Lipid profile in antipsychotic drug users: A comparative study

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Original Article

Abstract

BACKGROUND: Schizophrenic patients who receive antipsychotic drugs may be highly prone to metabolic disorders such as weight gain, dyslipidemia, and insulin resistance. The objective of the present study was to compare the effect of atypical and conventional antipsychotics on lipid profile.

METHODS: 128 schizophrenic patients were enrolled into the study. Patients were divided into two groups. One group had received one type of atypical antipsychotic drug, and, the other, one type of conventional antipsychotic drug. They were considered as atypical and conventional groups. Moreover, both groups had not used any other antipsychotic drugs during the past year. Demographic data and food frequency questionnaire were completed by the participants. Serum triglyceride, total cholesterol (TC), high-density lipoprotein and low-density lipoprotein (LDL) cholesterols, and apolipoprotein A and B (Apo B) were tested by blood sample drawing after 12 hours of fasting through the antecubital vein. Student's t-test was used to compare atypical and conventional groups.

RESULTS: There was no significant difference in age, gender, duration of illness, period of drug consumption, and age at onset of illness in the two groups. Patients in the atypical group used clozapine and risperidone (46.9%) more than olanzapine. In the conventional group 81.3% of patients used phenothiazines. Comparison between lipid profile in the conventional and atypical groups showed a significantly higher mean in TC (P = 0.01), LDL (P = 0.03), and Apo B (P = 0.01) in conventional group than the atypical group.

CONCLUSION: In schizophrenic patients, the level of lipid profile had been increased in both atypical and conventional antipsychotic users, especially conventional users, so the effect of antipsychotic drugs should be investigated periodically.

Keywords: Atypical Antipsychotic, Conventional Antipsychotic, Lipid Profile

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Introduction

Antipsychotic agents are mainly used for prevention or treatment of schizophrenia and serious psychotic diseases. There is no suitable monitoring method for the selection of antipsychotic agents, forecast of curative effect, and adjustment of dose. Therefore, to study the curative and toxic effect, and side effects, and to improve the physical health and remote therapy for the prevention and treatment of mental diseases it has become an issue of international concern.[1]

The data generated from studies of schizophrenia patients exposed to conventional antipsychotics illustrate that agents with similar modes of therapeutic action may have significantly different metabolic profiles. Several studies emerged examining the metabolic profiles of this class of antipsychotics. In general, these antipsychotic drugs

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were found to elevate serum triglycerides (TG) and total cholesterol (TC), but with greater effects on TG concentrations. Subsequent studies confirmed the finding that high serum TG seemed to be the primary significant dyslipidemia, but elevated TC could also be found.[2]

Over the past decade, atypical (or second-generation) antipsychotics have been increasingly used in the treatment of schizophrenia in preference to conventional (first-generation) drugs.[3] However, there have been numerous studies that certain atypical antipsychotics have been associated with a greater risk of metabolic abnormalities, including weight gain, hyperlipidemia and new-onset type 2 diabetes mellitus, and elevations of blood cholesterol, triglyceride, and lipid levels.[4-6]

Due to long term consumption of these drugs in schizophrenic patients, their side effects on metabolic syndrome is notable and should be considered. Thus, in this study, we tried to compare lipoprotein and apolipoprotein serum levels in schizophrenic patients under treatment of conventional or atypical antipsychotic drugs.

Materials and Methods

This case-control study was carried out on 128 schizophrenic patients in 2009. All patients had the criteria for schizophrenia of the fourth edition of Diagnostic and Statistical Manual of Mental disorders (DSM-IV, American Psychiatric Association, 1994); they had received one type of atypical or conventional antipsychotic drug for at least one year before sampling.[7]

Patients, who have received one type of atypical antipsychotic drug and have not received any other antipsychotic drug during the past year, with age range of 21-46 years were considered as atypical group. Patients, who have received one type of conventional antipsychotic drug and have not used any other antipsychotic drug during the past year, with age range of 20-40 years were considered as conventional group.

Inclusion and Exclusion criteria

Patients with an Axis I disorder other than schizophrenia, with an Axis II disorder, or patients at significant suicide risk were excluded via a semistructured psychiatric interview.

