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WEIGHT GAIN - AS POSSIBLE PREDICTOR OF METABOLIC SYNDROME

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SUMMARY

Rapid weight gain among patients with mental disorders can further compound psychological distress and negatively influence compliance. Weight gain associated with treatment with atypical antipsychotic medication has been widely recognized as a risk factor for the development of diabetes type II and cardiovascular diseases.

This paper describes a 33-year old female patient treated for schizoaffective disorder. Within two months after introducing quetiapine the patient experienced considerable weight gain amounting to 19 kg. The replacement of antipsychotic during inpatient psychiatric care resulted in weight loss.

Key words: *metabolic syndrome- quetiapine- weight gain*

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INTRODUCTION

Most atypical antipsychotics used in clinical practice may cause weight gain and its possible effects may develop into metabolic syndrome.

The NCEP/ATP III panel defined metabolic syndrome as the presence of any three or more of the following criteria: central or abdominal obesity (measured by waist circumference) for men greater than 40 inches (102 cm), for women greater than 35 inches (89 cm), fasting blood triglycerides greater than or equal to 150 mg/dL (1.69 mmol/L), blood

HDL cholesterol for men less than 40 mg/dL (1.04 mmol/L), for women less than 50 mg/dL (1.3 mmol/L), blood pressure greater than or equal to 130/85 mmHg and fasting glucose greater than or equal to 100 mg/dL (5.55 mmol/L) (Grundy et al. 2004).

Metabolic syndrome is a high risk factor for the development of diabetes type II and cardiovascular disorders. It occurs more frequently among patients affected by schizophrenia, but it is also increasing in general population probably due to lifestyle factors, nutritional habits, stress, smoking and lack of physical activity (Kozumplik et al. 2010, Newcomer 2007).

Metabolic syndrome is also known as insulin resistance syndrome, metabolic syndrome X, cardiometabolic syndrome and the deadly quartet. This syndrome is characterised by central obesity, i.e. when main deposits of body fat are localised around the abdomen.

Overweight and obesity are commonly assessed by using body mass index (BMI) defined as weight in kilograms divided by the square of the height in meters (kg/m^2). A BMI > 25 kg/m^2 is defined as overweight and a BMI > 30 kg/m^2 as obesity.

Causes of metabolic syndrome are both hereditary and acquired. Not all atypical antipsychotics have the same amounts and patterns of weight gain. Some studies do indicate weight gain liability of quetiapine (Sajatovic et al. 2008, Meyer 2001) although olanzapine and clozapine cause most weight gain and have the greatest maximal weight gain liability (Bushe et al. 2010, Hotujac et al. 2002). Long-term treatment with quetiapine monotherapy is associated with moderate weight gain (Brecher et al. 2007).

Quetiapine is an atypical antipsychotic, a dibenzothiazepine derivate. In human serum quetiapine and its active metabolite N-desalkyl quetiapine have greater affinity at serotonin ($5HT_2$) and dopamine D_1 and D_2 receptors. They also have high affinity at histamine and adrenergic Alpha 1 receptors, and moderate affinity to Alpha 2 adrenergic and serotonin $5HT_1A$ receptors. However, they have no significant affinity for cholinergic muscarinic or benzodiazepine receptors (Stahl 2008).

Quetiapine is indicated for the treatment of schizophrenia, bipolar disorders and other mood spectrum disorders. Low doses of quetiapine prescribed for insomnia also affect weight gain (Cates et al. 2009) and significant weight gain was also revealed in patients treated with quetiapine as add-on therapy of treatment resistant depression (Anderson et al. 2009).

CASE REPORT

A 33 year-old female patient, employed as a shop assistant, visited a psychiatrist for the first time four years ago. She claimed to feel apathetic and complained of undefined body agitation, difficulties in falling asleep and sleep maintenance and lack of appetite. She is the

older child (of two) and was raised in a two-parent family. Since early childhood she used to isolate herself, was quiet and shy and did not have many things in common with her peers. She claimed she had always been "in her brother's shadow". She never established an emotional relationship or intimate contacts. After graduating from vocational school, she found an employment for which she was trained and stated that she "manages to do everything she is expected to which brings her personal fulfilment".

Due to depressive disorders fluvoxamine (200 mg/day) and alprazolam (1.5 mg/day) were prescribed. Over the next several years the patient maintained normal social and occupational functioning, occasionally visited the psychiatrist and selectively took the prescribed medication.

In August 2010 the patient was admitted to hospital. She stated she felt psychophysically exhausted and overworked and believed her brother's marital problems to be the trigger. She also claimed to have a number of somatic symptoms such as heart-beat perception, chest pressure, face flushing, arm weakness and lumbar back pain. The patient felt tense and irritable, forgetful and distracted, was socially isolated, experienced sleep impairment and was completely dysfunctional.

Upon the admission to hospital and during psychiatric examination the patient's verbal output was abundant and spontaneous, anxiety and psychotic symptoms were detected while her thought process appeared accelerated. The patient also verbalised fear of death and abundant somatisation, while in longer conversations she revealed paranoid elements. The patient displayed attention deficit and impaired self-criticism and was emotionally cold.

