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Short communication

Inflammatory profile in depression and associated clinical and sociodemographic features in a Middle-Eastern North-African population

Lilia Bahrini, Sami Ouanes*, Rym Ghachem

Razi Hospital, Manouba, Tunisia

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ABSTRACT

Background: Evidence of the presence of an inflammatory syndrome in depressive disorders has aroused great interest among researchers but results were heterogeneous and almost all previous studies involved patients from Europe or North America. The objectives of the current study were to determine the prevalence of biological inflammatory syndrome among patients with depression in a Middle-Eastern/North-African population and to examine the associated sociodemographic and clinical factors.

Methods: We conducted a cross-sectional descriptive and comparative study including 65 patients and 30 healthy controls. The patients had an untreated major depressive episode and no inflammatory medical conditions; they were recruited in the psychiatry outpatient clinic in Razi hospital – Tunisia over an eight-month period ranging from May to December 2012.

We examined sociodemographic and clinical characteristics and both groups had an inflammatory balance including: high sensitive C-reactive protein, interleukin 6, serum protein electrophoresis, haptoglobin and orosomucoid. A standardized inflammatory protein profile for age and sex was performed.

Results: High sensitive C-reactive protein levels did not differ significantly between patients with depression and controls. The assay results of Interleukin 6 in our study showed higher values in patients with depression than in controls ($p=0.024$). Albumin was found to be increased in patients with depression ($p<0.001$).

The dosage of the alpha-1-globulin including the orosomucoid and of the alpha-2-globulin including haptoglobin, showed that patients with depression had higher values than controls ($p<0.001$).

The inflammatory protein profile (which consists of a synthesis of three inflammatory proteins: high sensitive C-reactive protein, haptoglobin and orosomucoïd) showed a trend towards higher levels of inflammation among patients with depression than among controls.

Limitations: The relatively small number of subjects decreased the statistical power and the cross-sectional setting does not allow us to draw any conclusions about cause-to-effect relationships. Although we tried to exclude people with current infections, a small percentage of subjects may have had subclinical infections. The Body Mass Index, a parameter that might affect the levels of the investigated inflammatory markers, was not measured.

Conclusion: The existence of inflammation in depression has been proven by the results of four meta-analyses and over a hundred studies. However, the generalization of this finding is yet to be confirmed. It seems more likely that inflammation concerns a subgroup of patients with depression. Studies targeting this particular subgroup could provide new therapeutic approaches.

1. Introduction

Alterations in the neuro-immuno-endocrine response were highlighted in subjects with depressive disorders, suggesting that depression might be associated with a dysregulated inflammatory response (Medzhitov, 2008). Three main findings bolster this hypothesis. Firstly, an increase in key proinflammatory cytokines, such as IL1, IL6 and TNFα, has been reported in patients with depression (Dean et al., 2010; Maes et al., 1991a). Secondly, depression has been associated with increased serum levels of positive proteins of the inflammatory reaction (PRI+) such as Haptoglobin (Hp), α1-antitrypsin, α1-acid-glycoprotein or orosomucoid (ORO), ceruloplasmin, and α1 and α2 globulins (Joyce et al., 1992; Maes, 1993; Sluzewska et al., 1997; Song et al., 1994), and decreased

* Correspondence to: Hôpital Razi, 1 Rue des orangers, Manouba 2010, Tunisia.
E-mail address: sami.ouanes@gmail.com (S. Ouanes).

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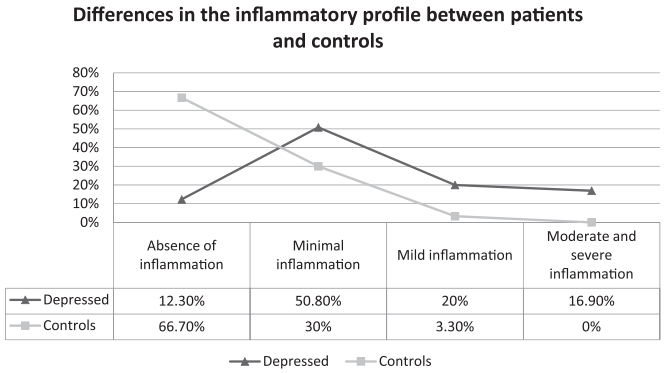

Fig. 1. Differences in the inflammatory profile between patients and controls. The Cochran–Armitage test showed a trend towards higher levels of inflammation among patients with depression than among controls.

serum levels of negative proteins of the inflammatory reaction (PRI−), such as albumin (Alb) and transferrin (Maes, 1993; Song et al., 1994). Thirdly, high plasma levels of C3 and C4 fractions of the complement system were observed in patients with depression (Berk et al., 1997; Maes et al., 1997; Song et al., 1994). (Fig. 1).

