Metabolic effect of Olanzapine medication on weight gain

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Abstract: Since increased use of antipsychotics in people, their endocrine and metabolic side-effects (weight gain, obesity, and related metabolic deviations) are of particular disturbing, that appears antipsychotic-induced metabolic adverse events. Aim of the study is to evaluate metabolic effects of olanzapine on weight gain. This 8 week, controlled study was carried out during a prearranged treatment protocol in an outpatient service, thus enabled to control effects of energy outlay and other life style related factors. Subjects were randomly allocated into olanzapine (n=217). Weight and calorie intake were measured daily. Serum lipids were measured at baseline and 8th week. Olanzapine treatment were showed associated weight gain (F=0.85% p<0.05). Our finding shows that olanzapine has significant effect in weight gain.
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Introduction

Olanzapine metabolic syndrome acts as effective agent in the treatment of schizophrenic symptoms with a favorable side effect profile. Adverse metabolic effects such as weight gain and dyslipidemia have increasingly been recognized with the use of typical antipsychotic drugs. However various antipsy-chotics have distinct metabolic effects. Olanzapine treatment has been consistently associated with weight gain (1) in a prolonged treatment period from the first weeks of the treatment up to the end of the first year (2). The drug has been tested against conventional and some novel antipsychotics and found to be associated with a more severe weight gain (3, 4). Pooled data from studies on weight change with olanzapine use revealed that 24–37% of the patients experienced weight gain of 7% of their body weight (5). Despite increasing use of psychotropic medication in patients, their endocrine and metabolic side-effects (weight gain, obesity, and related metabolic abnormalities such as hyperglycaemia and dyslipi- demia) are of particular concern that appears to be at great risk for antipsychotic-induced metabolic side-effects. In addition to medication, many factors contribute to weigh gain in psychiatric patients, including sedentary lifestyle and poor diet control. Excessive weight gain has several deleterious effects in psychiatric patients, including stigmatization and further social withdrawal, and non compliance with medication. Furthermore, excessive corpulence may evolve to a metabolic syndrome with a high-risk state for future cardiovascular morbidity and mortality in adult age. Because youths are still developing at the time of psychotropic drug exposure, in a context of physiological changes in hormonal and endocrine levels and body composition, most reference values need to be adjusted for gender, age and growth charts. Hence, sex- and age-adjusted body mass index (BMI) percentiles are crucial to assess weight gain (6). Olanzapine is an atypical antipsychotic that belongs to the thienobenzodiazepine class. Olanzapine binds to a large number of neurotransmitter receptors, including the dopamine D1, D2, and D4 receptors, serotonin 5- HT2A, 5-HT2C, 5-HT6, and 5-HT3 receptors, histamine H1 receptor, muscarinic receptors, α- and β-adrenergic receptors, γ-amino butyrate (GABA) a1receptor, and the benzodiazepine binding sites. Antagonism at the central H1, 5-HT2C, M1, and α-1 noradrenergic receptors have been suggested as possible molecular mechanisms of antipsychotic induced dys-regulation of food intake and weight gain (7,8). Antipsychotic use has also been associated with dyslipidemia. Olanzapine treatment was associated with a marked hypertriglyceridaemia and hypercholesterolaemia (9,10). Although dyslipidemia was generally accepted to be a result of weight gain, recent studies revealed that some antipsychotics may have direct and immediate effects on serum lipids independent from their effects on weight (11) and inter-relations between life style related factors, dyslipidemia, and weight gain requires further investigation (12). Although the pathophysiology of the metabolic side effects of atypical antipsychotic drugs is not completely understood, the final effect of olanzapine on the metabolic parameters is probably the end result of a complex interaction between many factors such as life style, diet related factors, endocrine factors and receptor profile of the antipsychotic drug.

We evaluate the metabolic effects of olanzapine in a randomized prospective design, recording individual parameters such as diet and calorie intake, and controlling energy outlay and other life style related factors.