Exclusion criteria for the atypical and conventional group included lipid lowering agent and beta blockers consumption and organic diseases such as hypertension, diabetes, cardiovascular, adrenal, hepatic, and thyroid disease documented through physical examination and laboratory tests. In order to screen organic diseases, laboratory tests including complete blood count, serum electrolyte assay, thyroid function tests, liver function tests, urine analysis, and ECG were performed for all participants.

In addition, informed consents for this study were obtained from participants and their families after complete explanation.

Measurements

All individuals completed a self-administered questionnaire to determine demographic characteristics such as age, gender, duration of illness, the age at onset of illness, duration, and type of drug consumption.

According to their dietary habits, each patient completed a Food Frequency Questionnaire. This instrument was designed according to the WHO's Food Frequency Questionnaire; however, some additions were made. Validity of the questionnaire was confirmed by the Medical Education Development Centre, affiliated to Isfahan University of Medical Sciences, Iran, before being used.[8]

Blood sample was drawn after 12 hours of fasting through the antecubital vein. All the blood sampling procedures were performed in the central laboratory of Isfahan Cardiovascular Research Center, using enzyme-linked method. Serum triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL)-cholesterol, and apolipoprotein A (Apo A) and B (Apo B) were analyzed at sampling date. TC and TG levels were measured within 24 hours by an enzymatic method in Elan2000 autoanalyzer. HDL was assayed with direct method, while LDL was calculated by the Friedewald et al. formula; in cases that TG $\geq$ 400 mg/dl it was measured directly.[9] Apolipoprotein A and B cases were measured by the Immunoturbidometric technique by Pars Azmon-Iran.

Statistical Analysis

Data was analyzed by SPSS for Windows version 15.0 (SPSS, Inc., Chicago, IL). $P \leq 0.05$ was considered significant. All continues variable data were expressed as mean $\pm$ SD and t-test was used for case-control group comparison. Data regarding qualitative variables was expressed as frequency and chi-square was used for the two groups.

Results

There were 128 participants in this study, 96 (75%) male and 32 (25%) female with the mean age of 46.15 $\pm$ 12.41 years. They were divided into two equal groups; atypical and conventional groups.

Table 1 shows the characteristics of participants.

In the atypical and conventional groups, there was no significant difference in age, gender, duration of illness, and age at onset of illness. Patients in the atypical group, used olanzapine in 4 (6.3%), clozapine in 30 (46.9%) and risperidone in 30 (46.9%) cases. In the conventional group 56 (81.3%) patients used phenothiazines, 4 (6.3%) thiothixene, and 8 (12.5%) haloperidol.

Table 2 shows drug consumption other than conventional or atypical antipsychotics in the two groups.

Finally, table 3 shows lipid profile in conventional and atypical group. Comparison between the two groups shows a higher mean in TC, LDL, and Apo B in the conventional group than the atypical group, with a significant difference in TC (P = 0.001), LDL (P = 0.001), and Apo B (P = 0.001).

Discussion

The current study is a case-control study of schizophrenia in regard to lipid profile, especially close consideration of serum lipoprotein levels and apolipoproteins A and B, in patients receiving conventional or atypical antipsychotic drugs. In total, we observed that serum lipoprotein levels were high in the two groups. The mean level of HDL and Apo A in the two groups was not significantly different. The mean level of total cholesterol (TC), Apo B, and LDL were statistically higher in the conventional group than the atypical group.

There is no clear evidence to whether atypical antipsychotics are more effective or are better tolerated than conventional antipsychotics.[10]

Table 1. Characteristics of patients in the two groups

	Conventional group n = 64	Atypical group n = 64	P
Age (Mean ± SD) y	47.16 ± 11.22	45.13 ± 12.12	0.320
Gender (%)	52.00 (81%)	42.00 (67%)	0.060
Duration of illness (Mean ± SD) y	17.21 ± 11.25	18.54 ± 12.41	0.520
Drug consumption duration (Mean ± SD) m	15.21 ± 3.11	17.31 ± 4.22	0.001
Age onset of illness (Mean ± SD) y	15.81 ± 10.78	14.64 ± 11.83	0.550

