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Estimation of Prolactin and Some Biochemical Parameters in Some Psychotic Male Patients Treated with Risperidone in Tikrit City

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ABSTRACT

The primary purpose of this research is to examine the impact of taking risperidone by psychotic individuals on serum levels of prolactin hormone as well as a few biochemical indicators (total protein and liver enzymes AST and ALT). The experiment required collecting fifty blood samples and dividing them into two groups: the first group consisted of normal, healthy persons who served as a control. In contrast, the second group consisted of psychotic patients treated with risperidone at a dosage of two milligrams per day. The findings of this study showed that There were significant increases in total protein content at levels (P≤ 0.05) of the group 2 compared to control, and there were significant gains in liver enzymes (AST and ALT) concentration range at levels (P ≤0.05) of the second group in comparison to the control group, and there were substantial improvements increases in prolactin hormone concentrations at levels (P≤ 0.05) of the second group in compared to control.

Keywords- Risperidone, Prolactin, Total protein, AST, ALT.

I. INTRODUCTION

Risperidone, a benzisoxazole derivative, was initially used in treating schizophrenia and other psychotic diseases for the first time in 1994. Risperidone is an antipsychotic medication that belongs to the second generation. It has an antagonistic effect on dopaminergic (D1, D2, D3, D4), serotoninergic (5-HT1A, 5-HT2A, and 5-HT2C), adrenergic α1 and α2, and histaminergic receptors (H1). As a result, it exhibits a strong affinity for serotonin2a (5-HT2a) and dopamine (D2) receptors and a medium affinity for histamine1 (H1) and α1 and α2 adrenergic receptors. Risperidone's mechanism of action involves an antagonistic action on post-synaptic D2 receptors. It also involves an antagonistic action on 5-HT2a in post-synaptic receptors, which can have direct antipsychotic effects as well as indirect antipsychotic effects (via promoting D2 antagonism). In addition, antagonism on post-synaptic 5-HT2a receptors can regulate the firing of dopamine (DA) neurons, leading to an increase in the amount of DA released by the dorsal striatum, the prefrontal cortex, and the nigrostriatal region [1, 2]

The lactotrophs in the anterior pituitary gland are largely responsible for synthesizing prolactin and its subsequent release. Prolactin is a single-chain protein with 199 amino acids and a molecular weight of 23 kilodaltons. Dopamine in the hypothalamus is the primary inhibitor of the secretion, and it is regulated in a negative feedback process, with prolactin functioning as the afferent signal: short-loop feedback prolactin's principal functions throughout pregnancy and lactation are the growth of the mammary gland, milk synthesis, and milk secretion maintenance. During pregnancy, there is a rapid rise in serum prolactin levels, accompanied by an increase in the size and number of lactotrophs. During lactation, a neuroendocrine reflex route leads to fast prolactin production caused by suckling. In the absence of pregnancy, hyperprolactinemia may manifest as symptoms of hypogonadotropic hypogonadism. These symptoms may include menstrual disruption and infertility. As a result, prolactin plays a vital role in human health and disease, especially in its role in metabolic homeostasis, which includes the regulation of body weight, adipose tissue, skin and hair follicles, the pancreas, bone, the adrenal

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response to stress, the management of lactotroph cell homeostasis, and maternal behaviour. [3, 4].

A plasma prolactin level greater than 20 ng/mL in men is considered hyperprolactinemia, whereas a level greater than 25 ng/mL is considered to be hyperprolactinemia in women. A lower libido, erectile dysfunction, gynecomastia and ejaculatory dysfunction are potential side effects of increased prolactin levels in men; Chronic hyperprolactinemia is linked to an increased risk of developing osteoporosis, breast cancer, and cardiovascular disease [5]. The use of antipsychotic medications such as risperidone, which block the inhibition of prolactin secretion, is one cause of hyperprolactinemia. The prevalence of hyperprolactinemia is caused by the use of the antipsychotic drug risperidone due to the potency of its ability to block D2 receptors. The reproductive system is affected by drug-induced hyperprolactinemia, which causes prolactin levels to rise 2–4 times above the maximum limit of the normal range of 15–25 g/L in men and women. The release of the hypothalamic gonadotropin-releasing hormone is inhibited by elevated prolactin levels, which can influence sex hormone dysfunction. The production of luteinizing hormone and follicle-stimulating hormone from the pituitary is therefore inhibited once gonadotropin-releasing hormone is inhibited. [6].

