also, the mean level of testosterone showed a significant increase in psychiatric patients when compared with healthy individuals (P.value = 0.000) (table 1).

There was a significant decrease in LH hormone in patients taking olanzapine drugs compared to those taking Risperidone treatments (p value = 0.03) (table 2). Diagnosis and stages showed no effect on the level of testosterone and luteinizing hormones in psychiatric patients (figure 1 and 2).

In the correlation analysis, the study showed negative insignificant correlation of LH level (r =-0.049, p = 0.07) and testosterone level (r =-0.250, p = 0.8) with the duration of disease per years (figure 3, 4).

Table 1 A comparison of testosterone and luteinizing hormone statistical results across study groups

Hormones	case group (n=50)	control group (n=50)	p value
LH(IU/L)	3.8 ± 0.54	6.01 ± 0.56	0.000
Testosterone (ng/l)	8.3 ± 0.92	4.45 ± 0.83	0.000

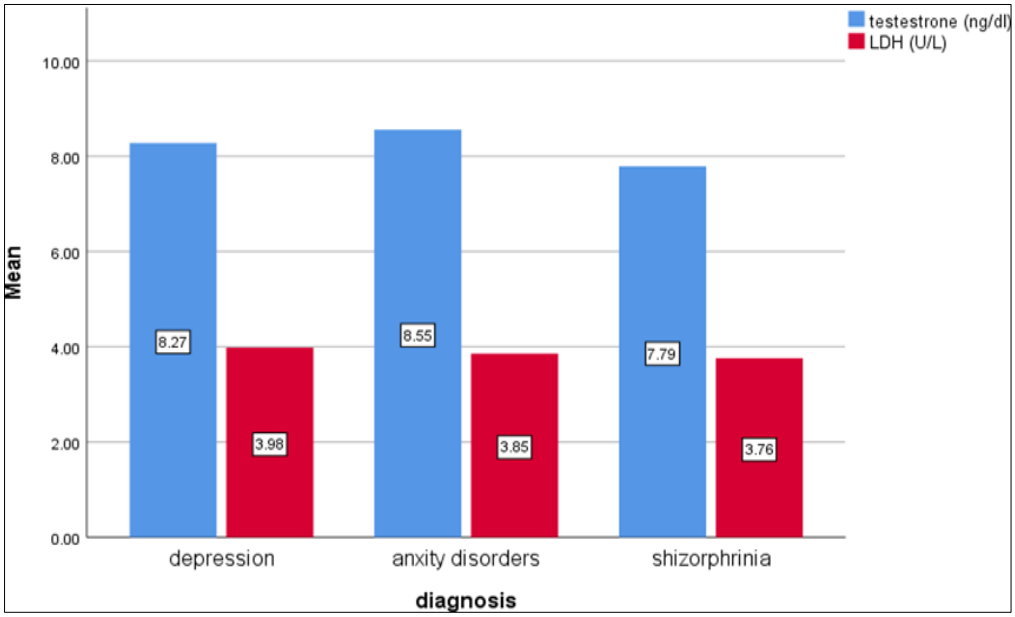

Figure 1 Mean levels of testosterone (ng/l) and LH (IU/L) based on disease diagnosis

Table 2 Compares testosterone and LH levels in case studies based on treatment type

	OLANZPIN tab (n= 28)	RISPERIDONE (n= 22)	P value
LH(IU/L)	3.7 ± 0.5	4.1 ± 0.5	0.03*
Testosterone (ng/l)	8.3 ± .89	8.4 ± .9	0.6

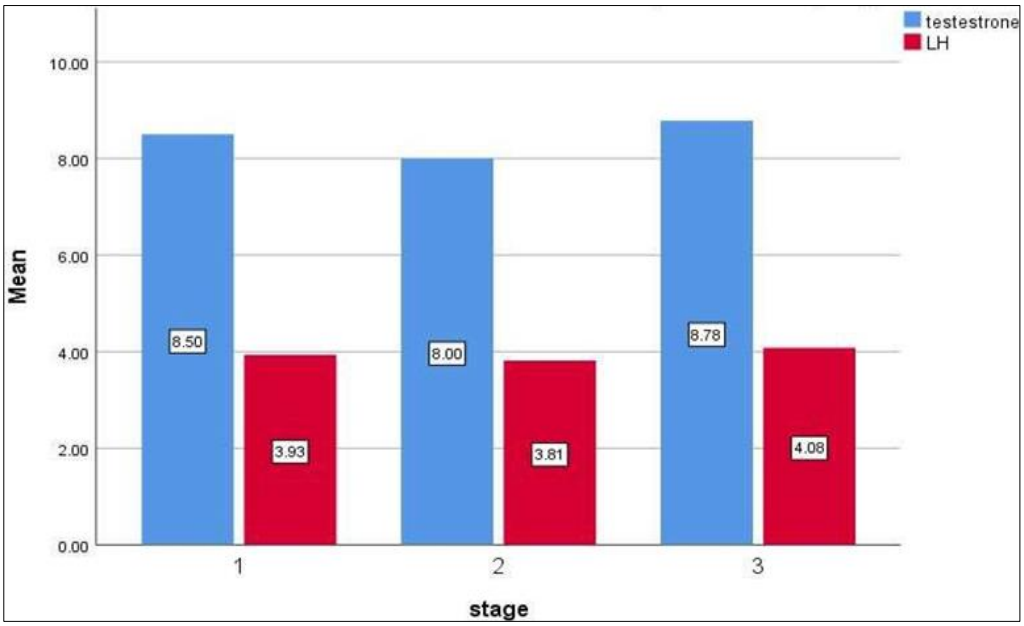

Figure 2 Mean of testosterone (ng/l) and mean of LH (IU/L) according to stage of disease

