Psychiatria Danubina, 2010; Vol. 22, No. 2, pp 275–277 *Conference paper*

C-REACTIVE PROTEIN AND METABOLIC SYNDROME IN PATIENTS WITH BIPOLAR DISORDER COMPARED TO PATIENTS WITH SCHIZOPHRENIA

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SUMMARY

Introduction: *Infectious and inflammatory processes could potentially play an important role in the etiology and pathogenesis of psychotic disorders. The aim was to investigate is there any differences in CRP levels in patients with bipolar disorder compared to patients with schizophrenia and if there is an association beetwen increased CRP levels and the presence of MS in theese two groups of patients.*

Subjects and methods: *Patients with bipolar disorder (N=60; 32 males and 28 females) and schizophrenia (N=63, 33 males and 30 females). MS was defined according to NCEP ATP III criteria. The cut-off point for elevated CRP was set at 5 mg /L.*

Results: *The prevalence of the MS was 31% in bipolar group compared to the 37% in schizophrenia group. No statistically significant differences in mean CRP values was observed between bipolar and schizophrenia group. CRP >5 mg /l was significantly associated with the presence of MS.*

Conclusion: *Measurement of serum inflammatory parameters in psychiatric patients may be beneficial in order to obtain a better assessment of their metabolic risk profile.*

Key words: *c-reactive protein - metabolic syndrome - bipolar disorder - schizophrenia*

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INTRODUCTION

Beside genetic factors, infectious and inflammatory processes could potentially play an important role in the etiology and pathogenesis of bipolar disorder (Liu et al. 2004, O Brien et al. 2006).

C-reactive protein (CRP) is one of positive acute phase protein and it is synthesized in the liver and then excreted in the blood. CRP levels can be increased more than 10000 times as a response to an infection and represent direct and quantitative measure of acute inflammatory reaction. Increased CRP levels are associated not only with acute but with chronic infections too.

There are many studies showing that patients in acute manic phase have increased levels of CRP and other inflammatory markers compared to depressive, euthymic patients and healthy controls (Huang and Lin 2008, Cunha et al. 2008, Wadee et al. 2002) and that the intensity of manic symptoms is associated with CRP levels (Dickerson et al. 2008).

Inflammatory markers in patients with bipolar disorder and shizophrenia (TNF -1 and CRP) are significantly higher than in healthy controls (Hope et al. 2009). Results of abovementioned study showed specific alteration of endothelium inflammatory reactions shared by both disorders. Some authors defined metabolic syndrome (MS) as a chronic mild inflammatory state (Newcomer 2007). Furthermore, the presence of MS is the most important predictor of premature onset of cardiovascular disease (CVD). CRP, as the most specific biomarker of inflammation, is the independent risk factor for CVD, too. Laboratory and epidemiological data showed that CRP is associated mostly with insulin resistance and obesity, but with the other subcomponents of MS too (Devaraj et al. 2009).

Aim of this study is to investigate is there any differences in CRP levels in patients with bipolar disorder compared to patients with schizophrenia and if there is an association beetwen increased CRP levels and the presence of MS in theese two groups of patients.

SUBJECTS AND METHODS

Subjects were patients with bipolar disorder (N=60; 32 males and 28 females) and schizophrenia (N=63, 33 males and 30 females) treated at the Department of Psychiatry, University Hospital Centre Zagreb during the period of 36 months. The average age of all participants was 40.76 ±12.19.

The diagnosis of bipolar disorder and schizophrenia was made according to diagnostic criteria of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10), (WHO 1996).

All bipolar patients who entered the study were in at least one month euthymic phase defined with HAMD-17 score 7 or less and YMRS score 5 or less. The most recent episode in 25 bipolar patients was manic and in 35 patients was depressive episode. All patients with schizophrenia were in a stable phase which means that pharmacotherapy was not changed within a month. Written informed consent was obtained from all participants, under procedures approved by the Local Ethics Committee and in accordance with the Helsinki Declaration.

