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BRIEF COMMUNICATION

Peripheral chemokine levels in women with recurrent major depression with suicidal ideation

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DESCRIPTORS
Suicide;
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Mood Disorders;
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Immunity.

Abstract
Objective: To compare serum levels of MCP-1/CCL2, RANTES/CCL5, and Eotaxin/CCL11 between female patients with recurrent major depressive disorder (MDD) and healthy controls, verifying if there is a difference in the levels of these mediators between those with or without current suicidal ideation. *Methods*: Thirty female outpatients with recurrent MDD were divided in two groups accordingly the presence or absence of suicidal ideation. These groups were compared with 16 healthy controls. Serum levels of MCP-1/CCL2, RANTES/CCL5, and Eotaxin/CCL11 were determined. Depression severity was evaluated by Beck Depression Inventory (BDI). Suicidal ideation was assessed by SCID-I and BDI. *Results*: Patients with recurrent MDD and healthy controls did not differ in age, socioeconomic status, and education. All patients reported high scores of BDI (mean, SD, n; 29.75, 10.55, 28). Multivariable analysis of covariance adjusted for age and BMI showed that MDD patients with suicidal ideation presented lower levels of MCP-1/CCL2 and RANTES/CCL5 ($p < 0.001$) and higher levels of Eotaxin/CCL11 ($p = 0.04$) compared to healthy controls. These differences remained significant after adjusting for depression severity. *Conclusion*: The findings of this study indicated that the presence of recurrent MDD with suicidal ideation is associated with differences in inflammatory chemokines when compared to those without suicidal ideation.
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DESCRITORES:
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Transtorno Depressivo Maior;
Transtornos do Humor;
Inflamação;
Imunidade.

Níveis periféricos de quimiocina em mulheres com depressão maior com ideação suicida

RESUMO
Objetivo: Comparar os níveis séricos de MCP-1/CCL2, RANTES/CCL5 e Eotaxin/CCL11 entre pacientes do sexo feminino com transtorno depressivo maior (TDM) recorrente e controles saudáveis, verificando se há diferença nos níveis desses mediadores entre os indivíduos com ou sem ideação suicida. *Métodos*: Trinta pacientes do sexo feminino com TDM recorrente foram divididas em dois grupos de acordo com a presença ou ausência de ideação suicida. Esses grupos foram comparados com 16 controles saudáveis. Os níveis séricos de MCP-1/CCL2, RANTES/CCL5 e Eotaxin/CCL11 foram determinados. A gravidade da depressão foi avaliada usando o *Beck Depression Inventory* (BDI) e a ideação suicida foi avaliada usando o SCID-I e o BDI. *Resultados*: As pacientes com TDM recorrente e os controles saudáveis não diferiram em idade, *status* socioeconômico e educação. Todas as pacientes relataram altas pontuações no BDI (média, SD, n; 29,75, 10,55, 28). A análise de covariância multivariada ajustada para idade e de IMC mostrou que as pacientes com TDM e ideação suicida apresentaram níveis mais baixos de MCP-1/CCL2 e RANTES/CCL5 ($p < 0,001$) e níveis mais elevados de Eotaxin/CCL11 ($p = 0,04$) em comparação com os controles saudáveis. Essas diferenças permaneceram significantes após o ajuste para gravidade da depressão. *Conclusão*: Os resultados deste estudo indicaram que a presença de TDM recorrente com ideação suicida está associada a diferenças nas quimiocinas inflamatórias na comparação com os indivíduos sem ideação suicida.
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Introduction

Suicide is a major problem in public health, with approximately 1 million people dying from suicide per year.[1] Mental illnesses, particularly major depressive disorder, (MDD) are the main risk factor for suicide. Although several factors including personality and cultural and ethnic background may exert influence on suicidality of depressed patients, neurobiological factors involved in suicidal ideation and behavior has received considerable attention. Several studies have documented different biological changes in subgroups of individuals with MDD and suicidal behavior,[2] including serotonergic and noradrenergic system abnormalities. Hypothalamus-pituitary-adrenal (HPA) axis dysfunction has also been reported.

A growing body of evidence has indicated the presence of a longstanding pro-inflammatory state in MDD. Increases in inflammatory mediators such as cytokines were extensively shown in MDD, with interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1) being the most commonly associated with MDD.[3-5] The causes for this pro-inflammatory state are largely unknown, although both genetic and environmental factors have been proposed as relevant.[6] Chemokines, cytokines with chemoattractive properties, have received less attention regarding their role in MDD. Nevertheless, these inflammatory mediators may be of particular interest in these patients, given their effect on the amplification of inflammatory response, possibly resulting in increased neuronal and glial death.[3,7-9] For instance, peripheral chemokine levels seem to be altered in neurodegenerative disorders, such as multiple sclerosis[10] and Alzheimer's disease[11,12] and in neuropsychiatric disorders such as schizophrenia[13,14] and bipolar disorder.[15] To date, more than 50 chemokines and approximately 20 chemokine receptors, particularly G-protein-coupled receptors,[16] have been identified. The two largest families of chemokines, CCL and CXCL, attract mononuclear cells to sites of chronic inflammation. The binding of a chemokine to its receptor activates signaling cascades that lead to cell shape rearrangement and movement,[17] namely chemokine (C-C motif) ligand 11 (Eotaxin/CCL11).[18] Activation of these signaling pathways results in increased calcium concentrations and activation of mitogen-activated protein kinases, and also has a role in synaptic plasticity.[16] For instance, CCL and CXCL chemokines have been shown to help in the prevention of neuronal apoptosis.[19,20] Monocyte chemotactic protein-1 (MCP-1/CCL2) and regulated-on-activation normal T cell expressed and secreted (RANTES/CCL5) protein are important mediators of the immune and inflammatory responses.[21]

Studies exploring differences in inflammatory mediators across subgroups of depressive patients are scarce. A recent report indicated differences in cytokine concentrations among suicide attempters compared to non-suicidal depressed patients and healthy controls.[22] Suicide attempters have increased levels of IL-6 and TNF-α as well as decreased levels of IL-2 concentrations. Unfortunately there are very few studies investigating the role of chemokines in major depression and suicide.[23]

Because understanding the inflammatory mechanisms involved in MDD and suicide may potentially open new treatment possibilities, the aim of this study was to investigate chemokine differences between MDD individuals with and without suicidal ideation, in order to propose novel markers of suicidal ideation in MDD.

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