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CHANGES IN VALUES OF CHOLESTEROL AND TRYGLICERIDES AFTER WEIGHT LOSS DURING TREATMENT WITH ARIPIPRAZOLE IN A PATIENT WITH SCHIZOPHRENIA - Case report

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SUMMARY

Metabolic syndrome can contribute to significant morbidity and premature mortality and should be accounted for in the treatment of mental disorders. Patients with schizophrenia are at risk of undetected somatic comorbidity. Patients with schizophrenia have metabolically unfavorable body composition, comprising abdominal obesity, high fat percentage and low muscle mass, leading to increased risk of metabolic and cardiovascular diseases. Smoking, poor diet, reduced physical activity and alcohol or drug abuse are prevalent in people with schizophrenia and contribute to the overall cardiovascular disease risk. Side effects of antipsychotics may cause diagnostic problems in deciding regarding the origin of particular symptoms (somatic illness vs. side effects) during treatment of psychotic disorders. Bearing in mind frequent comorbidity between of psychotic and somatic disorders, early recognition of such comorbidity is important, as well as the selection of antipsychotics.

The aim of this article is to report a case of changes in values of cholesterol and triglycerides after weight loss, during treatment with aripiprazole in a patient with schizophrenia.

This case report emphasizes the importance of regular monitoring of values of cholesterol and triglycerides during treatment with antipsychotics.

Key words: *schizophrenia – aripiprazole – cholesterol – triglycerides – side effects*

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INTRODUCTION

Metabolic syndrome can contribute to significant morbidity and premature mortality and should be accounted for in the treatment of mental disorders (Jakovljević et al. 2007). Patients with schizophrenia are at risk of undetected somatic comorbidity. They present physical complaints at a late, more serious stage (Oud & Meyboom 2009). The leading cause of death for individuals with psychotic illnesses or bipolar disorder is cardiovascular disease, which is often the result of patients' health problems associated with their psychiatric disorders, including, but not limited to, obesity, metabolic syndrome, and diabetes. Such problems occur more often and have worse outcomes in patients with serious mental illness than the general population because of a combination of factors such as inadequate access to quality care, poor lifestyle choices, and the association between some antipsychotic medications and weight gain (McIntyre 2009). Evidence from data linkage analyses to clinical trials demonstrate that smoking, poor diet, reduced physical activity and alcohol or drug abuse are prevalent in people with schizophrenia and contribute to the overall cardiovascular disease risk (Barnett et al. 2007). Antipsychotic treatment, in particular with some second-generation antipsychotics, is associated with weight gain and other metabolic side effects (Birkenaes et al. 2008). Never the less, it is not clear in what extent side effects of antipsychotics contribute to such development, especially as a general conclusion (Kozumplik et al. 2010). Although lifestyle and genetics may contribute independent risks of cardiometabolic dysfunction in schizophrenia and other serious mental illness, antipsychotic treatment also represents an important contributor to risk of cardiometabolic dysfunction, particularly for certain drugs and for vulnerable patients (Stahl et al. 2009).

Side effects of antipsychotics may cause diagnostic problems in deciding regarding the origin of particular symptoms (somatic illness vs. side effects) during treatment of psychotic disorders. Bearing in mind frequent comorbidity between of psychotic and somatic disorders, early recognition of such comorbidity is important, as well as the selection of antipsychotics (Kozumplik et al. 2009a). Guidelines recommend that side effects should be monitored regularly, and the side effect profile of the prescribed antipsychotic should be considered. In case of unacceptable side effects, changing to a different antipsychotic is recommended (Kozumplik & Uzun 2009). In order to establish the side effects of treatment with antipsychotics, patients should be monitored from the beginning of treatment, enabling comparison of baseline values (e.g. body weight, fasting plasma glucose, A1c levels, lipid profile hemoglobin) and values of the same parameters during treatment. Guidelines for such monitoring are described in different guidelines for treatment of schizophrenia (American Psychiatric Association 2004; Royal Australian and New Zealand College of Psychiatrists

Clinical Practice Guidelines Team for the Treatment of Schizophrenia and Related Disorders 2005).

The aim of this article is to report a case of changes in values of cholesterol and tryglicerides after weight loss, during treatment with aripiprazole in a patient with schizophrenia.

