EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Contribution of Leptin to the Formation of Neuroleptic Obesity in Patients with Schizophrenia during Antipsychotic Therapy

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We studied the dynamics of serum leptin level and some anthropometric values in patients with schizophrenia treated with risperidone, olanzapine, and clozapine showed gender-dependent specific correlations between the studied parameters.

Key Words: *neuroleptic obesity; leptin; antipsychotic therapy; gender factor*

According to published data, 40-80% patients with schizophrenia treated with oral atypical antipsychotic drugs develop more than 20% body weight gain [2,4]. Some authors hypothesize a relationship between side effect of this drug and neurohumoral and neuropeptide disorders [1,5]. Leptin is assumed to play an important role in these processes. It is produced by adipose cells. Leptin is assumed to be involved in the regulation of appetite and lipid catabolism [2,6,8,10]. Elevated serum levels of leptin in schizophrenics treated with oral atypical antipsychotic drugs (for example, clozapine and olanzapine) were detected not once [7,9]. On the other hand, analysis of published data allows no unambiguous evaluation of the significance of leptin level in the development of neuroleptic obesity [2,11].

We studied the dynamics of leptin level during antipsychotic therapy and analyzed its values in comparison with anthropometric data with consideration for the gender factor.

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MATERIALS AND METHODS

The data used in this study were obtained in examinations of 69 patients (32 men and 37 women) aged 18-48 years (mean age 31.2±1.3 years) with the diagnosis of paranoid schizophrenia according to IDC-10 (F-20.0). The mean duration of the disease was 9.7±3.2 years. Risperidone was used in the treatment of 23 patients (10 men and 13 women), olanzapine in 23 (11 men and 12 women), and clozapine in 23 (11 men and 12 women) patients. Analysis of leptin levels and the main anthropometric values characterizing body weight changes in patients (body weight index (BWI), body weight gain, body weight, and waist/hip ratio, WHR), was carried out in the groups formed by the gender factor (group 1: men; group 2: women). The groups were comparable by the main clinical demographic characteristics. Previous therapy was discontinued for a period of 7-10 days before the treatment. Serum leptin level and anthropometric values were studied at the following stages of therapy: before drug therapy (basic level; stage 1), after 3-4 weeks (stage 2) and after 6-8 weeks of therapy (stage 3).

Serum leptin level was measured by enzyme immunoassay using commercial kits for leptin mea-

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TABLE 1. Dynamics of Leptin Level and Anthropometric Values

Parameter	Group 1 (men), *n*=32			Group 2 (women), *n*=37		
	stage 1	stage 2	stage 3	stage 1	stage 2	stage 3
Leptin, ng/ml	8.56±1.10^{+}	10.32±1.36*$^{+}$	11.63±1.22*$^{+}$	6.89±1.24	6.66±0.98	6.55±1.16
Body weight increment, kg	—	4.00±0.21	2.14±0.15	—	1.04±0.12	-0.34±0.03
BWI, kg/m^2	23.95±2.21	25.25±3.10	27.09±3.85*	23.94±0.98	24.35±1.19	24.94±2.05
WHR	0.85±0.89	0.85±0.11	0.83±0.13	0.87±0.03	0.88±0.04	0.87±0.07
Body weight, kg	68.56±6.59	72.56±9.05	74.70±10.94	70.19±3.29	71.23±3.84	70.89±6.03

Note. *p<0.01 differences between the groups (Wilcoxon test); ^{+}p<0.01 compared to group 2 (Mann—Whitney test).

surements. The results were processed using standard methods of statistical analysis.

RESULTS

Leptin level in the group of men significantly surpassed the normal value and significantly (p<0.01) increased from stage to stage (Table 1). The BWI corresponded to normal only at stage 1, while at stages 2 and 3 first-degree body weight excess was noted. These processes were associated with body weight gain by weeks 3-4 and 6-8 of therapy, but WHR corresponded to normal (<1.0), which can indicate the absence of android obesity.

In women, leptin level slightly decreased during 6-8-week therapy but remained within the normal range throughout the study. The mean BWI values were also normal and corresponded to normal body weight. By weeks 3-4, body weight increased by 1.04±0.01 kg, while by weeks 6-8 the BWI means were negative (-0.30±0.03 kg). The mean WHR was above 0.81 at all stages of the study, indicating abdominal form of fat deposition.

Coefficients of correlation between leptin level and anthropometric value (BWI, body weight increment, WHR) were calculated after Spearman. The correlations are presented in Table 2.

Positive correlations between leptin level and BWI and body weight increment were detected in male patients. These data suggest that leptin resistance contributes to the pharmacogenic increment of body weight in men, as normally body weight increment is associated with a decrease in leptin level. The detected positive correlations between leptin level and WHR in females corresponding to abdominal obesity (>0.81) in the presence of normal BWI indicate (in our case) predominant deposition lipids in the subcutaneous fat and the absence of abdominal obesity, which is in line with published data [2,3].

Measurements of leptin levels in all patients with BWI>25.0 carried out without consideration for the gender factor indicated a linear correlation between leptin level and BWI (r=0.684; p=0.0001). Reduced leptin level in patients with high BWI values can indicate reduction of adipose tissue volume at the moment of measurements, while high leptin concentration can indicate resistance of leptin receptors.

Hence, our findings confirm the modern hypothesis suggesting that body weight changes in schizophrenics, specifically, neuroleptic obesity, are caused by changes in leptin level and the gender factor.

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TABLE 2. Coefficients of Correlation between Leptin Level and Anthropometric Values (Weeks 6-8 of Therapy) According to Spearman

Parameter	Group 1 (men)		Group 2 (women)	
	r	*p*	*r*	*p*
BWI, kg/m^2	0.551	<0.0001	0.109	0.42
Body weight increment, kg	0.436	0.0017	0.31	0.182
WHR	-0.241	0.41	+0.341	0.0022

Note. *r*: coefficients of correlation; *p*: significant correlation.

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