The incidence of dyslipidemia (hypertriglyceridemia and hypercholesterolemia) in patients treated with the new generation of antipsychotic drugs compared to conventional therapy

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ABSTRACT

Aim To investigate the incidence of dyslipidemia (hypertriglyceridemia and hypercholesterolemia) in patients treated with antipsychotics of new generation compared to conventional therapy.

Methods This retrospective study included 116 chronic psychiatric patients divided into two groups: a test group who were on treatment with antipsychotics of the new generation and a control group who were treated with classical antipsychotics. Laboratory and vital parameters were monitored in a group of patients who were treated with new generation antipsychotics (clozapine, olanzapine, risperidone), as well as in the group of patients who were treated with classical antipsychotics (promazine, levopromazin, haloperidol, fluphenazine).

Results Mean triglyceride level in the test group was 3.13 mmol/L, and for the control group, 2.28 mmol/L, while the mean value for cholesterol test group was 6.12 mmol/L, and for the control group, 5.85 mmol/L. The average age of the test group was 49.6 years, while the control group was 51.47 years. There was a statistical significance in triglycerides (p = 0.004), while the cholesterol (p = 0.239) and age (p = 0.356) had no statistical significance in the test group compared to the patients who were treated by the new generation of antipsychotics, and the control group of patients who were treated with antipsychotics.

Conclusion Dyslipidemia in the form of hypertriglyceridemia occurs more frequently in patients on therapy with the new generation of antipsychotics compared to patients treated with conventional therapy. Hypercholesterolemia as a form of dyslipidemia had not been proven as significantly frequent during the therapy with new antipsychotics in relation to classical antipsychotic treatment.

Keywords: lipids, antipsychotics of new generation, disorder
INTRODUCTION

Dyslipidemia is an increasing problem in most industrialized societies and is a risk factor for coronary heart disease (CHD) (1,2). Imbalances in individual lipid components, including serum triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol have each been shown to contribute to this increased risk (3,4,5). Certain psychiatric patient populations, such as those afflicted with schizophrenia, are of particular concern. Psychiatric patients with schizophrenia are naturally at increased risk for dyslipidemia and obesity, in part due to poor diet and sedentary lifestyle, but these conditions can be exacerbated by some antipsychotic medications (6-9). Clozapine and olanzapine, for example, appear to be associated with hyperlipidemia, which may be associated with changes in body weight (5,10,11). Further, newer antipsychotic agents may exhibit less susceptibility for weight gain and the development of dyslipidemia (12). This review is intended to briefly highlight the association between dyslipidemia and certain type of antipsychotic therapies (Risk-benefit assessment) (12-14). Despite the adverse effects mentioned above, a number of factors should be considered while making a decision on a therapy (15). These include the nature of the patient’s psychiatric condition, specific target signs and symptoms, past history of drug response (both therapeutic and adverse), patient preference, history of treatment adherence, medication effectiveness, psychiatric and medical comorbidities, availability of appropriate formulations (e.g., fast-dissolving oral, short- or long-acting intramuscular), need for special monitoring, and cost of and access to medications (9,16). Nonetheless, the risks of obesity, diabetes, and dyslipidemia have considerable clinical implications in this patient population and should also influence drug choice (8,14,17).

Even for those medications associated with an increased risk of metabolic side effects, the benefit to specific patients could outweigh the potential risks (14). For example, clozapine has unique benefits for treatment-refractory patients and those at significant risk for suicidal behavior (18). Since treatment response in many psychiatric conditions is heterogeneous and unpredictable, physicians and patients can benefit from the availability of a broad array of different therapeutic agents (19,20).

PATIENTS AND METHODS

The clinical retrospective study was conducted at the Department of Psychiatry of the Cantonal Hospital Zenica. The study included 116 patients who were diagnosed and treated as chronic psychosis in General and Emergency Department of Psychiatry of the Cantonal Hospital in Zenica from 01 January 2009 to 31 May 2011. These patients were aged between 33 and 66 years with first or repeated hospitalization due to worsening of psychotic disorders. Aimed at homogenization of the groups, males and females in a similar ratio were selected in both groups. Patients who were admitted to the Emergency or General Department of Psychiatry, or who are refractory to classical antipsychotics, were treated with the new-generation of antipsychotics (clozapin,olanzapin,risperidon) and they were included into the test group of patients. Patients who had previously responded to conventional antipsychotics were included into the control group of patients. The test group had included 78 patients, of whom 39 men and 39 women who were admitted to the Department of General and Emergency Psychiatry because of repeated worsening of psychotic disorder, and were treated with some of the new generation antipsychotics as monotherapy or in combination with other psychoactive drugs, depending on the clinical status. The control group included 38 patients, of whom 19 men and 19 women, who were admitted under the same circumstances and who were treated with classical antipsychotics as monotherapy or in combination with other psychoactive drugs.