Venipuncture was performed for all subjects between 8 and 9 a.m. after 12 hours overnight fast. Immediately after collecting blood samples, serum concentration of total cholesterol, high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), triglycerides and serum glucose were determined using enzyme methods and commercial kits (Olympus Diagnostic, GmbH, Hamburg, Germany) on Olympus AU 600 automated analyzer. CRP serum levels were determined using immunoturbidimetric method. The cut-off point for CRP elevation was set at 5 mg/L.

MS was defined according to NCEP ATP III criteria (Expert panel JAMA, 2001).

Baseline characteristics were compared by t-test for independent samples when comparing 2 groups. For categorical variables chi-square test was used, or Fisher's exact test for 2x2 contingency tables. Contingency coefficient and Spearman coefficient of correlation were used as measures of association between variables. Analyses were done using SPSS for Windows Version13.0. Probability level of $p<0.05$ was considered to be statistically significant.

RESULTS

The prevalence of the MS was 31% in bipolar group compared to the 37% in schizophrenia group. There were no differences in the prevalence of MS between males and females in both groups. No statistically significant differences in mean CRP values was observed between bipolar and schizophrenia group (Table 1) We found significantly higher proportion of bipolar patients (33%) with CRP higher than 5 mg/L in comparison to the schizophrenia group (22%). (χ^2=6.371, ss=2, p=0.041)

In the whole sample we found significant association beetween high CRP and the prevalence of the MS (r=0.19, p=0.031). 40% patients with fullfilled criteria for MS had CRP higher than 5mg/L while 21% patients without MS had high CRP. CRP positively correlated with waist circumference(r=0.22, $p<0.05$) and systolic blood pressure(r=0.21, $p<0.05$).

CRP higher than 5 mg/L was a predictor for MS in both groups (Table 2). In bipolar group patients with high CRP had 2.627 times higher risk for MS. In the schizophrenia group patients with high CRP had 2.153 times higher risk for MS.

Table 1. CRP values in bipolar and schizophrenia group

	Mean	Std. deviation	Median	Interquartile Range	Minimum	Maksimum	N
Bipolar	4.24	4.09	2.60	1.22-5.88	0.20	17.10	60
Schizophrenia	4.94	9.94	2.40	0.90-4.50	0.10	60.40	63
Total	3.96	6.55	2.30	0.80-4.75	0.10	60.40	181

Table 2. Odds ratio, significance and confidence interval for CRP as a predictor for MS

CRP	Wald statistics	ss	P	Odds ratio (OR)	95% C.I.
Bipolar	0.687	1	0.160	2.627	0.683 ± 10.106
Sch	1.317	1	0.251	2.153	0.581 ± 7.797

DISCUSSION

The prevalence of MS in bipolar group was comparable to the prevalence of MS in schizophrenia group. Thus, we confirmed the results from recent studies (Birkenaes et al. 2007, Corell et al. 2008) reporting about almost the same risk for the development of MS in patients with bipolar disorder and schizophrenia. Regarding gender differences in the prevalence of MS our results did not confirmed the results from previous studies showing higher prevalence in male population (Regitz-Zagrosek 2006). It is noteworthy that forementioned study was performed on general population so we can raise the question if the gender distribution of MS is different in general and psychiatric population.

Our results are in line with the results of other studies showing no differences in CRP levels between patients with bipolar disorder and schizophrenia. (Akanji et al. 2009, Hope et al. 2009) .

Like in previous studies (Kirilmaz et al. 2010, Zeugman et al. 2009) our bipolar and sch patients with CRP>5mg/L had more than two times higher risk for having the MS than bipolar and sch patients with CRP levels <5mg/L.

We can conclude that elevated CRP levels are associated with increased risk for the development of MS in patients with bipolar disorder and schizophrenia.

MS, the most important predictor for the development of CVD and type II diabetes , is more prevalent in psychiatric population than in general population..Our results indicate the possibility for typization of psychotic disorders regarding biological parameters, (particularly CRP) and evaluation of its influence to the development of MS.

Inflammation plays an important role in atherosclerotic complications, which is activated in MS. Increased number of MS components are strongly associated with elevated inflammatory and metabolic markers. Measurement of serum inflammatory

parameters in psychiatric patients with MS may be beneficial in prediction, detection and management of cardiovascular events.

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