CASE REPORT

Patient, 32 years old, has been treated under diagnose of schizophrenia, according to DSM-IV diagnostic criteria, for the past eight years. At the beginning of treatment he was taking fluphenazine in therapy, in daily dosage of 10 mg. After two years of such therapy, malignant neuroleptic syndrome occurred, and flufenazine was discontinued. After that he was treated with olanzapine standard oral tablets in daily dosage of 10 mg, and gradually gained weight (10 kg) during period of eight months. Also, during that period no positive symptoms of schizophrenia were noticed, but he did not show interest for social life and was unemployed. He practiced sedentary lifestyle (at home, watching TV most of the time). He requested change of therapy because he was unsatisfied with weight gain and his lifestyle. He said that he was reading about aripiprazole on the Internet and requested such therapy. Aripirazole was introduced in therapy in daily dosage of 15 mg. At the beginning of therapy with aripiprazole the values of cholesterol and tryglicerides were in referent ranges. The daily dosage was gradually increased to 25 mg. Also, the patient was taking zolpidem, 5 mg in the evening, occasionally. The patient was taking 25 mg of aripiprazole daily for the period of one year. After aripiprazole was introduced in therapy the patient reported that he started a new diet, with less fatty foods and he lost 10 kg during period of six months. Also, during that period he finished higher education and found a job. The values of cholesterol and tryglicerides were performed each three months, showing normal values, but after one year of such therapy the value of cholesterol was 7,8 mmol/L and the value of tryglicerides was 4,5 mmol/L. The values of cholesterol and tryglicerides were elevated at the following examination, one month later. Specialist of internal medicine was consulted and he recommended therapy with atorvastatin. However, the patient refused to take atorvastatin in therapy. Patient's mental condition was still remitted, he was able to function at work and socially, and the daily dosage of aripiprazole was gradually decreased to 20 mg, and than to 15 mg. Six months after that the values of cholesterol and tryglicerides were in referent ranges, again. He was able to function at work and socially during that period, and without worsening in mental condition. He is in regular outpatient treatment; the values of cholesterol and tryglicerides are being monitored and are in referent ranges.

DISCUSSION

Before the treatment with aripiprazole was initiated, the patient was treated with olanzapine standard oral tablets in daily dosage of 10 mg, and gradually gained weight (10 kg) during period of eight months. Also, during that period he did not show interest for social life, he was unemployed, and practiced sedentary lifestyle (at home, watching TV most of the time).

An earlier article reported weight loss in two patients with schizophrenia after switching from olanzapine standard oral tablets to olanzapine orally disintegrating tablets. Switching patients from olanzapine standard oral tablets to olanzapine orally disintegrating tablets treatment resulted in significant weight loss that was maintained during 12 months in both patients (Kozumplik et al. 2009b). Second generation antipsychotics (SGAs) induce substantial weight gain but the mechanisms responsible for this phenomenon remain speculative. In the investigation that aimed to explore eating behaviors among SGA-treated patients and compare them with nonschizophrenic healthy sedentary individuals (controls), the findings suggested that patients under SGA seem to develop disordered eating behaviors in response to altered appetite sensations and increased susceptibility to hunger, a factor which may influence the extent of body weight gain triggered by these drugs (Blouin et al. 2008).

Furthermore, in the described case report aripirazole was introduced in therapy in daily dosage of 15 mg and the daily dosage was gradually increased to 25 mg. The values of cholesterol and tryglicerides were in referent ranges at the beginning of therapy with aripiprazole, but increased outside referent ranges after one year of such therapy (the values of cholesterol and tryglicerides were performed each three months).

The changes in values of cholesterol and tryglicerides were monitored in some previous investigations. In the 1-year follow-up study that aimed to evaluate changes in metabolic parameters after switching to aripiprazole in Japanese population - 32 patients with schizophrenia were observed and assessment was done of bodyweight, total cholesterol, triglyceride, serum prolactin level, and QTc interval - significant reductions were observed in these parameters other than QTc interval (Takeuchi et al. 2009). In another study that aimed to investigate the safety and efficacy of aripiprazole in first-episode drug-naive patients with schizophrenia - a total of 45 patients were enrolled in an open-label 12-week study - body weight and metabolic parameters such as cholesterol, triglycerides, and fasting glucose did not change during this study (Takahashi et al. 2009). The results of a post-hoc analysis that examined the efficacy, safety, and tolerability of aripiprazole in patients with schizoaffective disorder (data were obtained from a sub-sample of subjects with schizoaffective disorder (randomized: aripiprazole