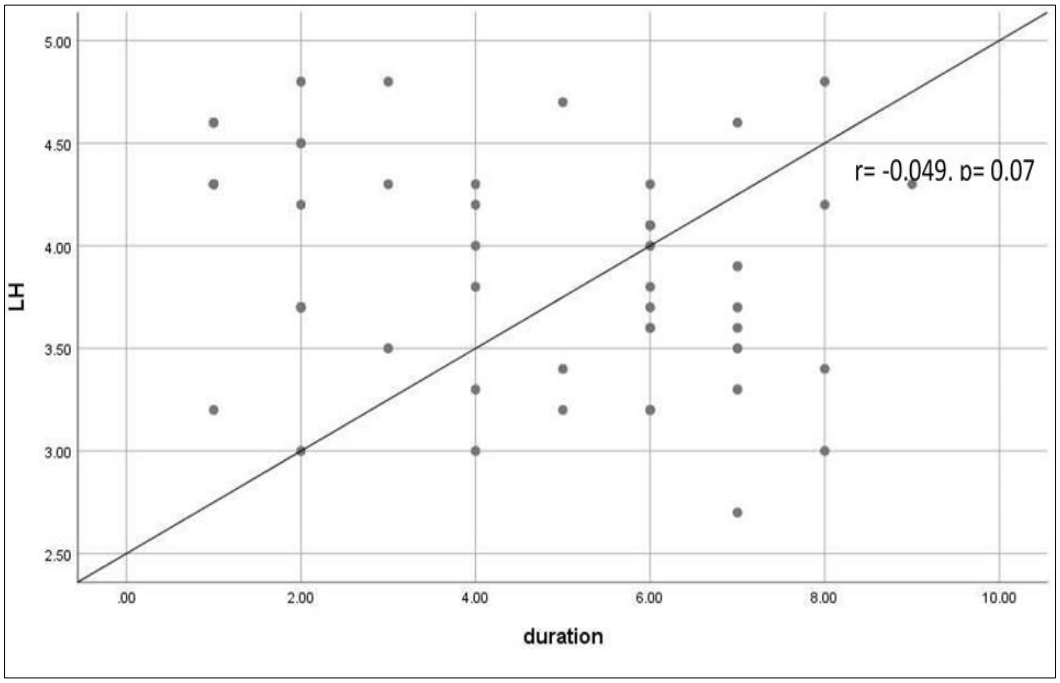

Figure 3 Correlation between LH (IU/L) and Disease Duration by Years

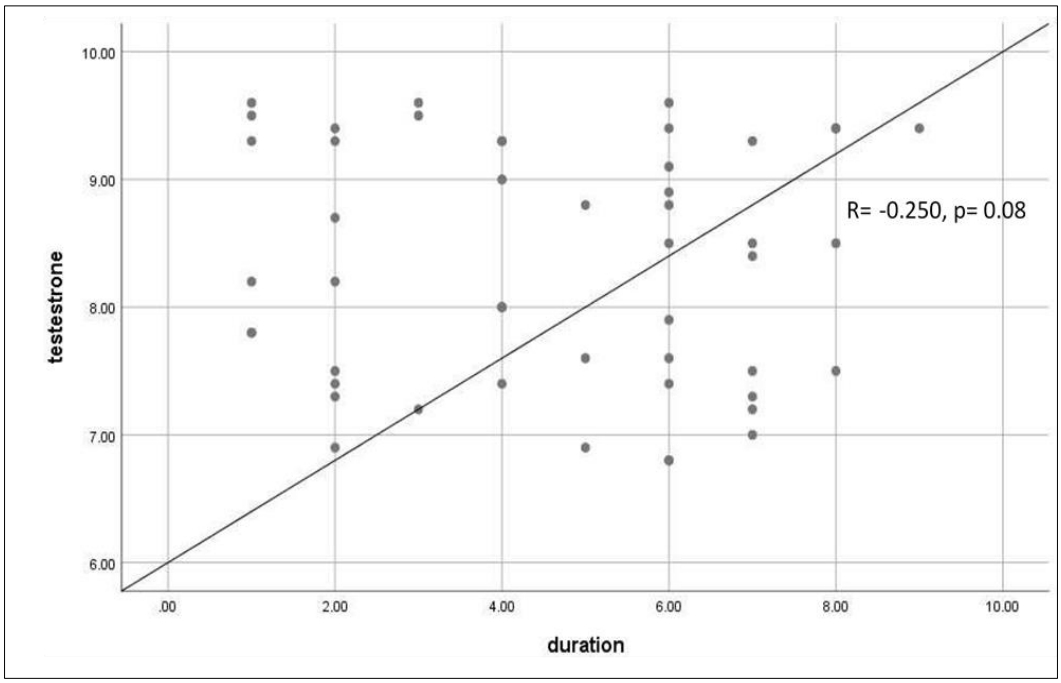

Figure 4 Correlation between testosterone (ng/l) and the duration of disease by years