Method

Sample and Procedure

Consecutive inpatients aged 15-60 within the indication spectrum of atypical antipsychotic monotherapy(n=217) were screened in Psychiatric Clinic. Patients with any overt metabolic or endocrine disorder diagnosed before or during hospitalization (n= 15) were excluded and finally 202 patient enrolled in the study. The study was approved by the local ethics committee. Subjects were randomly assigned into olanzapine (n=202), using a prearranged number chart that was rescheduled following a failure for any reason. The treatment procedure (i.e.; dosing, management of side effects, judgment for non response and decisions regarding antipsychotic medication change) was carried out by the assigned clinician. The patients who were added another antipsychotic agent or whose antipsychotic treatment was suspended were to be dropped out. Mean daily doses of the administered olanzapine was 10 mg/day. No serious adverse events were examined in group.

Clinical and Laboratory Assessments

The study setting permitted a structured treatment protocol including the daily physical activity for all inpatients. Standard hospital diet (average 2000 kcal/day) was served, however consumption of extra food and beverage was not restricted. Daily food intake was recorded and computed by the dietician in kilocalories (Kcal). Weight, BMI and calorie intake were measured daily. Weight was measured before breakfast at 8 am, with the same electronic weigher.

Analysis

Statistical analyses were carried out with the SPSS 16.0 program. Symptom severity was compared between the patients at baseline and at the end of the eight^{h} week. Weight gain, was compared within the patients. In some previous studies baseline BMIs were found to affect antipsychotic induced weight gain (13,14).

Results

8 months after olanzapine was introduced to therapy, an abrupt weight gain was observed. We measured and found that the patient's weight was 60.9 kg, which was a weight gain of 10 kg. Laboratory blood parameters at this point were changed, and revealed increased levels of glucose in blood, cholesterol and thyroid-stimulating hormone. The parameters have been checked constantly one time for every two months. During this period patient's weight in most subjects were continuously increased. Our result indicated that olanzapine use was associated with weight gain. We observed an average of 7.2 kilo-grams gained in the olanzapine group that was equivalent to 14.3 % of the patients' body weight at baseline. Olanzapine treatment were showed associated weight gain (F=0.85% $p<0.05$). At 27 patients because of severe weight gain drug consumption was stopped. At 10-16 case hyperglycemias were showed which are not discussed now.

Table 1. Olanzapine subjects for weight gain during 8 weeks

Olanzapine	Baseline	Week2	Week 4	Week 6	Week 8
Weight (kg) (Mean±SD)	60.9±14.0	63.2±14.5	65.1±14.8	67.7±14.6	70.8±15.2

Discussion and Concussion

In this clinical case report our aim was to present the effect of olanzapine on weight gain. Our finding was a randomized, controlling the individual parameters of calorie intake and energy outlay in a regular environment. Within a 8 weeks treatment period with olanzapine, it is observable that weight, calorie intake rise constantly. While it was previously proposed that different effects of different antipsychotics on weight gain may be related to H1, M1 and α-1 noradrenergic receptor affinities (8, 15). Our results reveal that the olanzapine are associated with weight gain and this result is parallel to previous findings (1,16). When two drugs are compared for their effects on serum lipids, it is evident that olanzapine disturbs lipid profile. This finding is in line with previous studies(17) Widely used guidelines for metabolic side effects of antipsychotic drug (18) recommend monitoring the lipid profiles of patients before treatment and at week 12. Indeed, olanzapine was associated with relatively high rates of food craving (48.9%) and binge-eating behavior (16.7%) in a recent randomized, double-blind study of patients with schizophrenia, schizoaffective disorder, or schizophrenic form disorder (19). In another study, hunger and satiety ratings were determined in a cohort of 48 healthy volunteers randomized to olanzapine, risperidone, or placebo for 2 weeks using a standardized feeding protocol (20). Measurement of body weight and calculation of BMI are very simple and easily applicable methods, as well as laboratory blood parameters, give a very good insight to some side-effects of antipsychotic therapy. Olanzapine has played a critical role in alerting

scientists to the metabolic consequences of most antipsychotics patients. Weight and metabolic changes observed in olanzapine-treated patients stimulated investigations of such effects in other antipsychotics for further long-term studies. It is extremely important to know very well all possible side-effects of the medications we prescribe, so we could promptly intervene, according to achievements and professional rules. The specificities of other disorders instruct us to the need of interdisciplinary approach and cooperation. Measurement of body weight and calculation of BMI are very simple and easily applicable methods, as well as laboratory blood parameters, give a very good insight to some side-effects of antipsychotic therapy.

