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Impact of Antipsychotic Medications on Lipid, Blood Sugar, and Hormonal Balance: A Clinical Perspective

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Abstract

Antipsychotic medications are regarded as indispensable in the treatment of psychiatric disorders; however, their administration has been associated with metabolic and hormonal adverse effects. In the present case-control study, the influence of such medications on lipid metabolism, glucose homeostasis, and hormonal balance was examined in 80 patients with chronic psychiatric disorders (schizophrenia, bipolar disorder, and drug-induced psychosis) and compared with 15 healthy controls recruited at Alhawary Psychiatric Hospital, Benghazi, Libya. Biochemical assessments included fasting blood sugar (FBS), glycated hemoglobin (HbA1c), lipid profile (cholesterol, triglycerides, HDL, LDL), prolactin, thyroid-stimulating hormone (TSH), serum albumin, C-reactive protein (CRP), and creatine kinase (CK). No statistically significant differences were observed in FBS, HbA1c, or lipid parameters ($p > 0.05$). Conversely, significant elevations in prolactin (20.22 vs. 8.8 ng/mL, $p = 0.000$), CRP ($p = 0.033$), and CK ($p < 0.05$), together with a reduction in serum albumin ($p = 0.001$), were detected among patients. These

findings suggest that antipsychotics exert pronounced effects on hormonal and inflammatory pathways, most likely mediated through dopaminergic and mitochondrial mechanisms, while exerting limited influence on lipid and glucose profiles in this cohort. It is therefore recommended that prolactin, CRP, and CK be routinely monitored to mitigate long-term risks. Further research is warranted to clarify underlying mechanisms and to optimize therapeutic strategies.

Keywords: Antipsychotics, lipid metabolism, glucose homeostasis, prolactin, psychiatric disorders, metabolic side effects.

تأثير استعمال الادوية النفسية على مستوى الدهون، مستوى سكر في الدم و التوازن الهرموني

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ملخص

أدوية الاضطرابات النفسية المختلفة تعتبر لا بديل لها في علاج الاضطرابات النفسية، وتناولها قد ارتبط بأعراض جانبية أيضية وهرمونية.

في الدراسة الحالية نقوم بدراسة تأثير مثل هذه الأدوية على أيض الدهون، توازن مستوى السكر والتوازن الهرموني.

قمنا بفحص 80 مريض مصاب باضطرابات نفسية مزمنة (الفصام، اضطراب ثنائي القطب، و الدهان المصاحب لتعاطي العقاقير) و بالمقارنة ب 15 شخص سليم، أنجزت الدراسة في مستشفى الهواري للأمراض النفسية، بنغازي، ليبيا.

التقييم البايوكيميائي تضمن مستوى سكر الدم الصيامي، السكر التراكمي (HbA1C)، فحص الدهون (الكوليسترول والدهون الثلاثية، HDL، LDL، البرولاكتين هرمون الغدة الدرقية، ألبومين المصل، بروتين سي التفاعلي (CRP)، كرياتين كايينز (CK). لم يلاحظ اختلاف في الأهمية الإحصائية بين مستويات سكر الدم الصيامي، السكر التراكمي وقياسات الدهون ($P > 0.05$) وبالمقارنة نجد ارتفاع ملحوظ في مستوى البرولاكتين ($P = 0.000$ ، 8 ± 22.20 نانوجرام/مل، $CRP = 0.032$) و CK ($P = 0.001$) مع انخفاض في مستوى ألبومين المصل. ($P = 0.001$) كما لوحظ بين المرضى.

هذه النتائج تشير الى أن أدوية الامراض النفسية تؤثر بشكل كبير على مسارات الالتهابات والهرمونات تحدث على الأرجح من خلال آليات الدوبامين والميتوكوندريا بينما تحدث تأثير محدود على مستويات الدهون والسكر في هذه الدراسة. لذلك ينصح بالمراقبة الدورية للبرولاكتين و CRP و CK لتقادي الخطورة على المدى البعيد.

المزيد من الأبحاث ضرورية لتوضيح الآليات المسببة ولوضع استراتيجية قصوى للعلاج.

الكلمات المفتاحية: مضادات الذهان، استقلاب الدهون، توازن الجلوكوز، البرولاكتين، الاضطرابات النفسية، الآثار الجانبية الأيضية.

Introduction

Antipsychotic medications have long been recognized as essential for the management of psychiatric disorders such as schizophrenia, bipolar affective disorder, and drug-induced psychosis. Nevertheless, their use has consistently been associated with metabolic and hormonal disturbances, thereby increasing the risk of cardiometabolic complications [1,2]. Both typical agents (e.g., haloperidol, chlorpromazine) and atypical drugs (e.g., risperidone, olanzapine) have been shown to effectively control psychotic symptoms. However, their administration has also been linked to dyslipidemia, hyperglycemia, and hyperprolactinemia, which collectively compromise patients' quality of life [3,4]. Consequently, an in-depth understanding of these adverse effects

is required in order to optimize clinical management, particularly in understudied populations such as those in Libya.

