



ISSN: 2277- 7695

TPI 2016; 5(4): 43-45

© 2016 TPI

www.thepharmajournal.com

Received: 07-02-2016

Accepted: 10-03-2016

**I.R. Romash**Department of Psychiatry,  
Narcology and Medical  
Psychology.Ivano-Frankivsk National  
Medical University, Ivano-  
Frankivsk, Ukraine.

## Endogenous insulin and glucose concentration in patients with paranoid schizophrenia treated with atypical antipsychotics

**I.R. Romash****Abstract**

The article presents the results of the investigation of changes in endogenous insulin indices and glucose level in blood serum during prolonged treatment (3 months) with atypical antipsychotics. Increase in both indices was observed in the studied groups. The index of endogenous insulin concentration significantly increased by 10.9% and constituted  $17.56 \pm 0.70$  uIU/mL ( $p < 0.05$ ) and glucose level in blood serum increased by 36.6 % and amounted  $7.01 \pm 0.29$  mmol/L ( $p < 0.05$ ). Long-term risperidone use caused significant increase in insulin concentration by 19.3% up to the level of  $19.85 \pm 1.50$  uIU/mL ( $p < 0.05$ ) and increase in fasting glycemia by 34.5% reaching  $8.44 \pm 0.23$  mmol/L ( $p < 0.05$ ). Treatment with quetiapine during 3 months caused a significant increase in insulin concentration in blood serum by 2.96% from  $15.05 \pm 1.73$  uIU/mL to  $15.49 \pm 0.69$  uIU/mL ( $p < 0.05$ ) as well as a significant increase in glycemia level by 20.3 % from  $5.39 \pm 0.78$  to  $6.76 \pm 0.27$  mmol/L ( $p < 0.05$ ).

**Keywords:** Insulin concentration; paranoid schizophrenia; atypical antipsychotics.

**Introduction**

The use of neuroleptic therapy in patients with paranoid schizophrenia causes metabolic syndrome. Its main symptoms are weight gain, lipid and carbohydrate metabolism disturbance. The development of comorbidities such as obesity, arterial hypertension and diabetes mellitus (DM) is a dynamic sequential process when steady deterioration in the patient's condition occurs. Such sequence is associated with a progressive decrease in hormones secretion by  $\beta$ -cells of pancreas and development of secondary metabolic insulin resistance [2, 3, 5].

Scientific publications by M.S. Popov provide the evidence that changes in insulin concentration cause brain neurons disorders. In case of hyperinsulinemia hyperglycemia occurs causing the development of oxidative stress with glycolysis of basal membrane proteins and neuronal overload with glucose and inability of its disposal [3]. Insulin has a widespread effect on brain tissue, particularly in the temporal lobes where insulin sensitive receptors are located [2, 4]. These parts of the brain are largely related to the memory consolidation processes. There is some evidence that insulin is directly involved in a number of cognitive functions and its metabolism disturbances may be accompanied by many neurological syndromes and cognitive disorders.

In addition to neurotransmitter functions in the brain insulin is involved in the regulation of amyloid precursor protein synthesis and its metabolism product A $\beta$  as the main component of amyloid complications and regulates tau protein phosphorylation as the basis of neurofibrillary formation [1, 6].

According to the literature data adipose tissue is the most sensitive to insulin. Dynamics of its content growth in the body indicates the degree of the body's sensitivity to the hormone [1, 6]. Increased incidence of patients with DM in direct ratio corresponds to the number of individuals with obesity [2, 9]. The risk for pre-diabetes and diabetes development includes not only the excess of adipose tissue, but also side effects of medication. The issue of diabetes developments as a part of the metabolic syndrome, insulin resistance and hyperinsulinemia causes a number of questions that require a detailed study of these changes.

The issue of hyperinsulinemia correlation as a biological factor that occurs in schizophrenia treatment with atypical neuroleptics becomes of particular relevance.

**The objective of the research** was to study changes in carbohydrate metabolism in patients with paranoid schizophrenia treated with atypical neuroleptics.

**Correspondence****I.R. Romash**Department of Psychiatry,  
Narcology and Medical  
Psychology.Ivano-Frankivsk National  
Medical University,  
Ivano-Frankivsk, Ukraine.