4. Discussion

1% of the world's population is at risk from psychiatric disorder. Psychotropic medication-induced changes in mood, cognition, and behavior may influence the hormone levels causing sexual dysfunction and other clinical symptoms. Antipsychotics, anticonvulsants, and other psychotropic medications all have detrimental effects on sperm quality and sexual function. These negative side effects differ amongst men and are less severe for some drugs, allowing their effects to be somewhat controlled. (6,7). The major function of olanzapine is to block certain dopamine receptors in the brain, which helps to balance out dopamine overactivity. Olanzapine also affects serotonin (5-HT), another neurotransmitter in the brain, which may potentially contribute to its advantageous effects. It is interesting that there is no research examining the harmful effects of olanzapine (OLZ), an atypical antipsychotic medicine, on the male reproductive system, despite the fact that it is known that OLZ causes sexual dysfunction in men (19). When compared to healthy people, the study found that luteinizing hormone levels were significantly lower in psychiatric patients. When compared to healthy people, the amount of the hormone testosterone was much higher in psychiatric patients. This result was in line with a Brazilian study that found a high correlation between psychiatric disorder and the concentration of these hormones (20). Antisychotics' hyperprolactinemia effect, which may obstruct the generation of sex hormones, is responsible for this impact. When compared according to disease stage, this study amply demonstrated that there was limited difference in the amount of testosterone and luteinizing hormones in psychiatric patients. This result was consistent with the earlier research (21) , who observed that over time, there was a minimal change in the levels of testosterone and luteinizing hormones in the case group.To measure the amount of blood testosterone and luteinizing hormones among Sudanese psychiatric patients, a study was carried out there at(22). . In psychiatric patients, they discovered higher levels of testosterone and lower levels of luteinizing hormones. Additional studies conducted in Brazil by Anna Maria Niccolai (23). Evaluate the hypothalamic-pituitary-gonadal (HPG) axis by contrasting the serum hormone profiles of newly admitted patients with psychotic disorders who were taking antipsychotic medications with those who had not taken any antipsychotic medications in the preceding six months. The mean [SD] of the patients in the treated group was significantly different. Hormone serum concentrations overall (treated vs. control). Contrarily, this research found that there was no discernible difference between the mean levels of LH and testosterone according to diagnosis (depression, anxiety disorders, and schizophrenia). These results were in conflict with earlier research (24) , who found that males with hypersexual diseases had elevated LH levels but unchanged testosterone levels. Because of the small sample size and usage of several instruments, this variation can be explained. In addition, olanzapine significantly decreased LH levels in patients compared to risperidone while having no effect on testosterone levels. These results are in line with a prior study (25). That discovered that olanzapine use was linked to disturbance of the reproductive hormone (LH). By reducing the sensitivity of LH receptors in leydig cells, olanzapine decreased the function of the testicles for the release of testosterone. Olanzapine also led to the suppression of steroid production enzymes by increasing the release of prolactin, melatonin, and serotonin. However, the study also found a weak negative association

between testosterone and LH and the length of the condition. Unfortunately, no research has comprehensively examined how gonadal hormones affect the length of psychiatric diseases. Finally, the study showed that there was no discernible relationship between testosterone and LH and age. This result was at odds with other research that claimed sex hormone levels start to decline beyond the age of 30, which is followed by a decline in sex libido (26). The difference can be attributed to ethnicity and age of participants.

Risperidone and olanzapine, two neuroleptics with differing receptor affinity profiles, were compared to one another in the study done to assess the influence of medications on the hypothalamo-pituitary-gonadal (HPG) axis in male schizophrenic patients. In comparison to olanzapine, risperidone caused a greater PRL elevation. Gonadotropin and testosterone (reproductive hormones) abnormalities may result from taking this drug (FSH). Further research is necessary to determine the reasons for the inhibin B level drop caused by olanzapine and the lack of a negative connection between FSH and inhibin B in patients with risperidone-induced hyperprolactinemia. When compared to patients using olanzapine, individuals taking risperidone displayed a higher level of sexual dysfunction and treatment non-adherence. (27). finally, the atypical antipsychotic drug olanzapine (OLZ) makes men have sexual dysfunction.

5. Conclusion

The present study concludes that: Treatment of psychiatric patients with these medications, olanzapine and risperidone, can be associated with disturbances in reproductive hormones testosterone and luteinizing hormone. The causes of olanzapine-risperidone-evoked reduction of LH and increases in the level of testosterone in psychiatric patients. Patients receiving olanzapine showed a higher testosterone than risperidone.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

Statement of ethical approval

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Statement of informed consent

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