Effect of Therapy with Atypical Antipsychotic Drugs on Prolactin Concentration in Patients with Schizophrenia and Schizoaffective Disorders

L. N. Gorobets

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Plasma prolactin concentration was measured in patients with schizophrenia and schizoaffective disorders receiving therapy with risperidone, olanzapine, and quetiapine and compared with the corresponding parameter in patient receiving typical neuroleptic drug haloperidol. We evaluated the specific effects of the test drugs on prolactin concentration in men and women.

Key Words: *atypical antipsychotic drugs; prolactin; neuroleptic hyperprolactinemia; gender factor*

An increasing interest in the effect of neuroleptic drugs on function of the anterior hypophysis (*e.g.*, prolactin secretion) is due to the development of new-generation medications [1,5,8]. A relationship was found between blood prolactin concentration and neuroleptic treatment [6]. The mechanism of neuroleptic-induced hyperprolactinemia includes blockade of D_2 receptors in the tuberoinfundibular region resulting in a decrease in hypothalamic dopamine concentration. It should be emphasized that dopamine produces an inhibitory effect on prolactin secretion by pituitary lactotropic cell. These changes are followed by hyperprolactinemia with typical clinical manifestations (galactorrhea, amenorrhea, and weak libido). Published data show that new-generation antipsychotic drugs have various effects on prolactin secretion [3,4,7,9].

Here we compared the effects of atypical antipsychotic medications risperidone, olanzapine, and quetiapine and classic neuroleptic haloperidol on prolactin concentration in men and women.

Department of Psychiatric Endocrinology, Moscow Institute of Psychiatry, Federal Agency of Public Health and Social Development. ***Address for correspondence:*** lav@nm.ru. L. N. Gorobets

MATERIALS AND METHODS

The samples were obtained from 231 patients (82 men and 149 women, 18-48 years, average age 31.1±1.3 years). According to international classification of diseases (ICD-10) there were 170 patients with paranoid schizophrenia (F-20.0), 25 patients with schizotypical disorder (F-21.0), and 36 patients with schizoaffective disorder (F-25.0). The mean duration of the disease was 9.1±3.7 years.

The patients were divided into groups depending on neuroleptic therapy: group 1, risperidone (83 patients), group 2, olanzapine (56 patients); group 3, quetiapine (37 patients); and group 4, haloperidol (55 patients). The groups were matched by clinical and demographic parameters. The patients received monotherapy with risperidone, olanzapine, quetiapine, and haloperidol in the average daily doses of 3.83±0.11, 13.58±0.62, 358.11±29.05, and 17.27±0.41 mg, respectively. Treatment with other drugs was discontinued for 7-10 days before the start of therapy. Prolactin concentration was measured in 3 stages: stage I, before treatment (basal level); stage II, 3-4 weeks after the start of treatment; and stage III, 6-8 weeks after the start of treatment.

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TABLE 1. Prolactin Concentration in Male Patients (mU/liter, *M*±*m*)

Stage	Risperidone (*n*=45)	Olanzapine (*n*=10)	Quetiapine (*n*=5)	Haloperidol (*n*=22)
I	883±62	560.0±174.3	658.0±87.5	731.6±110.0
II	1149.0±64.2*	399.0±114.8	381.0±56.3	1203.7±97.3*
III	1090.0±57.7	350.0±99.2+	301.0±47.8*	1032.0±86.5+

Note. Here and in Table 2: $p<0.05$: *compared to stage I; +compared to stage II.

TABLE 2. Prolactin Concentration in Female Patients (mU/liter, *M*±*m*)

Stage	Risperidone (*n*=38)	Olanzapine (*n*=46)	Quetiapine (*n*=31)	Haloperidol (*n*=33)
I	1998.0±209.5	1132.0±162.2	1676.81±237.50	1564.6±139.0
II	2543.0±174.6*	799.0±79.8*	648.87±188.10*	1892±141*
III	2490.0±163.6	696.0±76.2+	525.29±137.40	1843±126

Plasma prolactin concentration was measured by enzyme immunoassay with commercial kits for prolactin. The results were analyzed by standard statistical methods.

RESULTS

The effects of the test drugs on prolactin concentration were studied separately in men and women.

Basal prolactin level in men of various groups exceeded the normal (50-500 mU/liter), which was probably related to previous psychotherapeutic treatment (Table 1).

Prolactin concentration significantly increased in stage II of therapy with risperidone and haloperidol, but decreased after treatment with olanzapine and quetiapine. However, the differences in prolactin concentration in stages I and II were insignificant. In stage III prolactin concentration remained practically unchanged in group 1 patients, but significantly decreased in patients of groups 2, 3, and 4 (Table 1). In stages II and III prolactin concentration in patients of groups 2 and 3 did not differ from normal.

Basal prolactin level in women exceeded the normal (similarly to men, 70-700 mU/liter, Table 2). Prolactin concentration in female patients was much higher than in male patients. However, prolactin concentration underwent similar changes in women and men. In stage II prolactin concentration significantly increased in patients of groups 1 and 4, but decreased in patients of groups 2 and 3. In stage III prolactin concentration slightly decreased in patients of groups 1, 3, and 4. It should be emphasized that prolactin concentration progressively decreased in female patients of the olanzapine group (Table 2).

Our results indicate that atypical antipsychotic drugs produce different effects on prolactin secretion, which is associated with the specific neuroleptic profile of their activity [1-3,5]. Treatment with risperidone (antagonist of D_2 and 5HT-2a receptors) and classic neuroleptic haloperidol (selective antagonist of D_2 and D_3 receptors) stimulated prolactin secretion. Olanzapine and quetiapine have little effect on prolactin secretion in the pituitary, which is related to low affinity of these drugs for D_2 and D_3 receptors. These data illustrate the similarity of variations in prolactin concentration in male and female patients. Differences in prolactin concentration in men and women at various stages of antipsychotic therapy suggest that the factor of sexual dimorphism play a role in the gender-specific interaction between the hypothalamus and hypophysis.

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