Test group protocol

The test group patients who received therapy upon receipt of the new generation of antipsychotics (group or clozapin tablets in dose of 25-100 mg, risperidon tablets at a dose of 1-4 mg, and olanzapine tablets at a dose of 5-10 mg). Some patients were treated with paroxetin and benzodiazepines too. All these patients were tested by laboratory tests of serum triglycerides and cholesterol at the start of treatment and two years follow up period.

Control group protocol

Patients of the control group were treated by classical antipsychotics (promazin tablets in dose of
25 to 150 mg, levopromazin tablets in dose of 25 to 75 mg, flufenazin tablets at a dose of 1 mg to 2.5 mg, haloperidol tablets at a dose of 2 to 10 mg, or as a depot preparation of these classical antipsychotics). The control group was followed up according to the same parameters as the study group in same period of follow up.

**Statistical methods**

T – test was used to determine the significance of differences between individual characteristics of groups in the sample given in the parametric form. A p value of <0.05 was considered to be statistically significant. Graphical representation is made using Boxplot applied in descriptive statistics. Within Boxplot of 25% - 75% of the data, and the boundary lines are extreme data. It shows the difference between the samples, without any assumptions basic statistical distribution.

For this investigation, the approval of the Ethics Committee of the Cantonal Hospital in Zenica was obtained.

**RESULTS**

The study included 58 male and 58 female patients. Minimum age in the test group was 33 years and the maximum age was 65 years, while in the control group minimum age was 34 years and the maximum age was 79 years. The lowest value of triglycerides in the test group was 0.90 mmol/L, and the highest value of triglycerides was 8.60 mmol/L, while in the control group, the lowest value triglyceride 0.80 mmol/L, and the highest value of triglycerides was 7.70 mmol/L. The lowest value of cholesterol in the test group was 2.80 mmol/L, and the highest value 8.50 mmol/L, while in the control group, the lowest value of cholesterol was 3.70 mmol/L, and the highest value of cholesterol in the control group was 8.80 mmol/L (Figure 1).

The average age of the test group was 49.96 years, and the control group was 51.47 years (p=0.356). Mean triglyceride levels in the test group were 3.13 mmol/L, and for the control group, 2.28 mmol/L (p=0.004), while the mean value for cholesterol test group was 6.12 mmol/L, and for the control group, 5.85 mmol/L (p=0.239) (Table 2).

<table>
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<th>Group of patients</th>
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<th>Max.</th>
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<td>2.80</td>
<td>8.50</td>
</tr>
<tr>
<td></td>
<td>Triglycerides</td>
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<td>0.90</td>
<td>8.60</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>51.47</td>
<td>34</td>
<td>79</td>
</tr>
<tr>
<td>Control N=38</td>
<td>Cholesterol</td>
<td>5.85</td>
<td>3.70</td>
<td>8.80</td>
</tr>
<tr>
<td></td>
<td>Triglycerides</td>
<td>2.28</td>
<td>0.80</td>
<td>7.70</td>
</tr>
</tbody>
</table>

The minimum age in the test group was 33 years and the maximum age 65 years, while in the control group the average age was 79 years (Figure 1).

The lowest value of cholesterol in the test group was 2.80 mmol/L, and the highest value of cholesterol in the test group was 8.50 mmol/L, while in the control group, the lowest value of cholesterol was 3.70 mmol/L, and the highest value of cholesterol in the control group was 8.80 mmol/L (Figure 2).
The lowest value of triglycerides in the test group was 0.90 mmol/L, and the highest value of triglycerides in the test group was 8.60 mmol/L, while in the control group, the lowest value of triglycerides was 0.80 mmol/L, and the highest value of triglycerides in the control group was 7.70 mmol/L (Figure 3).

Figure 3. Difference in triglycerides between the test and control groups

DISCUSSION

Our study has shown that dyslipidemia was represented in the form of hypertriglyceridemia in patients on therapy with the new generation of antipsychotic drugs compared with patients treated with antipsychotics. Despite the adverse effects or the impact of new antipsychotics, primarily clozapine and olanzapine in the development of hyperlipidemia and obesity, a number of factors should be considered when choosing among the antipsychotic medications (15). These include the nature of the patient’s psychiatric condition, specific target signs and symptoms, past history of drug response (both therapeutic and adverse), patient preference, history of treatment adherence, medication effectiveness, psychiatric and medical comorbidities, availability of appropriate formulations (e.g., fast-dissolving oral, short- or long-acting intramuscular), need for special monitoring, and cost of and access to medications (9,16). Nonetheless, the risks of obesity, diabetes, and dyslipidemia have considerable clinical implications in this patient population and should also influence a drug choice (8,14,17).