n=123, placebo n=56) who participated in two 4-week, multicenter, double-blind trials of subjects with schizophrenia or schizoaffective disorder), showed that there were no statistically significant differences at endpoint between groups in the mean change from baseline to endpoint in weight, glucose, or total cholesterol (Glick et al 2009). According to results of a search of MEDLINE (1999-May 2009) that was conducted for reports of short- and long-term clinical studies of atypical antipsychotics (including aripiprazole) and meta-analyses of randomized controlled trials comparing first- and second-generation antipsychotics (including aripiprazole) that aimed to review the efficacy and tolerability of aripiprazole in the context of recommended management strategies for schizophrenia and schizoaffective disorder, and in comparison with first-generation and other second-generation antipsychotics in the treatment of schizophrenia or schizoaffective disorder, the evidence suggested that aripiprazole is unlikely to be associated with clinically significant weight gain or dyslipidemia, increased prolactin levels, or prolongation of the QTc interval. Compared with placebo, aripiprazole has been reported to have a relatively low potential for inducing metabolic syndrome (Stip & Tourjman 2010).

In the described case report, after aripiprazole was introduced in therapy the patient reported that he started a diet with less fatty foods and lost 10 kg during period of six months. Also, during that period he finished higher education and found a job.

The results of the study that examined the detailed body composition of people with different psychotic disorders in a large population-based sample showed that individuals with schizophrenia have metabolically unfavorable body composition, comprising abdominal obesity, high fat percentage and low muscle mass. This leads to increased risk of metabolic and cardiovascular diseases (Saarni et al. 2009). Investigations are aiming to evaluate effectiveness of different nonpharmacological approaches, such as diet and exercise in the prevention and treatment of metabolic disorder. The results of a previous investigation showed that physical inactivity had profound negative effects on lipoprotein metabolism. Modest exercise prevented this. Moderate-intensity but not vigorous-intensity exercise resulted in sustained very-low-density lipoprotein (VLDL)-triglyceride lowering. Thirty minutes per day of vigorous exercise, like jogging, had sustained beneficial effects on high-density lipoprotein (HDL) metabolism (Slentz et al. 2007). The results of another investigation showed that weight loss induced by increased daily physical activity without caloric restriction substantially reduced obesity (particularly abdominal obesity) and insulin resistance in men, while exercise without weight loss reduced abdominal fat and prevented further weight gain (Nicklas et al. 2009).

Monitoring of cholesterol and triglycerides did not show elevation of these parameters in the phase when patient was gaining weight. Quite the opposite, the elevation of values of cholesterol and triglycerides was registered after the patient had lost weight and became more active.

The results of a MEDLINE search that aimed to provide an overview for practicing clinicians on the pharmacological basis of cardiometabolic risk induced by antipsychotic drugs in patients with serious mental illness, to propose hypotheses to explain these risks and to give tips for managing cardiometabolic risk during antipsychotic treatment, showed that strong evidence exists for significant cardiometabolic risk differences among several antipsychotic agents, and that convincing data indicate that hypertriglyceridemia and insulin resistance may occur in the absence of weight gain with certain antipsychotics (Stahl et al. 2009).

Furthermore, the decrease of values of cholesterol and triglycerides was registered after the daily dosage of aripiprazole was decreased from 25 mg to 15 mg.

The results of a review of the available literature that aimed to explore a possible relationship between dosage of SGAs and the degree of metabolic side effects, the preliminary evidence suggested a dose-response relationship between clozapine and olanzapine serum concentrations and metabolic outcomes, although the association between administered daily dose and metabolic outcomes is not clear. Also, data were controversial with regard to risperidone, while for the other SGAs, there was little evidence to suggest a dose-response relationship. It was concluded that the finding that metabolic complications may be associated with clozapine and olanzapine plasma concentrations provides further evidence for a causal contribution to the metabolic disturbances observed with these agents (Simon et al. 2009). The results of another review of the literature concerning the relationships between plasma concentrations of SGAs and clinical responses by dividing the studies on the basis of the length of their observation periods showed no direct evidence concerning optimal plasma concentration ranges of ziprasidone, aripiprazole or sertindole (Mauri et al. 2007).

CONCLUSION

In this article we reported about changes in values of cholesterol and triglycerides after weight loss, during treatment with aripiprazole in a patient with schizophrenia. This case report emphasizes the importance of regular monitoring of values of cholesterol and triglycerides during treatment with antipsychotics.

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