Alterations in body weight and biochemistry in patient treated with different psychotropic drugs in a clinic in Istanbul

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ABSTRACT

Aim Was to compare adult female patients receiving psychiatric drugs with obese adult females who didn’t receive any drug treatment with respect to the alterations in body weight and biochemistry, and find out the contribution of a team approach for the management of these alterations.

Methods A total of 102 female patients aged mean 40.9±12.4 years who had been followed up and treated in the Psychiatry Outpatient Clinics in Istanbul University for their psychiatric disorders and were complaining about increased body weight in the treatment period were included. The controls were composed of 261 females aged mean 39.8±13.0 years who had been referred by various departments to dietitians due to exogenous obesity but had no endocrine-metabolic or psychiatric disorders or history of drug use. Initially, anthropometric measurements and biochemical tests were performed for all patients.

Results In the group receiving psychiatric treatment, the mean body weight, BMI, waist and hip circumferences, body fat percentage (p<0.001), blood insulin, triglyceride, TSH, fibrinogen and homocysteine levels, and HOMA-IR were found to be higher than those of the controls (p<0.05), whereas the total protein, albumin, zinc and folate levels were significantly lower (p<0.001).

Conclusion The results of this study showed that patients who need psychopharmacotherapies were also more susceptible to several metabolic and cardiovascular disorders. Therefore, it would be useful if psychiatric patients are treated with a multidisciplinary team approach consisting of an endocrinologist, psychiatrist and a dietitian specialized in this area to prevent or delay the metabolic disorders caused by psychiatric disorders and treatments.

Key words: body composition, obesity, psychotropic drugs
INTRODUCTION

During psychiatric treatment, body weight usually increases and this is frequently accompanied by an increase in appetite (1). This side effect, which is difficult to foresee in terms of its development and timing, finally causes obesity and results in the cessation of an effective treatment in some of the patients. Obesity not only affects the psychological state of the patient, but also increases the risk of development of several chronic diseases such as coronary artery disease, hypertension, hyperlipidaemia, diabetes, some types of cancer, cerebrovascular diseases, osteoarthritis, pulmonary diseases and sleep apnoea (2-4). Therefore, reduction of body weight plays a pivotal role in the prevention of several chronic diseases and improvement of the prognosis of an ongoing disease.

In this research, we aimed to compare the changes in anthropometric and biochemical parameters in patients treated with psychiatric drugs with ones who did not, and to find out the contribution of a dietitian specialized in this area for the treatment of nutrition related metabolic problems arising out of psychiatric pharmacotherapies.

PATIENTS AND METHODS

In order to determine patients’ group for this research the records of all patients who admitted to outpatient clinic of Psychiatric Department in Cerrahpasa Medical Faculty University of Istanbul in the 2004 to 2008 period retrospectively analyzed. It has chosen two groups among 363 patients who suffer from obesity and were followed by a dietician. All patients are informed and accepted their inclusion in the research.

The study group included 102 (28.1%) adult female patients taking psychiatric pharmacotherapies and complained about increased body weight within this period. The mean ±SD age of study group was 40.9±12.44 years.

Medications that patients in the study group have taken were antipsychotics 34 (38.2%), mood stabilisers 36 (40.4%), antidepressants 72 (80.9%) or anxiolytic 9 (10.1%) which were mostly taken as combined pharmacotherapy.

The controls included 261 (71.9%) adult females who had no endocrine, metabolic or psychiatric disorders or history of drug use and had been referred to dietitians due to exogenous obesity. The mean ±SD age of control group was 39.8±13.0 years.

As body composition depends on age, sex and severity of obesity (5, 6) both groups included adult females with body mass index (BMI) ≥25.

