Letter to the editors

Metabolic alterations due to the use of antipsychotics in schizophrenic patients: molecular and neuroendocrinological considerations

Dear Editors,

It was with great interest that we read the article "Metabolic side effects of antipsychotics and mood stabilizers,"[1] in which extremely important aspects for clinical practice were discussed. We would like to contribute by citing points we consider relevant and that could not be analyzed in detail in the article.

Firstly, many works have demonstrated that the chronic use of antipsychotics directly interferes with the gene expression and with mechanisms of cell signaling. Recently, those changes have been confirmed in pathways directly or indirectly related to certain components of the metabolic syndrome, especially in those regarding changes in glucose homeostasis.

Zhao et al. observed changes in cell signaling secondary to the stimulation of the insulin receptor in the prefrontal cortex of schizophrenic patients receiving clozapine, compared with material taken from untreated patients.[2] Mice submitted to treatment using the same drug presented, in the striatum, an increase of up to 200% in the glucose-dependent insulinotropic polypeptide (GIP) gene expression, besides higher levels of that insulinotropic factor in the serum and small intestine.[3] In addition, another study, using olanzapine in the cerebral cortex of animals, showed downregulation of 31 genes and upregulation of 38 genes involved with cell signaling transduction, metabolism of nucleic acids, immune system, neurotrophic factors and metabolic and energetic pathways.[4] Similar changes were also demonstrated using risperidone.[5]

Furthermore, we would like to stress that there is also significant evidence of those patients being predisposed to develop the metabolic changes discussed in the article, independent of the use of drugs.[6]

Schizophrenic patients have higher prevalence of overweight and obesity, with distribution of visceral fat up to 3.4 times higher, independent of any drug effect. It is clear that care should be taken when interpreting this information, since these patients present inadequate eating habits, higher rates of sedentary lifestyle and precarious primary clinical care.[6,7]

Another issue to be considered is the already known activation of the hypothalamus-pituitary-adrenal axis in schizophrenic patients. Chronic increase in cortisol may lead to a pseudo-Cushing's syndrome, characterized by increased visceral fat, hyperinsulinemia, insulin resistance, dislipidemias and hypertension, all of them markers of the metabolic syndrome.[6,7]

In a recent Canadian study, schizophrenic patients without pharmacological treatment, through examinations of glucose tolerance and dosage of adiponectin, presented higher rates of insulin resistance and tendency to type II diabetes.[8]

Those data are extremely important, since, besides clarifying the possible causes of metabolic changes resulting from the use of those drugs, they show probable ways for a better understanding of schizophrenia pathophysiology, considering that many of these changes seem to be directly or at least indirectly connected to the disorder origin.

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