It has been well established that lipid metabolism plays a critical role in supporting synaptic plasticity and myelin production in the central nervous system [5]. Antipsychotic medications—especially olanzapine and clozapine—have frequently been associated with dyslipidemia, manifested by elevated triglycerides (TG) and low-density lipoprotein (LDL), or reduced high-density lipoprotein (HDL) [6]. Disruptions in glucose homeostasis, including insulin resistance and impaired pancreatic beta-cell function, are known to increase the risk of type 2 diabetes [7]. Furthermore, hormonal imbalances—particularly hyperprolactinemia resulting from dopamine D2 receptor blockade—can negatively affect gonadal function and bone integrity [8]. Additionally, inflammatory biomarkers such as C-reactive protein (CRP) and creatine kinase (CK) have been reported to rise, reflecting systemic inflammation and muscle membrane alterations [9].

Accordingly, the present study was undertaken at Alhawary Psychiatric Hospital, Benghazi, Libya, to evaluate the impact of antipsychotic medications on lipid profiles, glucose regulation, and hormonal parameters in a cohort of patients with chronic psychiatric disorders. Through the measurement of FBS, HbA1c, lipid profile, prolactin, TSH, serum albumin, CRP, and CK, patterns of biochemical dysregulation were investigated with the aim of clarifying their clinical implications.

Materials and Methods

Study Design and Participants

A case–control study design was employed, comprising 80 patients with chronic psychiatric disorders (schizophrenia: 48.42%, drug-induced psychosis: 27.37%, bipolar disorder: 8.42%) and 15 age- and sex-matched healthy controls. Participants were recruited from inpatient and outpatient departments of Alhawary Psychiatric Hospital, Benghazi, Libya, between 2023 and 2024. Patients were included if they had been diagnosed with chronic psychiatric conditions or drug-induced psychosis (e.g., cannabis or alcohol-related). Exclusion criteria encompassed heart disease, liver disease, or diagnosed endocrine disorders, which were verified through medical records and baseline laboratory investigations, in order to minimize confounding variables. Controls were selected

only if no systemic illnesses were documented. Ethical approval was obtained from the University of Benghazi, and informed consent was secured from all participants.

Biochemical Assays

Fasting blood samples were collected at 9:00 AM via antecubital venipuncture. Samples were clotted for 10 minutes, followed by centrifugation at 3000 rpm for 5 minutes to separate sera. Parameters analyzed included FBS, HbA1c, lipid profile (total cholesterol, triglycerides, HDL, LDL calculated via Friedewald's equation), serum calcium, renal function tests, CK, CRP, TSH, prolactin, uric acid, and serum albumin. Assays were performed using enzymatic colorimetric methods (e.g., glucose oxidase for FBS, bromocresol green for albumin), or boronate affinity chromatography (HbA1c) on standardized equipment (e.g., CERAGEM MEDISYS). Prolactin and TSH concentrations were determined using the QDX Instacheck Reader, whereas CRP was measured via turbidimetric immunoassay. Manufacturer protocols were strictly followed, including the use of reagent blanks at appropriate wavelengths (e.g., 520 nm for glucose, 620 nm for albumin).

Statistical Analysis

Data were processed using SPSS version 23 (Chicago, IL, USA). Descriptive statistics (mean, median, interquartile range [IQR]) and frequencies were calculated. Group comparisons were performed using the Mann–Whitney U test, as the data were not normally distributed, with a p-value of <0.05 considered statistically significant. Correlations between continuous variables were assessed using Pearson or Spearman methods as appropriate. Adjustments for multiple comparisons were not applied, owing to the exploratory nature of the investigation.

Table 1: Descriptive Statistics of Biochemical Parameters in Cases and Controls

Parameter	Cases (n=80) Median (IQR)	Controls (n=15) Median (IQR)	p-value
FBS (mg/dL)	87.30 (80–95)	87.50 (82–93)	>0.05
HbA1c (%)	5.50 (5.2–5.8)	5.40 (5.1–5.7)	>0.05
Total Cholesterol (mg/dL)	150.00 (135–170)	155.00 (140–175)	0.312

Triglycerides (mg/dL)	87.50 (70–110)	91.00 (75–115)	0.736
HDL (mg/dL)	41.00 (35–48)	41.00 (35–48)	0.577
LDL (mg/dL)	88.50 (75–100)	93.00 (80–105)	0.242
Prolactin (ng/mL)	20.22 (15–30)	8.80 (7–10)	0.000
TSH (μIU/mL)	1.64 (1.2–2.0)	1.47 (1.1–1.9)	0.213
CRP (mg/L)	3.50 (2.5–5.0)	2.00 (1.5–3.0)	0.033
CK (U/L)	150.00 (100–200)	100.00 (80–120)	<0.05
Serum Albumin (g/dL)	4.10 (3.8–4.3)	4.30 (4.1–4.5)	0.001
Uric Acid (mg/dL)	5.33 (4.5–6.0)	4.93 (4.2–5.8)	0.706

Lipid Metabolism

Lipid parameters likewise demonstrated no statistically significant differences ($p > 0.05$). Median total cholesterol was 150.00 mg/dL (IQR: 135–170) in patients and 155.00 mg/dL (IQR: 140–175) in controls ($p = 0.312$). Triglycerides were 87.50 mg/dL (IQR: 70–110) in patients and 91.00 mg/dL (IQR: 75–115) in controls ($p = 0.736$). HDL was 41.00 mg/dL (IQR: 35–48) in both groups ($p = 0.577$), whereas LDL was 88.50 mg/dL (IQR: 75–100) in patients and 93.00 mg/dL (IQR: 80–105) in controls ($p = 0.242$).