The transfer of -amino groups from aspartate and alanine to the -keto group of ketoglutaric acid is catalyzed by enzymes known as aspartate aminotransferase and alanine aminotransferase. This results in the production of oxalacetic and pyruvic acid, which are essential components of the citric acid cycle. The liver contains an exceptionally high concentration of both aminotransferases. ALT concentrations are low in skeletal muscle and kidneys; AST is also present in the heart, kidneys, brain, and red blood cells. While AST is present in the liver's cytosol (20% of total activity) and mitochondria (80% of total activity), ALT is only in the cellular cytoplasm. A higher concentration of AST is observed in zone 3 of the hepatic acinus. Sinusoidal cells in the liver are responsible for carrying out the process of aminotransferase clearance. Total AST in circulation has a half-life of around 17 hours, while mitochondrial AST has a half-life of 87 hours, and ALT has a half-life of around 47 hours. [7, 8, 9]. Increases in AST and ALT liver enzyme levels have been linked to the usage of the drug risperidone[10]. Risperidone can cause damage to the liver either directly through hepatotoxicity or indirectly through metabolic side effects such as weight gain, obesity, and metabolic syndrome [10, 11].

II. MATERIALS AND METHODS

2.1. Patients and Blood Collection

Carried out this research between July 2021 and November 2021 using a total of sixty blood samples, thirty of which came from psychotic patients between the ages of 15 and 35 who had been taking risperidone at a dosage of 2 milligrams per day for at least eight weeks. Blood samples are collected from the private psychiatric clinics in Tikrit and then divided into two distinct groups: The first group includes thirty blood samples from psychotic patients who were taking risperidone. In contrast, the second group includes twenty blood samples from healthy normal individuals who acted as the study's control group. Five millilitres of venous blood were drawn using a disposable syringe and clean, dry plain tubes that lacked anticoagulants to obtain blood samples. The blood was then allowed to clot at room temperature. The serum was then centrifuged for 10 minutes at 2000 rpm to remove any hemolysis.

2.2. Determination of parameters

The serum studied determined parameters such as prolactin, total protein, and liver enzymes (AST and ALT) by using their kits from (MyBioScourse) company (USA) of ELISA technique.

2.3. Statistical Analysis

(SAS, 2001) used software to analyze the data using one-way ANOVA and the Duncan Range Test at a statistical value of 0.05. ($p \leq 0.05$).

III. RESULTS AND DISCUSSION

There was a marked increase in the risperidone-treated group's prolactin hormone concentrations (p0.05) compared to the control group during the experiment period figure (1) (81.43 ± 16.77 ng/ml).

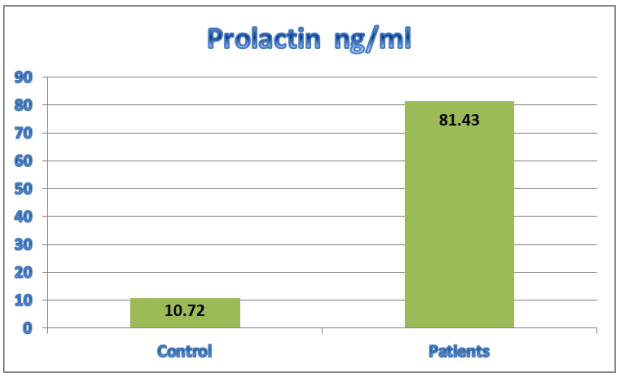

Figure 1: The study groups' concentrations of prolactin hormone (ng/ml).

These findings are consistent with those obtained by Magari et al. (2015) [12]; who discovered a significant increase in prolactin hormone in psychotic patients treated with risperidone when compared to a control group risperidone is a monoaminergic antagonist that causes dopamine to be released in various brain areas, including the anterior pituitary gland. It is believed that the therapeutic actions of antipsychotic medications like risperidone are mediated in the mesolimbic tract by blocking the dopamine type 2 D(2). Prolactin levels rise as a result of this activity in the

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tuberoinfundibular system. Risperidone binds to the D(2) receptor with a reasonably high affinity and low dissociation rate. This explains why it is associated with elevated serum prolactin levels and a higher incidence of hyperprolactinemia [12, 13, 14].

Figure (2) (10.11 ± 0.98 g/dl) shows that the risperidone-treated group had a significantly higher total protein content ($p \leq 0.05$) than the control group during the study duration.

