Effects of Risperidone on Serum Testosterone and Metabolic Parameters Among Schizophrenic Patients in Khartoum State, Sudan.

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Research

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Abstract

Background: Antipsychotics (AP) are commonly and increasingly prescribed to children and adolescents effectively for the treatment of schizophrenia symptoms, but they are often associated with different side effects, many studies report a decrease in testosterone and gonadotropins due to an AP-induced hyperprolactinemic effect in men, it has been found that lower levels of testosterone is correlated with negative symptoms in patients with schizophrenia.

Aim: Study was aimed to determine the effect of Risperdone on testosterone level in patients with Schizophrenia in Khartoum State.

Materials and Methods: A cross sectional hospital based study recruited 100 patients diagnosed with Schizophrenia, attended at Military Hospital, Khartoum state, during January to March 2021. The plasma testosterone was estimated using ichroma^{TM} semi automated analyzer, the collected data were analyzed using SPSS version (25).

Results: A cross sectional study recruited 100 patients, diagnosed with Schizophrenia, attended Military Hospital during January 2021, their age range from 25 to 52 years old (mean±SD = 38.1±6.42), to estimate testosterone levels in their plasma beside determine BMI and signs and symptoms related to Schizophrenia. The study found that mean of testosterone level was 3.44±2.11, mean of glucose level was 146.4±22.57 SD while mean of uric acid was 6.51±0.85 with strong significant statistical differences *P. value =* 0.001, 0.001 and 0.002 respectively, reverse correlation was observed between testosterone and body mass index, age, duration of the disease, glucose and uric acid levels (R= -0.33, -0.32, -0.37, -0.22 and -0.20 respectively).

Conclusion: Risperidone drug used in treatment patients with Schizophrenia was lowering the level of testosterone hormone. And also there was association between testosterone with blood glucose, uric acid, age and duration of disease.

Introduction

Schizophrenia is a chronic psychiatric disorder with a heterogeneous genetic and neurobiological background that influences early brain development and is expressed as a combination of psychotic symptoms such as hallucinations, delusions and disorganization and motivational and cognitive dysfunctions. Although Schizophrenia affects men and women with equal frequency. Schizophrenia is not as common as other mental diseases it can be very disabling as approximately 7-8 individuals out of 1000 will have this disorder. Schizophrenia is a word used to describe a mental disorder which has a spectrum of symptoms including alterations in perception, thought and sense of a self-decrease in violation, psychomotor slowing and displays of antisocial behaviour (Shahid, et al., 2018). We inherit our genes from both parents. Scientists believe several genes are associated with an increased risk of schizophrenia, but that no gene causes the disease by itself (Cardno and Gottesman, 2000).

In fact, recent research has found that people with schizophrenia tend to have higher rates of rare genetic mutations. These genetic differences involve hundreds of different genes and probably disrupt brain development (Harrison and Weinberger, 2005).Other recent studies suggest that schizophrenia may result in part when a certain gene that is key to making important brain chemicals malfunctions. This problem may affect the part of the brain involved in developing higher functioning skills (Walsh, et al., 2008). Also, in small ways the brains of people with schizophrenia look different than those of healthy people. For example, fluid-filled cavities at the center of the brain, called ventricles, are larger in some people with schizophrenia. The brains of people with the illness also tend to have less gray matter, and some areas of the brain may have less or more activity. Studies of brain tissue after death also have revealed differences in the brains of people with schizophrenia. Scientists found small changes in the distribution or characteristics of brain cells that likely occurred before birth (Huang, et al., 2007).

All antipsychotics are dopamine antagonists. Dopamine is involved in sexual arousal and orgasm. Dopamine blockade might contribute to libido loss and orgasm disturbance (Knegtering, 2003). In treating psychotic depression, besides antidepressives and anxiolitics, atypical risperidonehas proven useful. To patients who did not respond well on SSRI treatment, risperidone was added to their therapies which resulted in amelioration in the regulation of sleep biorhythm and sexual dysfunction. This effect was due to the risperidone increase in dopamine activity (Tanja, and et al., 2010). The onset of schizophrenia in males, most frequently encountered during adolescence, and characterized by an increase in testosterone levels (Labad, et al., 2015).

Women with schizophrenia usually experience less severe psychotic symptoms during periods of high estrogen such as during pregnancy and experience symptom exacerbationduring times of low estrogen such as during postpartum and menopause (Shirayama, et al., 2002). Furthermore, studies have shown that exogenous testosterone supplementation may reduce negative symptoms in men with schizophrenia (Kulkarni, et al., 2015), and that exogenous estrogen supplementation is associated with a reduction in psychotic symptoms in women with schizophrenia and possibly in men (Strous, et al., 2004).

Materials And Methods

Study design

The study conducted was a descriptive, cross-sectional study.

Study area and Duration

The study was carried out in Military Hospital, Khartoum from January to February 2021.

Study population

100 patients diagnosed with schizophrenia in the Military Hospital, Khartoum during January 2021 were selected by a convenience sampling technique.

Inclusion criteria

Any male diagnosed with Schizophrenia attended Military Hospital, during January 2021 was enrolled in this study.

Exclusion criteria

Any male suffering from a pituitary tumor, hypothyroidism, stress, inflammatory conditions, radiation exposure, obesity or undergoing an exercise programme was excluded from this study.

Sample size

Sample size was calculated according to the following formula:

$N= Z^2 *P*Q/ D^2$

N= Number of samples.

Z= Confidence interval which = 1.96.

P= prevalence of the disease.