All patients underwent antropometric assessment, body composition analysis using a Bioelectrical Impedance Analyzer (Bodystat Quadscan 4000, England). Biochemical parameters of patients were studied with overnight fasting blood samples taken from the antecubital vein. Biochemical parameters, serum fasting blood glucose (FBG), total protein, albumin, uric acid, triglyceride, and total, HDL and LDL cholesterol were measured using an Olympus AU 800 autoanalyzer (Olympus, Japan). FBG was analysed using the hexokinase method. The methods were biuret for total protein, BCG for albumin and the uricase / PAP method for uric acid. Levels of total, HDL cholesterols and triglycerides were measured using enzymatic methods in all samples. Serum hsCRP concentrations were determined with immunonephelometry using the BN II Systems Analyzer (Dade Behring, Malburg, Germany). FT3, FT4, third-generation thyroid stimulating hormone (TSH) were measured on Immulite 2000 (DPC; Los Angeles, USA). FT3 and FT4 were measured by a competitive analog-based immunoassay. TSH levels were determined by two-side chemiluminescent immunometric assay. Insulin and cortisol were measured with Immulite 2000 analyzer (DPC,USA) by chemiluminescent immunometric assay. Insulin resistance (IR) was determined by HOMA- IR index, e.g. serum insulin (mg/dl) x plasma glucose (mg/dl) / 405. Serum B12, folic acid levels were measured by radioimmunoassay (RIA) (DPC, USA). Plasma level of homocysteine was determined by high-performance liquid chromatography (HPLC Agilent 1100 Series), coupled with fluorescence detector. Plasma fibrinogen levels were measured by BCT (Dade Behring, Malburg, Germany) analyser. Serum zinc, and copper concentrations were determined using the standard atomic absorption spectrophotometry.
The data have been analysed with the Student’s t-test and correlations were calculated using Pearson correlation. All data are expressed as mean ± standard deviation (SD).

RESULTS

The results of anthropometric measurements and body composition analyses of study and control groups are shown in Table 1, while the biochemical parameters are shown in Table 2.

In the study group, the mean body weight, BMI, waist and hip circumferences, the waist/hip ratio, body fat percentage, and serum insulin, triglyceride, TSH, fibrinogen and homocysteine levels were found to be significantly greater while the percent of body water and lean body mass, total protein, albumin, zinc and folate levels were significantly lower than those of the controls.

In the study group, there was a positive correlation between BMI, waist and hip circumferences, body fat percentage, basal metabolic rate, insulin, HOMA-IR and ferritin levels (r=0.779, p<0.001; r=0.895, p<0.001; r=0.438, p<0.001; r=0.593, p<0.001; r=0.379, p<0.001; r=0.340, p<0.001; r=0.470, p<0.001; respectively). However, there was a negative correlation between BMI and the percentage of body water and lean body mass (r=0.548, p<0.001; r=-0.423, p=0.006; respectively). But BMI showed negative correlation with the percentage of body water and lean body mass, and HDL-C level (r=-0.554, p<0.001; r=-0.323, p=0.001; r=-0.210, p=0.002; respectively).

Mean duration for being treated with psychotropic drugs of patients in the study group was found median 2 years (Interquartile range, IQR: 1-4) and the increase in body weight was 11.9 ± 5.0 kg in this period.

In study group there was a positive correlation between the duration of drug treatment and body weight, BMI, waist and hip circumferences, body fat percentage, insulin, triglycerides, TSH and homocysteine (r=0.293, p=0.005; r=0.272, p=0.010; r=0.339, p=0.002; r=0.280, p=0.016; r=0.310, p=0.009; r=0.262, p=0.019; r=0.241, p=0.025; r=0.273, p<0.001; r=0.368, p<0.001; r=0.416, p<0.001; respectively).

