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Full Length Research Paper

Effects of Antipsychotic Drugs on Serum Biochemical Tests

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Abstract

Background: Accumulating evidence suggests that the typical and atypical antipsychotic drugs have serious metabolic disturbance. Objective: To compare the effects of atypical (Olanzapine) and typical (Haloperidol) antipsychotic medications on lipid profiles, plasma parathyroid hormone, bone minerals, glucose and insulin hormone levels in Sudanese schizophrenic patients. Method: Descriptive case control study conducted in patients with schizophrenia who were inpatients at two hospitals. One hundred fifty samples were collected, one hundred patients and fifty healthy individuals as controls. Covariates, including patients age, the duration of disease and antipsychotic treatment, other medications that may affect on lipid profiles, plasma parathyroid hormone, bone minerals, glucose and insulin hormone levels. During period from April to November 2013. Results: The means of cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), parathyroid hormone (PTH), calcium, magnesium and glucose were statistically significant differences among patients receiving Olanzapine and Haloperidol, (P<0.05) but were not clinically significant differences. Except in triglyceride, phosphors and insulin in, which was not statistically and clinically significant difference, (P>0.05). A significant positive correlation was noted between the means of lipid profile, plasma parathyroid hormone, bone minerals, glucose and insulin with duration of disease in patients treated with typical and atypical drugs. No significant correlation was noted between the means of lipid profile, parathyroid hormone, bone minerals, glucose and insulin with age of patients treated with typical and atypical drugs. Conclusions: Cholesterol, HDL, LDL, parathyroid hormone, calcium, magnesium and glucose level in schizophrenic patients treated with atypical and typical drugs were clearly higher than that of control. Hence, routine monitoring of lipid profile, parathyroid hormone, bone minerals, glucose and insulin during treatment with antipsychotic drugs is highly recommended for schizophrenic patients.

Keywords: PTH, antipsychotic, Sudan, Cholesterol, Lipids.

INTRODUCTION

Schizophrenia is a serious disorder of the mind and brain. The incidence rate of schizophrenia seems consistent across the world for the last half-century, (Hafner and Ander, 1997) and target number of persons with schizophrenia in Sudan needing treatment about 65,517 persons, Chisholm *et al.,* 2007. It is diagnosed 1.4 times more frequently in males than females, and typically

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appears earlier in men, Pichioni and Murray, 2007. The peak ages of onset are 20-28 years for males and 20-32years for females, Castle *et al.,* 1991. Onset in children is much rarer, Kumra *et al.,* 2001 as is onset in middle or old age.

The primary treatment of schizophrenia is antipsychotic medications, often in combination with psychological and social support. Cardiovascular risk in psychiatric disorders is partly related to antipsychotic therapy, especially atypical antipsychotic medications. Some antipsychotic medications are associated with pro-atherogenic conditions including insulin resistance and dyslipidemia, Parminder *et al.,* 2001. Weight gain is a common consequence of antipsychotic drug treatment and can lead to further morbidity, as a result of loss of the normal inhibitory control of leptin on body mass, Sukhwinder and Shergill, 2004.

Hyperglycemia and type 2 diabetes mellitus is more common in schizophrenia than in the general population. Glucoregulatory abnormalities have also been associated with the use of antipsychotic medications themselves, Newcomer *et al.,* 2002. Hyperprolactinemia is often seen among persons with schizophrenia, most commonly as a result of antipsychotic drugs that act as D2 receptor antagonists on pituitary lactotrophs, Meltzer *et al.,* 1983. Sustained hyperprolactinemia secondary to prolactin secreting adenomas is known to result in bone mass loss, leading to osteoporosis, Klibanski *et al.,* 1980; Greenspan *et al.,* 1986.

No data was found to indicate the effects of antipsychotic drugs on the patient's lipids level parathyroid hormone, bone minerals, glucose and insulin were previously examined in Sudan, so the goal of this study is to compare the effects of atypical and typical antipsychotic drugs in schizophrenic Sudanese patients.