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References

1. Newcomer JW.Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. CNS Drugs 2005; 19(1): 1-93.
2. Taylor DM, McAskill R. A typical antipsychotics and weight gain- a systematic review. Acta Psychiatr Scand 2000; 101: 416-32.
3. Wirshing DA, Wirshing WC, Kysar L, *et al*. Novel antipsychotics: comparison of weight gain liabilities. J Clin Psychiatry 1999; 60(6): 358-63.
4. Sikich L, Hamer RM, Bashford RA, Sheitman BB, Lieberman JA. A pilot study of risperidone, olanzapine, and haloperidol in psychotic youth: a double-blind, randomized, 8-week trial. Neuropsy-chopharmacology 2004; 29(1): 133-45.
5. Haddad P. Weight change with atypical antipsychotics in the treatment of schizophrenia. J Psychopharmacol 2005; 19(6): 16-27.
6. Goeb JL, Marco S, Duhamel A, Kechid G, Bordet R, Thomas P, Delion P, Jardri R.: Metabolic side effects of risperidone in early onset schizophrenia. Encephale 2010;36:242-252.
7. Tecott LH, Sun LM, Akana SF, Strack AM, Lowenstein DH, Dallman MF, *et al*. Eating disorders and epilepsy in mice lacking 5-HT2c serotonin receptors. Nature 1995; 374: 542-6.
8. Han M, Deng C, Burne THJ, Newell KA, Huang X-F. Short- and long-term effects of antipsychotic drug treatment on weight gain and H1 receptor expression. Psychoneuroendocrinology 2008; 33: 569-80.
9. Osser DN, Najarian DM, Dufresne RL. Olanzapine increases weight and serum triglyceride levels. J Clin Psychiatry 1999;60(11): 767-70.
10. Meyer JM, Davis VG, McEvoy JP, *et al*. Impact of antipsychotic treatment on nonfasting triglycerides in the CATIE Schizophrenia trial phase 1. Schizophr Res 2000; 103(1-3): 104-9.
11. de Leon J, Susce MT, Johnson M, *et al*. A clinical study of the association of antipsychotics with hyperlipidemia. Schizophr Res 2007; 92(1-3): 95-102.
12. Nasrallah HA. Atypical antipsychotic-induced metabolic side effects: Insights from receptor-binding profiles. Mol Psychiatry 2008; 13(1): 27-35.
13. 36. Lane HY, Chang YC, Cheng YC, Liu GC, Lin XR, Chang WH.Effects of patient demographics, risperidone dosage, and clinical outcome on body weight in acutely exacerbated schizophrenia. J Clin Psychiatry 2003; 64: 316-20.
14. Lee E, Leung CM, Wong E. A typical antipsychotics and weight gain in Chinese patients: a comparison of olanzapine and risperi- done. J Clin Psychiatry 2004; 65: 864-6.
15. Kroeze WK, Hufeisen SJ, Popadak BA, *et al*. H1-histamine recep- tor affinity predicts short-termweight gain for typical and atypical antipsychotic drugs. Neuropsychopharmacology 2003; 28(3): 519-26.
16. Allison DB, Mentore JL, Heo M, *et al*. Antipsychotic-induced weight gain: a comprehensive research synthesis. Am J Psychiatry 1999; 156: 1686-96.
17. Melkersson K, Dahl ML. Adverse metabolic effects associated with atypical antipsychotics: literature review and clinical implications. Drugs 2004; 64(7): 701-23.
18. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for The Study of Obesity. Consensus devel- opment conference on antipsychotic drugs and obesity and diabe- tes. Diabetes Care 2004; 27: 596-601.
19. Kluge M, Schuld A, Himmerich H, et al. Clozapine and olanzapine are associated with food craving and binge eating: results from a randomized double-blind study. J Clin Psychopharmacol. 2007;27:662-666.
20. Roerig JL, Mitchell JE, de Zwaan M, et al. A compari- son of the effects of olanzapine and risperidone versus placebo on eating behaviors. J Clin Psychopharmacol. 2005;25:413-418.

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