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Letter to the editor

Orlistat in the treatment of clozapine-induced hyperglycemia and weight gain

Second generation antipsychotics are the treatment of choice for schizophrenia spectrum disorders, mainly due to their improved tolerability compared to conventional drugs. However, the use of atypical antipsychotic is associated with weight gain, glucose and lipid abnormalities. These unwanted effects might involve centrally regulated alterations in appetite and feeding and possibly associated metabolic abnormalities. For clozapine, genetic predisposition and its high affinity for 5-HT_{2c} serotonin and H_1 histamine receptors have been linked with the extent of induced weight gain and metabolic changes [1].

Orlistat is a pancreatic lipase inhibitor, which non-systematically decreases gastrointestinal fat absorption without affecting psychotropic drug plasma levels [2]. Studies in healthy overweight patients with or without type 2 diabetes have shown that Orlistat helps with weight loss properties and improves lipid levels and glucose serum levels as well as insulin concentration [3,4]. It may therefore be particularly helpful in the treatment of metabolic side-effects of atypical antipsychotics as modification of eating habits and increase in physical activity are more difficult to instigate and would thus represent additional burden for immediate family members.

We report on a 35-year old man with chronic schizophrenia disorganized type, diagnosed at the age of 19. He had no family history of obesity, hypertension, hyperglycemia, diabetes or dyslipidemia. He had responded poorly to conventional antipsychotics and optimal treatment with risperidone. However he responded very well to clozapine at a dose of 600 mg/day. Laboratory assessments were performed at baseline and at 3-month intervals after initiation of clozapine treatment. Hyperglycemia of 7.1 mmol/l (reference value 3.6-6.1 mmol/l) was observed after 12 months of continuous clozapine treatment. At that time his Body Mass Index was 30 kg/m^2 and his waist circumference was 120 cm. Treatment with Orlistat 120 mg (1 tablet) before each meal was initiated. After 12 weeks this resulted in total weight loss of 6%, and an decrease of 7 cm in waist circumference. His fasting blood glucose levels were 5.9 mmol/l. No adverse events were reported by the patient or his family.

Orlistat might be an effective and well tolerated treatment option for hyperglycemia and weight gain associated with clozapine use. Long-term placebo-controlled studies with larger samples are necessary, in order to determine the value of Orlistat in the management of the metabolic side-effects of atypical antipsychotics.

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