Effect of antipsychotic medications in glucose and lipid metabolism at the fasted state in drug-naïve first-episode patients with psychosis after six months of treatment

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Abstract: Diabetes and dyslipidemia are common in patients with psychosis and this association may be partly related to adverse metabolic effects of antipsychotic medications. We assessed glucose and lipid metabolism during the fasted state in 54 newly diagnosed drug-naïve, first-episode patients with psychosis (FEPs) and in the same group of patients six months after the initiation of antipsychotic treatment. Measurements were obtained for fasting serum concentrations of total cholesterol, triglycerides, high density lipoprotein (HDL), glucose, insulin, connecting peptide (C-peptide), homeostatic model assessment index (HOMA-IR), glycated hemoglobin (HbA1c) and body mass index (BMI). Total cholesterol and triglyceride levels were significantly increased in the study group after six months of antipsychotic treatment ($Z = -4.875$, $p < 0.001$ and $Z = -3.656$, $p < 0.001$ respectively), while fasting glucose, fasting insulin, C-peptide, HbA1c, HOMA-IR index and HDL did not differ before and after treatment. A statistically significant difference in BMI was also observed after antipsychotic treatment ($p < 0.001$).

Results

Description of the patients' group

The median age of the study group was 27 ranged from 18-48 years. The patient group consisted of 33 (61%) males and 21 (39%) females. The mean duration of untreated psychosis (DUP) in our study population at the beginning of the study was 11.46 weeks (SD=7.56), as these patients were investigated during the acute phase of their illness. Positive and negative syndrome scale (PANSS) was used to assess patients' psychopathology before and six months after antipsychotic treatment.

Baseline comparison with controls

The mean age of FEP patients was similar to that of the healthy control subjects (25.50 years range=18-49 years versus 27 years range=18-48 years respectively, $p=0.7$). The patient group did not differ from healthy controls with respect to BMI. HbA1c percentage was similar in patients compared to healthy controls. FEP patients were more insulin resistant as reflected by their higher HOMA-IR score ($U=728$, $p<0.001$). Total cholesterol levels were, marginally lower in the healthy group. Finally, FEP patients had significant different levels of HDL, fasting insulin and fasting C-peptide compared to healthy controls ($U=766.5$, $p<0.001$, $U=759.5$, $p<0.001$ and $U=746.5$, $p<0.001$).

Glucose and lipid parameters before and after treatment

We observed a statistically significant increase for total cholesterol and triglycerides. HDL levels did not differ. Fasting glucose levels remained similar. The same was observed for fasting insulin levels, fasting C-peptide levels, HOMA-IR index and HbA1c.

Discussion

In this study we found significant increases in total cholesterol and triglyceride levels in drug-naïve, first-episode patients with psychosis after six months of antipsychotic treatment. A statistically significant difference in BMI was observed after antipsychotic treatment ($t = 5.9$, $p < 0.001$). In addition, at baseline drug-naïve patients had significantly higher levels of fasting insulin, fasting C-peptide, triglycerides and were more insulin resistant compared to matched for age, sex, BMI and smoking healthy controls, lower levels of HDL and slightly lower levels of total cholesterol. In a previous study (Petrikis et al., 2015) we compared glucose and lipid metabolism parameters between a group of forty drug-naïve first episode patients and forty healthy controls matched for age, sex, BMI and smoking status. Patients were more insulin resistant as reflected by their higher HOMA-IR score and had higher levels of fasting insulin and C-peptide compared to controls. HDL levels were marginally lower in the patient group while fasting glucose, HbA1c, total cholesterol and triglyceride levels were similar in the two groups. Patients with schizophrenia present metabolic abnormalities even before the initiation of any antipsychotic treatment. As our study group consisted of drug-naïve, FEP patients with relatively small DUP and the follow-up period was six months, we consider the impact of possible life-style changes due to the illness as minimal. We support the hypothesis that the observed changes in total cholesterol, triglycerides and BMI should be attributed mainly to the administered antipsychotic medications. Fasting insulin and insulin resistance, although already increased even before the initiation of antipsychotic treatment, did not increase further during six months of treatment. In these parameters, the impact of antipsychotic treatment with risperidone and olanzapine seems to be far less pronounced in the studied period. Although we tend to consider metabolic and glycaemic disorders in patients with psychosis as a whole, we should probably consider them separately. Glycaemic disorders seem to pre-exist in those patients and to worsen slowly over time (at least do not worsen in six months' treatment) under antipsychotic treatment, while lipid disturbances worsen significantly in the first months of treatment.

Conclusions: Changes in lipid parameters (total cholesterol, triglycerides) and BMI occur early after the initiation of antipsychotic treatment in antipsychotic naïve FEP patients treated with olanzapine and risperidone. Glycaemic disturbances seem to exist prior to any antipsychotic treatment but they did not change after six months. Monitoring of lipid and glycaemic parameters at frequent intervals during antipsychotic treatment is of utmost importance in order to detect and treat dyslipidaemias that seem to appear early in the course of antipsychotic treatment.