Hormonal and Inflammatory Markers

By contrast, significant elevations in prolactin (20.22 ng/mL, IQR: 15–30 in patients vs. 8.8 ng/mL, IQR: 7–10 in controls, $p = 0.000$), CRP ($p = 0.033$), and CK ($p < 0.05$) were detected among patients. Serum albumin levels were significantly reduced (4.10 g/dL, IQR: 3.8–4.3 in patients vs. 4.30 g/dL, IQR: 4.1–4.5 in controls, $p = 0.001$). In contrast, TSH (1.64 μIU/mL vs. 1.47 μIU/mL, $p = 0.213$) and uric acid (5.33 mg/dL vs. 4.93 mg/dL, $p = 0.706$) did not differ significantly.

Correlations

No significant correlations were found between age, disease duration, or antipsychotic dosage and lipid or glucose parameters. However, prolactin and CRP were positively correlated with risperidone and olanzapine use ($p < 0.05$).

Discussion

The results of this study demonstrate that antipsychotic medications exert significant effects on hormonal and inflammatory markers, while minimal influence was observed on lipid metabolism and glucose regulation within this Libyan cohort. In contrast to earlier studies associating antipsychotic agents—particularly olanzapine and clozapine—with dyslipidemia and hyperglycemia [6,7], no such differences were identified in the present sample. This discrepancy may be attributable to relatively low doses of high-risk antipsychotics (e.g., olanzapine, mean 9.76 mg), the exclusion of patients with pre-existing metabolic disorders, or population-specific factors such as genetic or dietary influences. For instance, Oddur et al. [10] reported significantly elevated triglycerides in patients with schizophrenia, particularly among females, findings that diverge from the present results. Similarly, Thelma et al. [11] identified reduced HDL levels in schizophrenia patients, whereas comparable HDL values were observed here ($p = 0.577$). Collectively, these differences highlight the heterogeneity of antipsychotic effects across populations, dosages, and treatment regimens, thereby underscoring the need for individualized monitoring strategies.

Significant prolactin elevation ($p = 0.000$) observed in this study aligns with established literature, as dopamine D2 receptor antagonism by agents such as risperidone and haloperidol has been shown to increase prolactin secretion [8,12].

Hyperprolactinemia (median 20.22 ng/mL) is clinically relevant, as it may result in galactorrhea, sexual dysfunction, or osteoporosis, warranting routine monitoring in clinical practice [13]. Likewise, elevated CRP ($p = 0.033$) and CK ($p < 0.05$) indicate systemic inflammation and muscle membrane changes, findings consistent with Yi Zou et al. [14] and Meltzer et al. [15]. These outcomes may be mechanistically linked to mitochondrial dysfunction, as suggested by Gustavo and Samira [16]. Reduced serum albumin ($p = 0.001$) further suggests impaired protein metabolism or possible nutritional deficiencies, consistent with prior findings [17]. Albumin's critical role in drug transport [18] reinforces the importance of this observation.

The absence of significant differences in TSH and uric acid contrasts with studies reporting thyroid dysfunction in patients

receiving antipsychotics [19]. Such inconsistencies are likely attributable to drug-specific or population-specific effects.

Limitations of this study include the relatively small control group ($n = 15$), the cross-sectional design, and potential selection bias. Lifestyle-related confounders (e.g., diet, physical activity) were not assessed, which may have influenced glucose and lipid outcomes. Future investigations should incorporate larger, longitudinal samples and account for lifestyle interventions to better delineate long-term consequences.

Conclusion

It has been demonstrated that antipsychotic medications significantly elevate prolactin, CRP, and CK, while reducing serum albumin in patients with chronic psychiatric disorders. By contrast, minimal effects were observed on lipid and glucose profiles within this Libyan cohort. These findings underscore the importance of routine monitoring of hormonal and inflammatory markers in order to mitigate potential risks such as hyperprolactinemia and cardiovascular complications. Clinical management should be tailored to achieve a balance between psychiatric efficacy and metabolic safety. Further research is required to clarify underlying mechanisms, evaluate longitudinal effects, and assess lifestyle interventions in modulating biochemical outcomes.

Author Contributions

Dr. Abdalla M. Jarari supervised the study and provided overall guidance throughout its execution. Dr. Salima M. Hawada contributed to the collection of clinical data and provided intellectual input during manuscript preparation. Ms. Hala Abd Elrasol carried out the thesis work as part of her student research, including data collection, laboratory assays, and initial analysis. Dr. Jagannadha Rao Peela contributed to the intellectual content and assisted in refining the manuscript. All authors reviewed and approved the final version of the manuscript.

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