METHOD

This study was a hospital based case control descriptive study conducted at the Abdul AalEledrisy psychiatric hospital and psychotic clinic of elselah Elteby, Sudan, between April2013 and November 2013.From an original sample of 150 subjects, 100 patients with psychosis ranging in age from 20-50 years (mean=35, SD=15), and 50 well health persons ranging in age from 20-50 years (mean=35, SD= 15).

Mean duration of illness was 4 years (SD=3). Patients remained on regimens of atypical (N=50) or typical (N=50) monotherapy throughout the 4-months study. Extensive inclusion and exclusion criteria resulted in a group of patients with psychosis and control who were in good general health and clinically stable before treatment with either olanzapine or haloperidol.

In brief, subjects were excluded for any medical condition or treatment known to alter lipid, insulin hormone, glucose, PTH, or bone minerals. For each subject demographic details, clinical finding and laboratory results were recorded on a questionnaire sheet, including age, sex, type of antipsychotic medication, duration of disease and treatment. Venous blood (5.0 ml) was drawn from each volunteer by using a disposable plastic syringe. The sample was then analyzed by automated chemical analyzer (ELISA and Mindary Bs-200). Approval was taken from faculty and hospital management. Written informed consent was obtained from all subjects. The paper is done according to the ethical comity of AL-Neelain University.

Statistical analysis

Statistical evaluation was performed using the Microsoft Office Excel (Microsoft Office Excel for windows; 2007) and SPSS (SPSS for Windows version 19). The Student T-test was used to assess significant differences in the means of plasma Parathyroid Hormone and Bone Minerals. Correlations between plasma Parathyroid Hormone and Bone Minerals, age, sex and duration of disease were assessed using bivariate correlation. $P< 0.05$ was considered statistically significant.

RESULTS

The study covered 195 subjects in Khartoum state Sudan, 65 patients treated with atypical drugs, 65 patients treated with typical drugs, and 65 healthy controls. Lipid profile, glucose and insulin were done in 100 male patients, 50 male patients treated with atypical drugs, 50 male patients treated with typical drugs and 50 well health persons ranging in age from 20-50 years (351±5) while bone minerals and parathyroid hormone in 100 patient (50 schizophrenic patients treated with A typical antipsychotic medication (15 female and35 male) and50 schizophrenic patients treated with Typical antipsychotic medication(15 female and 35 male) all those have a rising prolactin and normal vitamin D with average of (17±1) years, ranging between 20- 50 years and duration ranging between (6month -12years),50 volunteer with average age (16±1) years ranging between(20- 51 years) were selected as control group.

The mean value of all lipid,glucose, bone minerals and parathyroid hormone levels in patients treated with atypical and typical drugs were significantly increased

Table 1. Mean of plasma lipid in control and patients treated with a typical drugs

Parameter	Patients treated with a typical No 50 M±SD	Control No 50 M±SD	P. value
Cholesterol	143.1±28.5	123.0±20.8	0.000
Triglyceride	102.2±34.9	94.9±25.6	0.209
HDL	45.0±13.3	39.2±8.7	0.000
LDL	77.4±26.8	65.3±18.6	0.000
Glucose	110.6±8.03	97.54±6.99	0.03
Insulin hormone	19±3.56	18.4±2.73	0.12
PTH	50.27±8.3	46.20±9.05	0.021
Calcium	9.75±0.85	9.22±0.42	0.000
Magnesium	**2.**74**±**0.22	2.01**±**0.22	0.000
Phosphors	3.87**±**0.58	3.74**±**0.59	0.268