Even for those medications associated with an increased risk of metabolic side effects, the benefit to specific patients could outweigh the potential risks (12-14). The population of schizophrenic patients is at greater risk for developing obesity, type-2 diabetes, dyslipidemia and hypertension in the general population (21). The treatment with new generation antipsychotics is also associated with weight gain and other metabolic side effects (21). The relationship between weight gain caused by antipsychotic drugs and the occurrence of dyslipidemia is not yet entirely clear. Some studies suggest that weight gain and metabolic syndrome are certainly associated with the treatment with antipsychotics, but the occurrence of dyslipidemia was significantly associated with antipsychotic treatment (22). Clozapine and olanzapine significantly increase the risk of diabetes and dyslipidemia, with risperidone and quetiapine, the risk is possible, and ziprasidone and aripiprazol no risk for diabetes and dyslipidemia.

The results of this study have shown the increase in the triglycerides value when using the new generation of antipsychotic therapy compared to patients with conventional therapy, while for cholesterol there was no increase in the value when using the new generation of antipsychotic therapy compared to the patients who were treated with antipsychotics. A comprehensive study in a mental hospital in Italy investigating the comparison between the 76 patients treated with new-generation antipsychotics and 36 control patients who were not psychiatric patients, has shown that patients who were treated with new-generation antipsychotics had a significant prevalence (four times greater chance) of hypertriglyceridemia compared with controls (17). Similar values for hypertriglyceridemia were found in our study comparing the test and control groups. In several studies it was found that in patients who were not obese and were not treated with antipsychotics, the concentration of triglycerides for two weeks after the treatment with the new generation of antipsychotics significantly increased (23,24). Most antipsychotics may cause dyslipidemia indirectly through an increase in body weight, leading to abdominal obesity and hyperlipidemia. However, some antipsychotics (especially olanzapine and clozapine) may cause hyperlipidemia direct mechanisms that cause the lowering of HDL cholesterol and an increase in total cholesterol, triglyceride and LDL-cholesterol (25).
Dyslipidemia in the form of hypertriglyceridermia occurs more frequently in patients on therapy with the new generation of antipsychotics compared to patients treated with conventional therapy. Hypercholesterolemia, on the other hand, as a form of dyslipidemia, does not occur significantly more frequently in the therapy with the new antipsychotics in relation to the application of usual, classic treatment. Our study confirmed the previous view that the new generation of antipsychotics affects lipid disorder, primarily of triglycerides.

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**TRANSPARENCY DECLARATION**

Competing interests: none to declare.
Incidenca dislipidemije kod pacijenata liječenih novom generacijom antipsihotika u odnosu na pacijente koji su tretirani klasičnim antipsihoticima

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SAŽETAK

Cilj Utvrditi incidencu dislipidemije (hipertrigliceridemije i hiperholesterolemije) kod pacijenata koji su tretirani antipsihoticima nove generacije u poređenju s pacijentima koji su na terapiji klasičnim antipsihoticima.

Metode Ova retrospektivna studija obuhvatala je 116 hroničnih psihijatrijskih pacijenata podijeljenih u dvije grupe: ispitnu grupu pacijenata koji su na terapiji antipsihoticima nove generacije i kontrolnu grupu pacijenata koji su tretirani klasičnim antipsihoticima. Laboratorijski i vitalni parametri praćeni su i u grupi pacijenata koji su tretirani antipsihoticima nove generacije (clozapin, olanzapin, risperidon), kao i u grupi pacijenata koji su tretirani klasičnim antipsihoticima (promazin, levopromazin, haloperidol, flufenazin), te su dobiveni podaci statistički obrađeni.

Rezultati Srednja triglicerida za ispitnu grupu bila je 3,13 mmol/L, a za kontrolnu 2,28 mmol/L, dok je srednja vrijednost holesterola za ispitnu grupu bila 6,12 mmol/L, a za kontrolnu 5,85 mmol/L. Prosječna starost ispitne grupe bila je 49,6 godina, a kontrolne 51,47 godina. Ustanovljena je statistička signifikantnost za trigliceride (p=0,004), dok za holesterol (p=0,239) i starosnu dob (p=0,356) nije postojala statistička signifikantnost u usporedbi ispitne grupe pacijenata koji su bili na terapiji antipsihoticima novog generacije i kontrolne grupe pacijenata koji su bili tretirani klasičnim antipsihoticima.

Zaključak Dislipidemija, u obliku hipertrigliceridemije, češće se javlja kod pacijenata koji su liječeni novom generacijom antipsihotika u odnosu na pacijente koji su tretirani klasičnom terapijom antipsihotika. Hiperholesterolemija, kao oblik dislipidemije, nije pokazala statističku signifikantnost u poređenju terapije novim i klasičnim antipsihoticima.

Ključne riječi: lipidi, antipsihotici nove generacije, poremećaj