**Materials and methods**

The research was conducted at Ivano-Frankivsk Psychiatric Hospital №3. 120 patients with paranoid schizophrenia were examined. An average age was  $38.7 \pm 2.3$  years. The patients were divided into three groups:

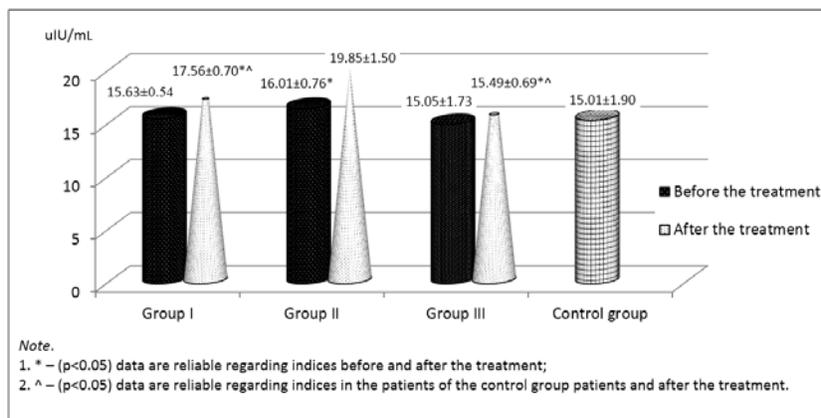
- Group I included 40 patients taking typical antipsychotic haloperidol in an average dose of  $4.6 \pm 1.3$  mg/day;
- Group II consisted of 40 patients taking atypical antipsychotic drug risperidone in an average dose of  $4.6 \pm 1.3$  mg/day;
- Group III amounted 30 patients taking atypical antipsychotic drug quetiapine in an average dose of  $413 \pm 116$  mg/day;

- Control group included 30 patients who did not undergo neuroleptic treatment during 6 months.

Basal insulin level was determined by immunoenzyme method in the fasted state from patients' venous blood using reagents kit "Accu-Bind ELISA Microwells INSULIN" manufactured by Monobind Inc, USA. Glucose level was determined by EasyGluco manufactured by US Diagnostics Inc, USA.

**Results of the research and their discussion**

The study of basal insulin level indicated that a significant increase in basal insulin level by 10.9% from  $15.63 \pm 0.54$  uIU/mL to  $17.56 \pm 0.70$  uIU/mL ( $p < 0.05$ ) was observed in Group I patients taking haloperidol (Fig. 1).



**Fig 1:** Dynamics of basal insulin level indices in patients with paranoid schizophrenia treated with atypical antipsychotics.

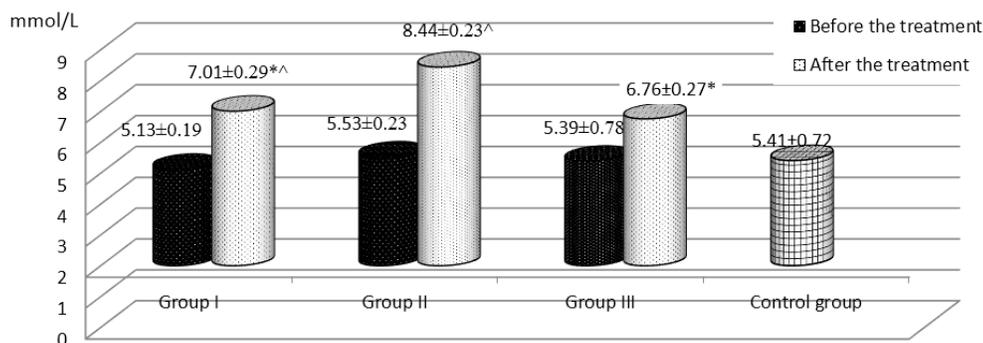
Prolonged use of the atypical antipsychotic risperidone caused significant increase in basal insulin level by 19.3% from  $16.01 \pm 0.76$  uIU/mL to  $19.85 \pm 1.50$  uIU/mL ( $p < 0.05$ ). According to recent scientific publications it was caused by the fact that this antipsychotic drug shows high affinity to serotonergic receptors type 2 (5-HT<sub>2</sub>), dopaminergic receptors type 2 (D<sub>2</sub>) and alpha-1 adrenergic receptors.

