Journal of Affective Disorders 163 (2014) 76–80

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Are ICAM, VCAM and E-selectin levels different in first manic episode and subsequent remission?

Çetin Turan, Sermin Kesebir*, Özgür Süner

Erenkoy Mental and Neurological Disease Training and Research Hospital, Sinan Ercan C. N: 29 Kadıkoy, İstanbul, Turkey

ARTICLE INFO

Article history:
Received 26 December 2013
Received in revised form
27 March 2014
Accepted 29 March 2014
Available online 12 April 2014

Keywords:
Bipolar disorder
ICAM
VCAM
E-selectin
Atherosclerosis

ABSTRACT

Objective: In bipolar patients, the rate of mortality from cardiovascular diseases is two-fold higher than that in other psychiatric disorders. The risk of cardiovascular diseases was found to be associated with some cellular adhesion molecules: Intracellular adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM) and E-selectin. The aim of this study was to compare ICAM, VCAM and E-selectin levels at first manic episode and subsequent remission period, and to investigate the presence of a relationship between adhesion molecules levels and clinical and metabolic variables.

Methods: In line with this purpose, 50 patients diagnosed with mania according to DSM IV-TR criteria, who had their first episode were evaluated consecutively. The control group consisted of 50 healthy individuals without any history of psychiatric admission and treatment, matched with the manic patients in terms of age, gender, BMI and smoking status. For the confirmation of subsequent remission period ($n=40$), Young Mania Rating Scale and Hamilton Depression Rating Scale were used. In three groups plasma ICAM, VCAM and E-selectin, fasting blood glucose, total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride levels were measured and compared.

Results: ICAM and VCAM levels were found to be higher in first manic episode than those in subsequent remission and healthy individuals. A weak correlation was found between ICAM levels and YMRS scores in manic patients. In first manic episode, a weak correlation was found between ICAM and total cholesterol and LDL cholesterol levels and a weak correlation was found between ICAM, VCAM and E-selectin levels and BMI.

Conclusion: In the present study, which is the first investigation of proinflammatory and prothrombotic state, which is defined as a risk for metabolic syndrome and cardiovascular disease, in bipolar disorder, ICAM and VCAM levels were found to be higher in first episode mania than those in subsequent remission and healthy individuals. As the study group included first episode mani cases, there was no effect of chronic psychotropic use. Probable risk of cardiovascular disease, reflected by increased ICAM and VCAM levels is already present in bipolar patients at the onset of the disease. In addition, ICAM and VCAM levels increasing in manic episode, return to normal in the subsequent remission period.

1. Introduction

Increasing evidence indicates that there is an inter-relationship between mood disorders and some physical diseases (Fagiolini, 2008; Fagiolini and Goracci, 2009). Glucocorticoid/insulin signal mechanisms and inflammatory effector systems are intersections pointing to pathophysiological relation between bipolar disorder (BD), and general medical conditions susceptible to stress (Evans et al., 2005). In BD, cardiovascular diseases (CVD) are more prevalent than general population (Kessler et al., 1994). A subgroup of bipolar patients has higher risk of developing CVD. Their habits, life styles, genetic susceptibility and choices of treatment are variables determining this subgroup (Kilbourne et al., 2007). Metabolic syndrome has been reported at the rate of 35–40% in bipolar patients (Vancampfort. et al., 2013). Metabolic syndrome comprises obesity, diabetes, hypertension and dysplipidemia as cardiovascular risk factors (Malhotra et al., 2013). Although they are not among diagnostic criteria of metabolic syndrome, proinflammatory and prothrombotic state are considered in the framework of metabolic syndrome (Gómez Rosso et al., 2008).

Plasma concentrations of adhesion molecules are thought to be potential biological markers playing part in the formation and progression of atherosclerosis (Troseid et al., 2005; Gray et al., 2010;

* Corresponding author. Tel.: +90 532 592 2080.
E-mail address: serminkesebir@hotmail.com (S. Kesebir).

http://dx.doi.org/10.1016/j.jad.2014.03.052
0165-0327/

Aalto et al., 2012; Bae et al., 2013). However, there relative prognostic value at present has not still been determined completely. Extensive research works revealing cardiovascular risk have focused on inflammatory markers such as intracellular adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM), and E-selectin. It has been proven that chronic inflammatory state in atherosclerotic disease involves vascular tissue components as well (Galkina and Ley, 2007). Adhesion molecules mediate leukocyte adhesion and migration throughout endothelial surface. It is thought that this plays a critical role in the early stages of atherosclerosis (Troseid et al., 2005). While ICAM is markedly increased by endothelial cells, VCAM is expressed by smooth muscle cells with special stimulation. That is, whilst, ICAM serves in endothelial activation at the first step of inflammation, VCAM becomes more active during smooth muscle proliferation, at a closer period to the formation of atheroma plaque. E-selectin is not marked in the absence of inflammation. However it is synthesized during the inflammatory process and is specific for endothelial cells. It acts as a rolling molecule for natural killer cells, B cells, regulatory T cells, neutrophils and monocytes.