Table 2. Comparison of the biochemical parameters of the groups*

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>Group</th>
<th>Study Mean ± SD</th>
<th>Control Mean ± SD</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mg/dL)</td>
<td></td>
<td>96.54 ± 11.29</td>
<td>94.02 ± 11.69</td>
<td>0.070</td>
</tr>
<tr>
<td>Insulin (mIU/mL)</td>
<td></td>
<td>17.20 ± 8.92</td>
<td>14.37 ± 9.45</td>
<td>0.019</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td></td>
<td>142.83 ± 78.34</td>
<td>117.21 ± 63.35</td>
<td>0.002</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td></td>
<td>205.69 ± 43.08</td>
<td>203.63 ± 42.48</td>
<td>0.687</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td></td>
<td>50.34 ± 15.46</td>
<td>50.68 ± 13.85</td>
<td>0.847</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td></td>
<td>129.05 ± 36.43</td>
<td>132.47 ± 37.69</td>
<td>0.459</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td></td>
<td>7.17 ± 0.54</td>
<td>7.40 ± 0.44</td>
<td>0.015</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td></td>
<td>4.12 ± 0.49</td>
<td>4.46 ± 0.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Homoglobin (g/dL)</td>
<td></td>
<td>12.95 ± 1.04</td>
<td>13.16 ± 1.02</td>
<td>0.149</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td></td>
<td>38.00 ± 2.96</td>
<td>38.57 ± 2.80</td>
<td>0.160</td>
</tr>
<tr>
<td>TSH (mU/mL)</td>
<td></td>
<td>2.2864 ± 2.1395</td>
<td>1.83 ± 1.36</td>
<td>0.036</td>
</tr>
<tr>
<td>FT3 (pg/mL)</td>
<td></td>
<td>2.93 ± 0.598</td>
<td>3.229 ± 0.956</td>
<td>0.159</td>
</tr>
<tr>
<td>FT4 (ng/dL)</td>
<td></td>
<td>1.532 ± 2.67</td>
<td>2.058 ± 3.31</td>
<td>0.472</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td></td>
<td>4.16 ± 2.39</td>
<td>3.39 ± 2.33</td>
<td>0.013</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td></td>
<td>437.81 ± 138.73</td>
<td>337.37 ± 90.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td></td>
<td>7.69 ± 6.87</td>
<td>6.45 ± 9.38</td>
<td>0.624</td>
</tr>
<tr>
<td>Cortisol (µg/dL)</td>
<td></td>
<td>14.58 ± 10.33</td>
<td>9.65 ± 5.32</td>
<td>0.966</td>
</tr>
<tr>
<td>Zinc (µg/dL)</td>
<td></td>
<td>78.21 ± 20.96</td>
<td>93.28 ± 22.01</td>
<td>0.005</td>
</tr>
<tr>
<td>Copper (µg/dL)</td>
<td></td>
<td>119.62 ± 32.46</td>
<td>118.85 ± 22.62</td>
<td>0.945</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td></td>
<td>4.94 ± 1.21</td>
<td>4.57 ± 1.28</td>
<td>0.175</td>
</tr>
<tr>
<td>Vitamin B12 (µg/dL)</td>
<td></td>
<td>328.04 ± 207.03</td>
<td>354.32 ± 192.89</td>
<td>0.477</td>
</tr>
<tr>
<td>Folic acid (ng/mL)</td>
<td></td>
<td>6.99 ± 3.32</td>
<td>9.31 ± 3.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Homocysteine (umol/L)</td>
<td></td>
<td>13.08 ± 3.55</td>
<td>10.55 ± 2.28</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*FBG, fasting blood glucose; TSH, thyroid stimulating hormone; FT3, free T3; FT4, free T4; HOMA-IR, homeostasis model of assessment-insulin resistance; CRP, C-reactive protein; *p-values below 0.05 were considered significant.
r=0.394, p=0.000; r=0.344, p=0.030; respectively), but there was a negative correlation between the duration of drug treatment and percentage of body water, percentage of lean body mass, and albumin (r=-0.278, p=0.020; r=0.293, p=0.013; r=0.415, p=0.006; respectively). It has also found a positive correlation in the study group between weight gain and length of drug treatment, BMI, waist and hip circumferences, body fat percentage, insulin, TSH and HOMA-IR (r=0.646, p=0.000; r=0.534, p=0.000; r=0.504, p=0.000; r=0.511, p=0.000; r=0.412, p=0.000; r=0.382, p=0.000; r=0.419, p=0.000; r=0.319, p=0.004; respectively), but there was a negative correlation between weight gain and percentage of body water, percentage of lean body mass, LDL-C and folat levels (r=-0.534, p=0.000; r=-0.388, p=0.001; r=-0.283, p=0.010; r=-0.247, p=0.041; respectively).

