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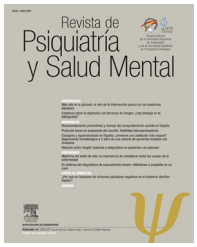

ORIGINAL ARTICLE

Oxidative stress biomarkers and clinical dimensions in first 10 years of schizophrenia☆

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KEYWORDS
Oxidative stress;
Lipid peroxidation;
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Negative symptoms

Abstract
Introduction: Several studies have described increased oxidative stress parameters in patients with schizophrenia. The objectives of the current study were to identify potential oxidative stress biomarkers in stable patients during first 10 years of schizophrenia and determine if they are associated with specific clinical dimensions.
Material and methods: Seventy-three clinically stable outpatients with schizophrenia and 73 sex and age-matched healthy controls were recruited. Sociodemographic, clinical and biological data were collected at enrollment. Blood biomarkers included homocysteine, the percentage of hemolysis, lipid peroxidation subproducts, and as an antioxidant biomarker, catalase activity in erythrocytes.
Results: Comparative analyses after controlling for smoking and metabolic syndrome evidenced a significant increase in catalase activity in patients. Also, lower lipid peroxidation levels showed an association with negative symptoms.
Conclusions: In conclusion, compensatory antioxidant mechanisms might be increased in stable patients with schizophrenia at early stages. Furthermore, there may be an inverse relationship between oxidative stress and negative dimension.

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PALABRAS CLAVE
Estrés oxidativo;
Peroxidación lipídica;
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Síntomas negativos

Biomarcadores de estrés oxidativo y dimensiones clínicas en los 10 primeros años de esquizofrenia

Resumen
Introducción: Diversos estudios han encontrado un aumento de los parámetros de estrés oxidativo en pacientes con esquizofrenia. Los objetivos de este estudio han sido identificar potenciales biomarcadores de estrés oxidativo en pacientes con esquizofrenia estables, durante los primeros 10 años de enfermedad, y determinar si se asocian con dimensiones clínicas específicas.
Material y métodos: Se evaluaron 73 pacientes clínicamente estables y 73 controles sanos pareados por edad y sexo. Se recogieron datos sociodemográficos, clínicos y parámetros biológicos. Los biomarcadores sanguíneos incluyeron homocisteína, porcentaje de hemólisis, subproductos de peroxidación lipídica y, como biomarcador antioxidante, actividad de la catalasa en eritrocitos.
Resultados: Los análisis comparativos tras controlar por tabaquismo y síndrome metabólico evidenciaron un aumento significativo en la actividad de la catalasa en pacientes. Asimismo, niveles inferiores de peroxidación lipídica se asociaron de manera significativa con la sintomatología negativa.
Conclusiones: Como conclusión, los mecanismos compensatorios antioxidantes podrían estar aumentados en pacientes con esquizofrenia estables durante las fases iniciales. Además, podría existir una relación inversa entre el estrés oxidativo y la dimensión negativa.

Introduction

Schizophrenia is a chronic and severe mental disorder characterized by heterogeneous symptoms and a long-term debilitating course. The diagnostic criteria are based on descriptive phenomenology of clinical symptoms and clinical course due to the lack of reliable and specific biomarkers.[1] However, in recent decades, several biological parameters such as inflammatory, metabolic, and neuroimaging biomarkers have been described in this population toward the goal of personalized, precision psychiatry.[2–6]

At present, the classical concept of schizophrenia has been reformulated,[7] and some authors suggest this disease has a multisystem impact from the early stages.[8] Indeed, blood biomarker studies have shown evidence of abnormalities in metabolic and immune response functions in subjects with schizophrenia.[9–11] Furthermore, oxidative imbalance has been involved in the pathophysiology of this disorder and some authors suggest a potential link between the oxidative stress and the increased risk of metabolic abnormalities in these patients.[12]

Several studies have documented changes in oxidative parameters (lipid peroxidation products, nitric oxide) and antioxidant enzymes (catalase, superoxide dismutase, glutathione peroxidase), although these results are not consistent, as increases or decreases in these parameters have been reported in patients.[13–16] More ambitious studies have attempted to determine a relationship between peripheral biomarkers and the severity of different clinical dimensions. Garcia-Alvarez et al. (2016) recently published a review of this issue.[17] Regarding inflammation, several cytokines and CRP, have been associated with positive, negative, and cognitive symptoms in several studies.[18–21] However, most studies have not identified a significant association between oxidative stress biomarkers and clinical severity in chronic schizophrenia patients or patients with first-episode psychosis.[22–25]

One of the probable reasons for these inconsistent results is the heterogeneity of schizophrenia and the difficulty of accurate categorization. Another underlying obstacle to studying peripheral markers is that different clinical disease stages may be associated with distinctive biomarkers, and they could fluctuate depending on whether patients are in their first-episode, an acute relapse, or a stable phase. Also, potential confounders as smoking, obesity or other metabolic disturbances were not considered in all the studies.[26]

Therefore, the main objective of the present study was to identify if peripheral levels of oxidative stress parameters are different in stable outpatients in the first 10 years of schizophrenia from those in matched healthy controls (HC). Secondly, the ultimate objective was to explore whether oxidative stress biomarkers are associated with different clinical dimensions in schizophrenia.

Material and methods

This was a multicenter, longitudinal, one-year follow-up study of patients with schizophrenia and HC, whose