There is a growing body of published research about inflammation in depression. However, almost all studies were carried out in European or North American populations. Whether the finding of these studies apply to patients from other regions, namely from the Middle-East/North-Africa (MENA) has not been previously examined.

Furthermore, since the results regarding biological inflammatory markers varied widely in the literature, we chose to examine several markers of inflammation, both acute and chronic. We also chose to study the most widely available and least expensive markers rather than the most specific ones, so that the findings can be applied to regions and countries with low resources.

The objectives of the current study were to determine the prevalence of biological inflammatory syndrome among patients with depression in a MENA population and to determine the associated sociodemographic and clinical factors.

2. Methods

2.1. Participants and psychiatric measures

This cross-sectional study was conducted in the outpatient department of psychiatry in Razi University Hospital in Tunis over a period of eight months from May to December 2012.

All consenting first-visit patients who scored at least eight on the 17-item Hamilton Rating Scale for Depression (HRSD-17) (Hamilton, 1960) were interviewed by a trained psychiatrist using the Mini-International Neuropsychiatric Interview (MINI) 6.0 (Sheehan et al., 1998) to confirm the diagnosis of major depressive disorder. The suicidal risk was assessed using the SAD-PERSONS scale (Patterson et al., 1983).

Exclusion criteria consisted of the following: present medical illness, co-occurring psychiatric disorder diagnosed by the means of the MINI, antidepressant or anti-inflammatory medication during the last six months.

Thirty age and gender-matched controls were recruited among health professionals in Razi Hospital. Exclusion criteria consisted of the following: present medical illness, present psychiatric disorder diagnosed by the means of the MINI, antidepressant or anti-inflammatory medication during the last six months.

2.2. Blood measures

Blood was collected on tubes containing lithium-heparinate (BIOSPHERE BIOMEDICAL Technics). The sample was centrifuged immediately and plasma was divided into several aliquots.

Serum protein electrophoresis (SPEP) was carried out the same day. The aliquots to measure highly sensitive C-reactive protein (hs-CRP), Hp, ORO and Interleukin-6 (IL-6) were preserved at −80 °C.

hs-CRP was measured by immunonephelometry (Dade Behring Marburg GmbH). Normal values were <3 mg/L with intra/inter-assay Coefficients of Variation (CVs) of 3.5% and 3.4% respectively.

Hp was measured by immunonephelometry (Siemens). Normal values were 0.5–2.5 g/L with intra/inter-assay CVs of 3.1% and 2.2% respectively.

ORO was measured by immunonephelometry (Siemens). Normal values were 0.5–1.5 g/L with intra/inter-assay CVs of 3.8% and 3.8% respectively.

IL-6 was measured by the sandwich method (Roche Diagnostics GmbH). Normal values were <4 ng/mL with intra/inter-assay CVs of 1.7% and 1.9% respectively.

SPEP was performed on agarose gel in the HYDRAGEL PROTEIN (E) K20 kit. Normal values were 35–44 g/L for Alb, 1–3 g/L for α1-globulins, 5–8 g/L for α2-globulins, 4–10 g/L for β-globulins and 5–12 g/L for γ-globulins.

An inflammatory profile using an inflammatory protein with fast kinetics (hs-CRP) and two inflammatory proteins with intermediate kinetics (Hp and ORO) was carried out by Protis® software-Dade Behring. This profile is the expression of inflammatory protein variations adjusted to age and sex. The profile was interpreted as follows: values $<100\%$ (of the normal values): absence of inflammation; values between 100% and 150%: minimal inflammation; values between 150% and 200%: mild inflammation; values between 200% and 300%: moderate inflammation; values $>300\%$: severe inflammation.

2.3. Ethical considerations

Ethical approval to conduct this research was provided by the Research Ethics Committee of Razi University Hospital. All participants gave informed consent.

2.4. Data analysis

Data were entered and analyzed using SPSS 20 for Windows.

Distributions were checked for normality using the Shapiro-Wilk test. Comparisons of two quantitative variables were performed using the Student *T* test. Comparisons of several quantitative variables (>2) were performed using the one-way ANOVA test. Comparisons of independent categorical variables were performed using the Pearson's chi-squared test, and in case of non-validity of this test by Fisher's exact test. Comparisons of dependent categorical variables were performed using the McNemar's test.

For multiple comparisons, significance levels were adjusted according to Holm-Bonferroni's method.

Confounding variables were controlled for by multiple regression.

3. Results

Sociodemographic and clinical features of both groups are presented in Table 1.

Comparison of mean levels of inflammatory markers between groups is presented in Table 2. Patients with depression had