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Letter to the Editors

Weight gain, serum leptin and triglyceride levels in patients with schizophrenia on antipsychotic treatment with quetiapine, olanzapine and haloperidol

Weight gain is a frequent adverse effect of most antipsychotic drugs (Baptista et al., 2002). Leptin is an adipocyte hormone regulating food intake and energy balance and provides the hypothalamus with information on the amount of body fat and affects the intracellular lipid concentration (Auwerx and Steals, 1998). Leptin administration results in reduced food intake and weight loss (Halaas et al., 1995), suggesting its role on weight regulation. The weight gain induced by clozapine and olanzapine has been reported to be associated with an increase in the leptin levels (Kraus et al., 1999). Quetiapine has similar receptor binding profile with clozapine and olanzapine. Therefore, we decided to evaluate whether quetiapine was associated with similar weight gain, leptin and triglyceride levels as olanzapine and a typical antipsychotic, haloperidol.

We examined 45 inpatients with DSM-IV schizophrenia who were administered these drugs as monotherapy by their clinicians: quetiapine ($n=15$, mean age: 28.6 ± 11.3 years), olanzapine ($n=15$, mean age: 29.2 ± 12.8 years) and haloperidol ($n=15$, mean age: 27.4 ± 10.6 years). All participants were free of all medications at least 2 weeks prior to beginning their current treatment. Exclusion criteria included the presence of a severe physical illness, history of alcohol and substance abuse or dependence, a previous history of lipid lowering treatment and the presence of any endocrinological disorder. All participants received a routine hospital diet. The patients were evaluated at baseline and sixth week with respect to the Positive and Negative Syndrome Scale (PANSS), Body Mass Index (BMI), weight, serum leptin and triglyceride levels. Leptin levels were measured by radioimmunoassay method. Triglyceride levels were measured by using an Olympus AU 600 autoanalyser. Statistical analysis was performed using the statistical package for social sciences (SPSS/PC 9.05 version, 1998). This study was not supported by any drug company.

The mean weight gain for the quetiapine, olanzapine and haloperidol groups were 3.9, 8.4 and 0.5 kg, respectively ($p<0.01$). There was a remarkable increase in triglyceride ($p<0.05$ for the olanzapine vs. quetiapine and quetiapine vs. haloperidol groups; $p<0.01$ for olanzapine vs. haloperidol groups) and leptin levels ($p<0.05$ for the olanzapine vs. quetiapine groups; $p<0.01$ for olanzapine vs. haloperidol groups) in the olanzapine group compared to quetiapine and haloperidol groups. At the evaluation of week 6, the significant difference in mean serum triglyceride ($F=3.29$, $p<0.05$ adjusted for BMI; $F=3.08$, $p<0.05$ adjusted for age) and leptin levels ($F=4.42$, $p<0.05$ adjusted for BMI; $F=4.24$, $p<0.05$ adjusted for age) among groups was found after BMI or age adjustment. There were significant positive correlations between the change in leptin levels and duration of illness in the quetiapine ($r=0.55$, $p<0.05$) and olanzapine groups ($r=0.72$, $p<0.01$) but not in the haloperidol group ($r=0.16$, $p>0.05$). The change in total PANSS scores correlated with change in leptin levels in all groups ($r=0.60$, $p<0.05$ for the olanzapine group; $r=0.58$, $p<0.05$ for the quetiapine group and $r=0.54$, $p<0.05$ for the haloperidol group).

Olanzapine led to a marked increase in weight gain, serum triglyceride and leptin levels, though increases in these variables were modest in patients receiving quetiapine and minimal in those receiving haloperidol. There was a greater increase in triglyceride and leptin levels in the olanzapine group compared with the quetiapine and haloperidol groups. Olanzapine induced increases in triglyceride levels have been previously reported (Melkersson et al.,

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2000). Leptin has been considered to interact with some neurotransmitters including histamine and serotonin which may cause these to be associated with weight gain (Morimoto et al., 1999; Dryden et al., 1999). Increases in serotonin receptor binding have been demonstrated to decrease food intake (Meguid et al., 2000) and there appears to be an interaction between leptinergic and serotonergic systems in the central nervous system (Leibowitz and Alexander, 1998). Probable different receptor binding profiles of antipsychotics among atypical antipsychotics may account for their different effects on leptin levels and related weight gain. It has been proposed that leptin mediates the beneficial effects of antipsychotics (Kraus et al., 1999). However, this observation has not been supported by Herran et al. (2001). In conclusion, our results suggest that leptin may be associated with quetiapine and olanzapine induced weight gain and that quetiapine seems to have modest effect on weight gain compared with olanzapine.

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