Table 2. Consumption of other drugs in the two groups

	Conventional group n = 64	Atypical group n = 64	P
Mood stabilizer	8 (12.5%)	18 (28.1%)	0.028
Tricyclic antidepressant	4 (6.2%)	10 (15.6%)	0.080
Anticholinergic agents	38 (59.4%)	26 (40.6%)	0.030
Selective serotonin reuptake inhibitors	6 (9.4%)	8 (12.5%)	0.570
Benzodiazepines	22 (34.4%)	36 (56.2%)	0.010
Phenobarbital	2 (3.1%)	0 (0.0%)	0.490
Amantadine	0 (0.0%)	2 (0.3%)	0.490

Table 3. Lipid profile and Apo A and B in the two groups

	Conventional group n = 64	Atypical group n = 64	P
Total cholesterol (Mean ± SD) mg/dl	249.75 ± 34.44	214.25 ± 50.32	0.001
Low density lipoprotein (Mean ± SD) mg/dl	149.96 ± 24.21	131.93 ± 36.81	0.001
High density lipoprotein (Mean ± SD) mg/dl	44.71 ± 11.81	45.18 ± 9.42	0.800
Apolipoprotein A (Mean ± SD) mg/dl	137.12 ± 23.69	134.05 ± 22.71	0.450
Apolipoprotein B (Mean ± SD) mg/dl	122.81 ± 20.51	104.56 ± 33.63	0.001

A study was conducted to determine the prevalence of hyperlipidemia in persons who did or did not take antipsychotic drug. High lipid levels were found in persons treated with both atypical and conventional drug. The prevalence of hypercholesterolemia, high LDL cholesterol, and hypertriglyceridemia was high in persons using all types of antipsychotic drugs; this was consistent with our results.[11]

One study comparing serum TC and TG levels among hospitalized male chronic schizophrenics receiving phenothiazines, or butyrophenones and age and sex-matched controls revealed the negligible effects of butyrophenones on serum lipids. However, it demonstrated significant elevations in serum TG levels for the phenothiazine group compared to the butyrophenone group and controls. There were no significant differences in TC values between the three groups. However, the phenothiazine-treated patients had significant elevations in low-density lipoproteins (LDL-c), and decreased high-density lipoprotein (HDL-c) concentrations.[2]

A five year naturalistic study on outpatients with schizophrenia or schizoaffective disorder showed that patients treated with clozapine experience significant weight gain and lipid abnormalities.[12] Serum glucose, and lipid were changed during the course of clozapine treatment. There were significant increases in serum triglyceride, total cholesterol, and glucose levels during the treatment. No significant changes were observed in high density lipoprotein (HDL) or low density lipoprotein (LDL).[13] The effects of olanzapine and risperidone exposure on risk of hyperlipidemia in schizophrenic patients were evaluated in a large health care database. Accordingly, olanzapine use was associated with nearly a 5-fold increase in the odds of developing hyperlipidemia compared with no antipsychotic drug and more than a 3-fold increase compared with those receiving conventional agents. Risperidone was not associated with increased odds of hyperlipidemia compared with no antipsychotic or conventional exposure.[5] These results are inconsistent with our study.

According to above studies, different atypical or conventional antipsychotic drugs have different effects on lipid profiles, but we did not investigate the effect of atypical and conventional antipsychotic drugs separately. In the conventional group patients used phenothiazines, and in the atypical group patients used clozapine and risperidone more than other types of antipsychotic drugs. Therefore, our results may not be consistent with other studies.

Limitation

The limitation of this study is that the effects of antipsychotic drugs on lipid profiles have been performed exclusively in populations with schizophrenia or schizoaffective disorder. Currently, antipsychotic drugs have widespread use for other psychiatric conditions, including major depression, anxiety disorders, and dementia. The generalizability of these prior studies to other patient populations is unclear. Extending generalizability is particularly important given that schizophrenia may in itself be a risk factor for the development of an adverse metabolic profile. The effect of each drug has not been investigated, so our study results differ from other studies.

Conclusion

In summary, our data suggest that patients treated with antipsychotics are at a higher risk for the development of lipid abnormalities than the general population. In patients who use antipsychotic drugs, lipid profile and metabolic risk factors should be investigated periodically.

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Conflict of Interests

Authors have no conflict of interests.

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