The aim of this study was to compare levels of adhesion molecules (ICAM, VCAM, E-selectin) in first manic episode and subsequent remission period of BD, to determine whether they differ from those in healthy individuals and to investigate whether adhesion molecule levels are related to some clinical and metabolic variables.

2. Methods

2.1. Sample

75 patients were screened consecutively for inclusion, who admitted to Erenkoy Mental and Neurological Diseases Training and Research Hospital outpatient clinics or emergency services between 01 April 2012 and 01 April 2013, diagnosed as BD according to DSM-IV criteria, who were at first episode.

Subjects with chronic inflammatory disease, hypertension, renal disease, hypertriglyceridemia, diabetes and severe or unstable medical illnesses ($n=2$) and other Axis I disorders were excluded ($n=2$). All subjects were medically healthy, as determined by physical and neurological examination and laboratory tests. The other exclusion criteria were as follows, being outside 18–45 age range, a BMI over 25, alcohol and substance use, and use of psychotropic drugs within last 24 h ($n=10$).

In addition, 8 patients were excluded from the study due to previous depressive episode, and 3 patients due to detection of hypertension and impairment in glucose tolerance in follow up period.

Control group comprised of 50 hospital personnel who were at similar mean age, sex, smoking status, and BMI with the patients group and without any previous history of diagnosis and treatment and current psychiatric complaints.

2.2. Tools

2.2.1. SCID-I (structured clinical ınterview for DSM-axis I disorders-SCID-I)

Turkish version of structured clinical interview for DSM-IV axis I disorders (Özkürkçügil et al., 1999).

2.2.2. SKIP-TURK (mood disorders diagnosis and following form)

Age of disorder onset, duration of the disorder, age at treatment initiation, physical and sexual abuse in the history, family history, academic and social functioning, age at menarche, premenstrual syndrome, stressor prior the first episode, type of the first episode, severity of the episode (Global Assessment of Functionality -GAF-score), postpartum onset, seasonality, depression subtype, psychotic episode, suicide, hospitalization, duration of the episode, the number of episodes, dominant course pattern, acute onset and remission, chronicity and rapid cycling, switch, cigarette smoking and substance use were inquired (Özerdem et al., 2004).

2.2.3. Hamilton depression rating scale (HDRS)

It was developed to measure the level of depression and changes in its severity (Williams, 1978). Its reliability and validity study in Turkish was carried out by Akdemir et al. (1996).

2.2.4. Young mania rating scale (YMRS)

It is used to measure the severity of manic symptoms before treatment in manic cases and to confirm the state of remission in recovery episode. This scale filled by the interviewer was developed by Young et al. (1978) and its validity and reliability study in Turkish was carried out by Karadağ et al. (2001).

2.3. Procedure

Ethical permission for this study was obtained from local ethical committee of our hospital. The cost of blood level measurements was met by our hospital investigation budget fund.

Blood sample necessary for the measurement of ICAM, VCAM and E-selectin, fasting blood glucose (FBG) and lipid levels was drawn from brachial vein after at least 8 h of starvation within first 24 h. Use of benzodiazepine was allowed by reason of agitation. For the measurement ICAM, VCAM and E-selectin levels, sera obtained from blood sample by separation in centrifuge were placed in 1.5 cc Eppendorf tube and stored at 20–80 °C until being submitted to analysis. After the necessary number of subjects were completed, MS201CE human sICAM-1 ELISA kit 96 test, BMS232 human sVCAM-1 ELISA kit 96 test and Ray Bio-human E-selectin ELISA kit 96 test kits were used in accordance with kit protocols and quantitative analysis was made in Farmasina medical and chemical products medical laboratories with the micro ELISA method. Simultaneous fasting blood glucose (FBG) and lipid levels were measured in the biochemistry laboratory of our hospital using standard enzymatic procedures.

Informed consent form was signed by one first degree relative of patients in manic episode. SKIP-TURK was collected in the remission period with the patient and at least one first degree relative of the patient. For conditions in which clear evaluation could not be done, information about the illness from the other relatives of the patient was taken.

Of 50 patients evaluated in manic period, 10 could not be evaluated because they did not come to their control. Number of evaluated patients in remission period were 40. For the confirmation of remission period, YMRS and HDRS were used weekly.

2.4. Statistical analysis

In the comparison of numerical variables, *t*-test and in groups comparisons, variance analysis was used. Bonferroni correction was applied in Post-hoc comparisons. In the determination of the interrelation between variables, Pearson correlation test was used. Regression analysis (Stepwise) was carried out to strengthen our results. All findings are double ended and p Value of $<.05$ was considered statistically significant.