Q= (1- P),

D= percentage of error which equal 0.04%, P = 53%.

Sample size = 519 samples.

Due to high costs and limitation of time, a total of 100 blood samples were collected from patients with schizophrenia in this study and stored at 4°C for further use.

Sample collection

2.5 ml of blood was collected in plain containers and let to stand for clotting, then centrifugated to obtain serum then preserved at 4°C for further use.

Data collection

Data was collected through a structured questionnaire, wit information on age, gender, weight and height recorded for each participant.

Data analysis

Collected data was analyzed by the Statistical Package for Social Sciences (SPSS, version 25).

Ethical Consideration

The study was approved by Alneelain University, Faculty of Medical Laboratory Sciences, Clinical Chemistry Department. Permission from participants was taken and they were aware with the study and the results obtained.

Results

A cross sectional study recruited 100 patients, diagnosed with schizophrenia, attended Military Hospital during January 2021, their age range from 25 to 52 years old (mean±SD = 38.1±6.42), to estimate testosterone levels in their plasma beside determine BMI and signs and symptoms related to Schizophrenia. The study found that the mean testosterone level was 3.44±2.11, mean glucose level was 146.4±22.57 SD, while the mean uric acid level was 6.51±0.85 with strong significant statistical differences (*P* = 0.001, 0.001 and 0.002 respectively), reverse correlation was observed between testosterone and body mass index, age, duration of the disease, glucose and uric acid levels (R= -0.33, -0.32, -0.37, -0.22 and -0.20 respectively).

Means and Standard Deviation of testosterone, Glucose and Uric acid level in Schizophrenic patients demonstrate a low testosterone level with slightly elevated glucose and uric acid, with strong significant statistical differences.

Table (3.1): Mean and SD of testosterone, glucose and uric acid levels in population study.

Parameters	Mean±SD	Mean (R.V)	*P-value*
Testosterone	3.44±2.11	6.5 (3-10)	0.001
Glucose	146.4±22.57	110 (80-140)	0.001
Uric acid	6.51±0.85	6 (4-8)	0.002

3.5 Reverse correlation was observed between testosterone and body mass index, age, duration of the disease, glucose and uric acid levels (R= -0.33, -0.32, -0.37, -0.22 and -0.20 respectively).

Discussion

Antipsychotic drugs have been used effectively for the treatment of schizophrenia symptoms, but they are often associated with metabolic side effects such as weight gain and endocrine disruptions and long-term hyperprolactinemia which can cause suppression of the hypothalamic-pituitary gonadal axis, so a decrease in gonadotropin-releasing hormone and consequently of luteinizing hormone (LH) and testosterone in males. This may cause sexual dysfunction such as loss of libido, loss of erection, ejaculation disorders, gynecomastia and galactorrhea. Few studies evaluating these hormonal effects in adult patients with Schizophrenia, these studies report a decrease in testosterone and gonadotropins due to an AP-induced hyperprolactinemic effect in men (Yvette, et al., 2012). The current study recruited 100

males withSchizophrenia, their age range from 25 to 52 years old (mean±SD = 38.1±6.42), to estimate testosterone levels in their plasma beside determine BMI and signs and symptoms related to Schizophrenia. The study found that mean of testosterone level was 3.44±2.11, mean of glucose level was 146.4±22.57 SD while mean of uric acid was 6.51±0.85 with strong significant statistical differences *P. value =* 0.001, 0.001 and 0.002 respectively, reverse correlation was observed between testosterone and body mass index, age, duration of the disease, glucose and uric acid levels (R= -0.33, -0.32, -0.37, -0.22 and -0.20 respectively). The study found that most patients with Schizophrenia treated with risperidone were had significantly low testosterone levels (53%) while the rest of them stayed within the normal range level (47%).

The study agreed with Yvette, *et al*., report that in 2012, patients with AP-induced hyperprolactinemia had significantly lower testosterone levels.

The results presented here also closely related to other study done by Xiao, *et al*., in which they report that serum testosterone level was significantly decreased after treatment with risperidone compared to baseline in a prospective study ($P < 0.05$).

The study was disagreed with Yasuhiro in which they report Prolactin (PRL) increased significantlyduring risperidone administration, however, luteinizing hormone, follicle-stimulating hormone, and testosterone did not change and also disagreed with another study done by Markianos, *et al*., in which they report that testosterone level was not change in patients with Schizophrenia, treated with risperidone (Markianos, *et al*.,1999).

However, risperidone used here in usual or lower-than-usual doses (1–8 mg/d) may be enough to cause low level in testosterone hormone, but levels of glucose and uric acid were slightly increased.

Conclusion

Risperidone drug used in treatment patients with Schizophrenia was lowering the level of testosterone hormone.

Recommendations

Patients with schizophrenia should be tested for testosterone and other fertility-related hormones. Further research works with larger sample size should be done to establish these findings. Schizophrenic patientd should also be aware about the side effects of risperidone during routine consultations.

Declarations

Ethical Approval and Consent to participate:

The study was approved by Alneelain University, Faculty of Medical Laboratory Sciences, Clinical Chemistry Department. Permission from participants was taken and they were aware with the study and

the results obtained.

Consent for publication:

Awarded by the Faculty of Medical Laboratory Sciences, Alneelain University, Khartoum, Sudan.

Availability of data and materials:

Data for this study is available from the authors upon request.

Competing interests:

None declared among the authors.

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Authors' contributions:

Authors MMAA and HAAM conceptualised the study, collected and analysed the data. Authors OKOE and MEAO wrote the manuscript and revised the first draft. GAH supervised the study.

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