DISCUSSION

Abdominal obesity is strongly associated with disorders of glucose, insulin and lipid metabolism (7-11). Waist circumference is among the fixtures of the diagnostic criteria of metabolic syndrome (12). In people with abdominal obesity, the presence of at least the two of the diagnostic criteria is regarded as indicative of metabolic syndrome (12). In these people, high serum uric acid, leptin, insulin, and CRP levels and high plasma fibrinogen as well as clinical depression, non-alcoholic steatosis, and polycystic ovary syndrome are more commonly encountered (12, 13). Recent studies have also indicated the association of insulin resistance and impaired glucose tolerance with decreased cortical functions and Alzheimer’s disease (AD) (14-20). In our study, higher levels of FBG, serum insulin, triglycerides and homocysteine levels in the study group (Table 2) may indicate that these patients have greater risk of not only cardiovascular and metabolic diseases, but also of AD.

In the present study, majority of patients on psychiatric pharmacotherapy use more than one drug. In addition, the proportion of antidepressant users was the highest (80.9%). It is possible that individual factors may have contributed to significant weight gain as well as the effect of antidepressants on appetite and body weight. When the factors such as premobid body weight, tendency to metabolic diseases, nutritional and physical activity habits, and coping levels with modification in appetite and sedation caused by psychotropic drugs are considered together, it may be possible to explain the development of weight gain and its relation with risk factors (26). Therefore, our suggestion is that patient should be evaluated in terms of other hormonal metabolic disorders that may develop during treatment, in addition to psychiatric disorders, and should be followed during the course of treatment.

Chronic lithium treatment has been shown in several studies to cause increased body weight (29-30). The extent of this increment varies among reports. It has been reported that weight gain occurs within the first 2 years, and body weight does
not increase significantly despite continuation of lithium intake (31, 32). Not all of the patients underwent lithium treatment in our study; however, thyroid stimulating hormone (TSH) levels were significantly higher in the study group than the controls. Because slowing down the functions of thyroid gland would contribute to obesity and other related risk factors by decreasing the basal metabolic rate, patients should be followed up regarding this issue.

Recent studies have proposed that clozapine, an atypical antipsychotic, is associated with insulin resistance (22, 26). It has been suggested that hyperleptinemia may form an important link between the development of obesity and insulin resistance syndrome, particularly in patients using atypical antipsychotics such as clozapine (22-24, 33). The majority of patients examined in our study used polypharmacy, which makes it difficult to ascribe insulin resistance established in the study group to solely antipsychotic use. In one study, a positive correlation was found between body fat and fibrinogen, while plasma leptin concentrations were shown to be correlated with fibrinogen and CRP (33). In our study, the mean fibrinogen level in the group receiving drugs was significantly higher from those of the controls (Table 2). While CRP was high in both groups (normal values; 0 to 5 mg/L), cortisol levels were higher in the study group. It is thought that higher cortisol levels in psychiatric patients are associated with their endogenous stress, and increased preference of sweet foods may be a mechanism developed for coping with this stress (8).

In this study, we have found that while the body weight, waist circumference and body fat ratio increase in patients undergoing pharmacotherapy for psychiatric disorders, increased circulating glucose, insulin, triglyceride and homocysteine levels accompanied by increased proinflammatory cytokines render these patients more susceptible to various metabolic and cardiovascular problems. Therefore, we conclude that it would be useful if candidates for psychiatric pharmacotherapy treated with multidiscipliner team approach consisting of an endocrinologist, psychiatrist and a dietitian to prevent or delay the metabolic disorders developing along with the psychiatric disorders and treatments.

Although the importance of team approach in the management of complex diseases has been stressed adequately in the literature, in clinical practice, while the dominant problem of the patient is given priority, other problems that may develop in time may be neglected. If a dietitian experienced in and informed on particularly disorders associated with endocrine metabolism and psychiatry fields and who is skilled in communicating with patients is included in the team, he/she may serve as a bridge in cooperating with other units and in maintaining this cooperation. In the present study, it was established that a dietitian experienced in and informed on this field may assume an important role in the treatment of nutritional, metabolic and cardiovascular diseases, which may develop in addition to psychiatric disorders in patients receiving psychiatric treatment. However, it will not always be possible to consult endocrinologists and dietitians for each patient receiving psychiatric treatment in the clinic. Therefore, family physicians and young psychiatrists should also be aware of the impact of various diseases and drug treatments on appetite and body weight and cardiometabolic diseases that may develop during treatment.

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Competing interests: none declared.

REFERENCES