Patients' taking the atypical antipsychotic quetiapine during 3 months significantly increased basal insulin level by 2.96% from  $15.05 \pm 1.73$  uIU/mL to  $15.49 \pm 0.69$  uIU/mL ( $p < 0.05$ ). According to scientific sources this is associated with the fact that this antipsychotic drug shows a higher affinity to brain serotonin receptors (5-HT<sub>2</sub>) than to dopamine receptors D<sub>1</sub> and D<sub>2</sub>. It has a high affinity with histaminergic and adrenergic alpha-1-receptors and less affinity with alpha-2 adrenergic receptors. It is not related to benzodiazepine receptor and

muscarinic receptors.

According to obtained data, prolonged three months use of drugs from the atypical antipsychotics group leads to disruption of secretion and insulin metabolism at the hormonal levels.

Analysis of the data depicted in Figure 2 established that the level of glucose in blood serum in the fasted state significantly increased by 34.5 % from  $5.53 \pm 0.23$  mmol/L to  $8.44 \pm 0.23$  mmol/L in group II patients after long-term treatment with risperidone. The increase in fasting glycemia level was significantly higher than in patients of the control group ( $p < 0.05$ ). This is clinically significant. This hyperglycemia leads to weight gain and is a common cause of patients' refusal of taking this medicine and this in turn promotes disease relapse.



Note:  
 1. \* - ( $p < 0.05$ ) difference is reliable regarding indices before and after the treatment;  
 2. ^ - ( $p < 0.05$ ) difference is reliable regarding indices in the patients of the control group patients and after the treatment

**Fig 2:** Dynamics of indices of glucose concentration in blood serum of patients with paranoid schizophrenia treated with atypical antipsychotics.

Three months use of quetiapine in patients of group III resulted in significant increase in fasting glycemia by 20.3% from  $5.39 \pm 0.78$  mmol/L to  $6.76 \pm 0.27$  mmol/L ( $p < 0.05$ ). Increase in glycemia by 36.6% from  $5.13 \pm 0.19$  mmol/L to  $7.01 \pm 0.29$  mmol/L ( $p < 0.05$ ) was observed in patients of group I during three months use intake of haloperidol. This index in group I patients was significantly higher than glycemia index in the patients of the control group ( $p < 0.05$ ).

### Conclusions

1. Changes in carbohydrate metabolism in patients with paranoid schizophrenia during three months treatment with atypical antipsychotics were caused by an imbalance of endogenous insulin accompanied by increase in insulin concentration in the blood serum by 19.3%, 10.9% and 2.96%.
2. Atypical antipsychotics intake during three months promotes carbohydrate metabolism disturbance leading to increase in glucose level by 36.6%, 34.5% and 20.3%.

**Prospects for further research** involve the study of the dynamics of insulin in the blood serum, glycemia indices and insulin resistance in patients with paranoid schizophrenia when treated with antihyperglycemic drugs.

### References

1. Mukhamediarov MA, Zefirov AL. Effect of beta-amyloid peptide on the function of excitable tissues: physiological and pathological aspects. *Uspekhi fiziologicheskikh nauk*. 2013; 44(1):55-71.
2. Orlovskiy MA. Activation of the expression of inducible nitric oxide synthase in the hippocampus during the development of experimental diabetes mellitus. *Ukrainian neurological journal*. 2007; 4:88-92.
3. Popova MS, Stepanichev MYu. Induction of cell cycle, amyloid beta and free radicals in the mechanism of free radical processes in the brain. *Neurochemical Journal*. 2008; 25(3):1-9.
4. Chubb SA, Hyde Z, Almeida OP. Lower sex hormone-binding globulin is more strongly associated with metabolic syndrome than lower total testosterone in older men: the Health in Men Study. *Eur. J. Endocrinol*. 2008; 158(6):785-792.
5. Lewis JG, Shand BI, Frampton CM. Plasma levels of sex hormone-binding globulin, corticosteroid-binding globulin and cortisol in overweight subjects who develop impaired fasting glucose: a 3-year prospective study. *Horm. Metab. Res*. 2009; 41(3):255-259.
6. Mohr BA, Bhasin S, Kupelian V. Testosterone, sex hormone-binding globulin, and frailty in older men. *J. Am. Geriatr. Soc*. 2007; 55(4):548-555.
7. Nestler JE. Sex hormone-binding globulin and risk of type 2 diabetes. *N. Engl. J. Med*. 2009; 361(27):2676-2677.