Table 2. Mean of plasma lipid in control and patients treated with typical drugs

Parameter	Patients treated with typical No 50 M±SD	Control No 50 M±SD	P. value
Cholesterol	145.1±33.8	123.0±20.8	0.000
Triglyceride	92.8±40.0	94.9±25.6	0.810
HDL	47.2±12.4	39.2±8.7	0.000
LDL	80.4±30.7	65.3±18.6	0.000
Glucose	119.6±7.56	97.54±6.99	0.000
Insulin hormone	18.2±5.41	18.4±2.73	0.231
PTH	51.01±10.21	46.20±9.05	0.014
Calcium	9.95±1.06	9.22±0.42	0.000
Magnesium	2.81±0.31	2.01±0.22	0.000
Phosphors	3.87±0.66	3.74±0.59	0.295

when compared with control group ($p<0.05$), except triglyceride, insulin hormone and phosphors in which were insignificantly different was observed ($P >0.05$) in typical and Atypical drugs, as illustrated in table (1) and (2). As shown in table (3) the patients treated with atypical drugs, there is insignificant negative correlation between lipid profile, glucose, insulin hormone, bone minerals and parathyroid hormone with age of patients and insignificant positive correlation with duration of disease. As shown in table (4) there is an insignificant negative correlation between lipid profile, glucose, insulin hormone, bone minerals and parathyroid hormone with age of patients treated with typical drugs and insignificant positive correlation with duration of disease.

DISCUSSION

Some antipsychotic drugs are associated with an increased risk of adverse metabolic outcomes, including weight gain, dyslipidemia and hyperglycemia. [The] high rate of osteoporosis in schizophrenic may result from the prolactin- raising effect of any antipsychotic medication. In this study, although the differences were statistically significant for Cholesterol, HDL, LDL ($p\leq0.05$) and insignificant for triglyceride ($p\geq0.05$), but clinically not significant. In both typical and atypical antipsychotic drugs, there is a reverse relation between lipid level and the age of patients and insignificant positive correlation between lipid level with duration of disease.

Table 3. Person correlation between plasma lipid, age and duration of disease in patients treated with a typical drug

Parameter	Statistic	Age	Duration of disease
Cholesterol	r.value	-0.42	+0.462
	P.value	0.114	0.233
Triglyceride	r.value	-0.751	+0.92
	P.value	0.065	0.027
HDL	r.value	-0.856	+0.723
	P.value	0.133	0.200
LDL	r.value	-0.867	+0.98
	P.value	0.138	0.100
Glucose	r.value	-0.543	+0.652
	P.value	0.246	0.341
Insulin hormone	r.value	-0.941	+0.766
	P.value	0.343	0.412
Calcium	r.value	+0.456	-0.678
	P.value	0.06	0.76
Magnesium	r.value	+0.660	-0.453
	P.value	0.54	0.33
Phosphors	r.value	+0.765	-0.865
	P.value	0.34	0.65
PTH	r.value	+0.889	-0.534
	P.value	0.35	0.65

Table 4. Person correlation between plasma lipid, age and duration of disease in patients treated with typical drug

Parameter	Statistic	Age	Duration of disease
Cholesterol	r.value	-0.324	+0.517
	P.value	0.094	0.512
Triglyceride	r.value	-0.821	+0.89
	P.value	0.128	0.333
HDL	r.value	-0.892	+0.823
	P.value	0.138	0.231
LDL	r.value	-0.801	+0.973
	P.value	0.072	0.340
Glucose	r.value	-0.675	+0.887
	P.value	0.541	0.600
Insulin hormone	r.value	-0.441	0.455
	P.value	0.411	0.451
Calcium	r.value	+0.564	-0.881
	P.value	0.09	0.65
Magnesium	r.value	+0.761	-0.386
	P.value	0.67	0.55
Phosphors	r.value	+0.123	-0.562
	P.value	0.55	0.67
PTH	r.value	+0.771	-0.362
	P.value	0.265	0.234

This study disagree with Wirshing DA, *et al.,* 2002 who studied the effects of novel antipsychotics on glucose and lipid levels in 950 patients, over one third of patients treated with any novel antipsychotics had clinically meaningful triglyceride elevations, Wirshing *et al.,* 2002. Also disagree with Lindenmaryer *et al.,* 2003 who studied the change in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics in one hundred fifty-seven patients; atypical drugs were associated with an increase in cholesterol levels, Lindenmaryer *et al.,* 2003.