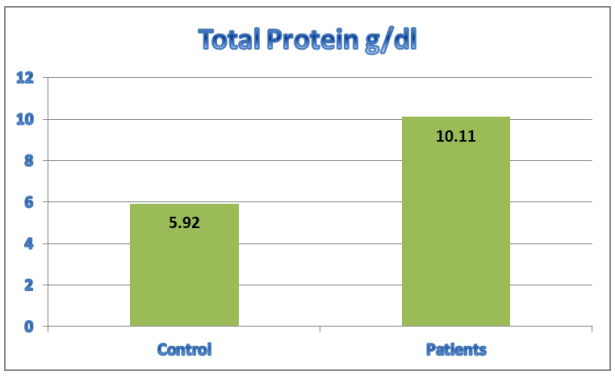

Figure 2: Concentrations of total protein (g/dl) in the study groups.

This rise in serum total protein in the risperidone treated group may be due to the pharmacological effects of the risperidone antipsychotic drug.

During the research period, the result showed that the risperidone-treated group significantly increased AST concentration ($p \leq 0.05$). **Figure (3) (14.17 ± 1.93 U/L)** Compared to the control group.

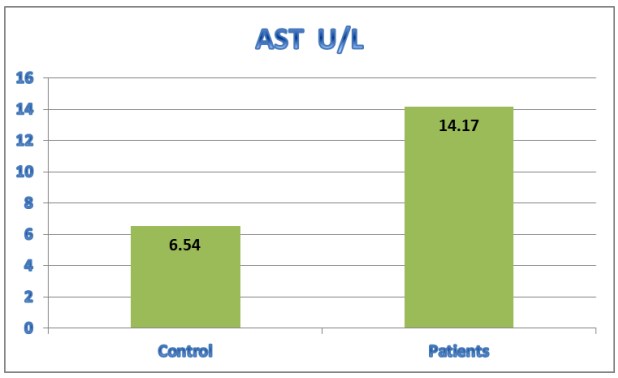

Figure 3: The study groups' concentrations of AST (U/L).

These findings agree with those observed in the research conducted by López-Torres et al. (2014) [15]; they observed a significant elevation of AST liver enzyme in psychotic patients treated with risperidone compared To the group that served as the control.

This research demonstrated a statistically significant rise in ALT concentration ($p \leq 0.05$) in the risperidone-treated group during the study duration Figure (12.27 ± 3.42 U/L) in comparison with the control group.

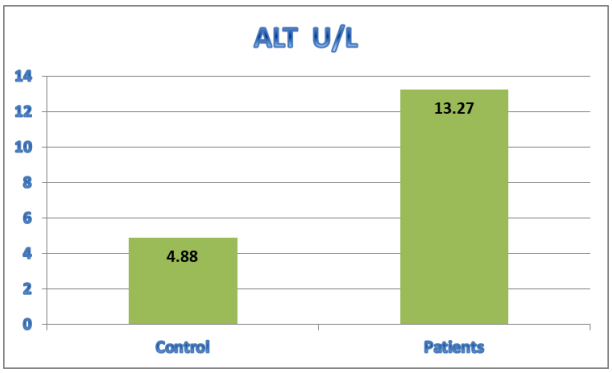

Figure 4: The study groups' concentrations of ALT (U/L).

These findings are consistent with the findings of Lopez-Torres et al. (2014) [15]; they discovered a significant elevation of ALT liver enzyme in psychotic patients treated with risperidone compared with the control group.

Antipsychotic medications, such as risperidone, can cause hepatotoxicity, causing AST and ALT levels to rise [16]. Hepatotoxicity could occur directly or indirectly; direct hepatotoxicity of antipsychotic drugs such as risperidone and direct effects can further promote other hepatic damage mechanisms such as immunity and inflammatory response. Adaptive immune responses are triggered in the host due to drug-metabolizing enzyme gene polymorphisms, transmembrane transporters and solute transport proteins gene polymorphisms, and human leukocyte antigen systems (HLA) gene polymorphisms. that increase the host's susceptibility to liver abnormalities. Antipsychotic drugs and their metabolic products have the potential to damage and death hepatocytes via several different molecular mechanisms, the most notable of which are the destruction of hepatic mitochondria and oxidative stress. Risperidone and other antipsychotic drugs, together with their metabolites, can activate several death signalling pathways, leading to cell necrosis and autophagic cell death [11]. Hepatocyte damage may develop indirectly due to an increased risk of metabolic syndrome complications, such as nonalcoholic fatty liver disease. Obesity and other metabolic syndrome traits are substantially linked to unexplained AST and ALT liver enzyme elevations; also, weight growth was found to be strongly linked to transaminase elevations at the start of psychotropic therapy [17].

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