While the patient was hospitalised a routine workup was performed. Laboratory and thyroid values as well as the ophathamologist's findings were within the normal range, while EEG revealed rhythmic activity to be mostly within alpha frequency range.

Psychological assessment revealed psychotic tendencies with dominant paranoid dimension as well as impaired ability to adjust to new situations.

Besides fluvoxamine (150 mg/day), the following substances were subsequently introduced: quetiapine XL (600 mg/day), fluphenazin (2 mg/day) and diazepam (20 mg/day).

Schizoaffective disorder (F25.2) was diagnosed according to ICD-10 and DSM-IV criteria. After discharge the patient participated in a hospital day care treatment programme for patients affected by psychotic disorders.

Two months later the patient was hospitalised again. The introduction of quetiapine XL (600 mg dose) induced considerable weight gain and the patient was quite discontented with it. Prior to quetiapine therapy she weighed 74 kg and upon the admission to hospital 93 kg. Her BMI was 36, waist circumference 107 cm and hip circumference 120 cm. Blood pressure maintained normal values - 120/75 mm/Hg.

As to the patient's psychopathology, disorders mostly occurred on affect plan. She had no spontaneity in contacts and had affective impairments. Her thought flow was slower but had no psychopathologic content. Her will and instinct dynamisms were lowered, while critical insight was adequate.

Upon the admission to hospital laboratory analyses showed as follows: cholesterol 6.5 mmol/L, HDL cholesterol 1.7 mmol/L, LDL- cholesterol 3.5 mmol/L, triglycerides 0.9 mmol/L, fasting glucose 5.7 mmol/L.

A week later the same values were measured: cholesterol 6.0 mmol/L, HDL- cholesterol 1.7 mmol/L, LDL- cholesterol 3.5 mmol/L, triglycerides 0.9 mmol/L, fasting glucose 4.9 mmol/L.

While the patient was hospitalised quetiapine was replaced with ziprasidone which was titrated up to 80 mg/day. Ziprasidone is generally associated with minimal mean weight gain and the lowest risk of more significant increases (Stahl 2008). Fluphenazine dose was reduced to 1 mg and at her discharge from hospital the patient's disorders were in favourable remission. The patient continued loosing weight (without additional interventions) so at discharge she weighed 91.3 kg.

One and a half month after the discharge at a control check-up the patient weight was 84 kg, BMI=33 cm, waist circumference 98 cm, and hip circumference 116 cm. Control laboratory analyses revealed: cholesterol 5.1 mmol/L, HDL-cholesterol 1.4 mmol/L, LDL-cholesterol 3.5 mmol/L, triglycerides 0.6 mmol/L, fasting glucose 4.8 mmol/L.

The patient was more adequate in contacts and spontaneity, stated to be more satisfied and psychomotorically calm. She did not experience any delusions and had good functioning. Regular monitoring of weight, fasting glucose, lipid levels and blood pressure was advised.

DISCUSSION

Weight gain may occur as an atypical antipsychotic side-effect and can have further negative effects on patients. As to the weight gain associated with atypical antipsychotics therapy, the following questions arise: to which extent can weight gain be tolerated as side-effect and at what stage of weight gain should an antipsychotic be replaced?

Most weight gain occurs within the first two months of treatment (Brecher et al. 2007, Vieta et al. 2005, Uzun et al 2005), as proved by the case described.

This side-effect often influences patients' compliance with treatment and impairs their life quality. Unattractive physical appearance may additionally stigmatise patients affected by mental disorders. In view of all this, patients often decrease medication dosages at their own initiative, which increases the risk of relapse and rehospitalisation.

Biologic, psychological and social methods are interwoven and combined in a comprehensive treatment of each patient affected by mental disorders. Metabolic

syndrome components themselves require continuous patient screening and monitoring and an active role of the psychiatrist, patient, patient's family and family doctor.

It is therefore advisable to establish preventive coaching and social programmes in order to help such patients change their lifestyle (balanced diet, regular exercise, smoking cessation) (Folnegović-Šmalc 2009).

It is crucial to establish whether the patient suffers from any physical disorder which might increase antipsychotic side-effects.

The choice of psychopharmaceutic drugs requires a rational approach. The patients receiving antipsychotic monotherapy have lower rates of metabolic syndrome (Correll et al. 2007), while antipsychotic polytherapy has higher rates of weight gain, dyslipidemia and insulin resistance (Dadić-Hero et al. 2010, Filaković 2003).

CONCLUSION

Although atypical antipsychotics show a higher degree of efficacy in the treatment of psychotic disorders, they also increase the risk of side-effects. Weight gain i.e. obesity is one of the recognised side-effects of such drugs.

Although weight gain is not one of the prominent side-effects of quetiapine, this symptom is to be monitored since it can be one of the first predictors of metabolic syndrome development. Social stigma attached to weight gain has additional negative impact on patients affected by mental disorders.

Reduction of prominent symptoms of mental disorders is the indication for atypical antipsychotics, although it should not be the only objective. Psychoeducational training aimed at informing the patient on antipsychotics effects, their possible side-effects and healthy lifestyle (balanced diet, physical activity) can be useful in prevention of obesity and metabolic syndrome. The objective of psychiatric treatment is to improve and encourage healthy lifestyle, life quality and social reintegration of patients affected by mental disorders.

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