This study agree with John W. Newcomer, MD; Dan who studied abnormalities in glucose regulation during antipsychotic treatment of Schizophrenia in 48 schizophrenic patients the result indicate that newer antipsychotic treatments such as clozapine and olanzapine, in comparison with typical agents, are associated with adverse effects on plasma glucose regulation, which can vary in severity independent of adiposity and age, Newcomer et al., 2002. Also agree with Jean-Pierre Lindenmayer and *etal*who assess the effects of clozapine, olanzapine, risperidone, and haloperidol on glucose and cholesterol levels in hospitalized patients with schizophrenia or schizoaffective disorder inone hundred fifty-seven patients with schizophrenia they conclude that clozapine, olanzapine, and haloperidol were associated with an increase of plasma glucose level, and clozapine and olanzapine were associated with an increase in cholesterol levels. The mean changes in glucose and cholesterol levels remained within clinically normal ranges, but approximately 14% of the patients developed abnormally high glucose levels during the course of their participation in the study, Lindenmaryer *et al.,* 2003.

In this study, although the differences were statistically significant, the means of PTH, calcium and magnesium were within normal range, but phosphors wasn't statistically and clinically significant, these treatment rises prolactin that effect on magnesium and lead to hypermagnesemia that lead to increased parathyroid hormone because insert in synthesis of it, increased of parathyroid hormone lead to increased calcium and hypercalcemia, and don't effect on phosphors in serum because have normal absorption with vitamin D. This study agree with Bergemann et al, investigated women with schizophrenia and found a high bone turnover but normal bone mineral density, Bergemann *et al.,* 2001. This study is disagree with study in Helsinki where 75 inpatients and outpatients suffering from schizophrenia. All patients had been treated with antipsychotic for at least 1 year, and only patients between the ages of 19 and 50 were studied to exclude patients with age-related idiopathic osteoporosis In men but not women with schizophrenia, bone mineral density was significantly lower than normal in the lumbar region, Hummer *et al.,* 2005.

Also disagree with Anna Maria et al., in Ireland who studies the decrease bone minerals density of Effects of long-term prolactin-raising antipsychotic medication on bone mineral density in Fifty-five patients who had been receiving prolactin-raising antipsychotic medication for >10 years underwent dual-energy X-ray absorptiometry of their lumbar and hip bones. Patients with schizophrenia were reported age -related reduced bone mineral density measures were found in 17 (57%) of the male and 8 (32%) of the female patients. This study disagree with Abraham et al reported an inverse relationship between prolactin level and bone mass in 16 patients (seven receiving typical antipsychotic, three risperidone, and six clozapine). Subjects had been receiving their respective antipsychotic for at least 6 months, Abraham *et al.,* 2003. Sex differences may return to the beginning of the disorder in male patients is about 5 years earlier than in female patients so male patients were more severely affected than female patients, Schweiger *et al.,* 2003. A similar finding has been reported in patients suffering from major depression.

The present study indicate that antipsychotic drugs have no or minimal effect on plasma lipids of schizophrenic Sudanese patients. In this study we found inverse relationship between duration of schizophrenic disease and plasma Parathyroid Hormone and Bone Minerals level were achievable in this study. There were several limitations in this study, the Only large-scale, prospective, longitudinal studies in which all potential confounders are controlled for will establish the precise nature of the association between all parameters in this study and schizophrenia, beside a small number of sample size and some problems in sampling procedure.

CONCLUSIONS

In conclusion, no different between effect of typical and a typical drugs on, lipid profile PTH, bone minerals, glucose, and insulin hormone in schizophrenic Sudanese patients, which cholesterol, HDL, LDL, PTH, calcium, magnesium, and glucose values in patients treated with atypical or typical drugs were significantly higher than that of control. Hence routine monitoring for schizophrenic patients during treatment with antipsychotic drugs is highly recommended. Antipsychotic treatment of schizophrenic patients can be

associated with adverse effects on glucose and lipid regulation, which can developed into type2 DM and cardiac problem.

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