Progress in Neuro-Psychopharmacology & Biological Psychiatry 35 (2011) 1261–1267

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

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

Thrombocyte serotonin and serum cholesterol concentration in suicidal and non-suicidal depressed patients

Nedjeljka Ruljancic [a,*], Mate Mihanovic [b], Ivana Cepelak [c]

[a] Psychiatric Hospital "Sveti Ivan", Department of Laboratory Diagnostics, Jankomir 11, 10 000 Zagreb, Croatia
[b] Head of Psychiatric Hospital "Sveti Ivan", Jankomir 11, 10 000 Zagreb, Croatia
[c] Pharmaceutical–Biochemical Faculty, Department of Medical Biochemistry and Hematology, University of Zagreb, A. Kovacic 1, 10 000 Zagreb, Croatia

ARTICLE INFO

Article history:
Received 14 September 2010
Received in revised form 3 February 2011
Accepted 15 February 2011
Available online 19 February 2011

Keywords:
Cholesterol
Depression
Gender
Suicidal behavior
Thrombocyte serotonin

ABSTRACT

Introduction: Numerous studies have confirmed the connection of reduced serum cholesterol and thrombocyte serotonin concentration with suicidal behavior in psychiatric patients. The purpose of such studies was to determine the link among cholesterol and serotonin concentration, comparing depressed patients with and without attempted suicide with phenotypically healthy control group.
Materials and methods: The examinees' groups consisted of 55 depressed patients with suicide attempt and 77 depressed patients with no suicide attempt. In accordance to ICD-10, the above patients were separated in two subgroups; F32.2 and F33.2. Phenotypically healthy control group was presented by the group of healthy blood donors. The fasting serum cholesterol concentration was established using standard enzymatic method, while the thrombocyte serotonin concentration was determined by the enzymatic immune-chemical method (ELISA).
Results: The ANOVA test ($N=228$, $F_{ratio}=8.26$, $p<0.001$) found significant difference of cholesterol concentration between groups, with lowest concentration in depressed patients with attempted suicide (SNK post hoc test, $p<0.05$). Upon gender stratification, the significance remained for the female patients (ANOVA, $N=125$, $F_{ratio}=6.06$, $p=0.003$). The serum cholesterol was shown to be statistically lower in the group of depressed patients with attempted suicide, diagnoses F32.2 ($p=0.031$) and F33.2 ($p=0.011$), compared to the group of depressed patients without attempted suicides. The thrombocyte serotonin was found to be significantly different in all examined groups, with the lowest thrombocyte serotonin in the group of depressed patients with no suicide attempt (SNK post hoc test, $p<0.05$, $N=187$, $F_{ratio}=37.69$, $p<0.001$). The same significance was found for the group of female (ANOVA, $N=103$, $F_{ratio}=11.81$, $p<0.001$) and the group of male patients (ANOVA, $N=84$, $F_{ratio}=30.40$, $p<0.001$). The thrombocyte serotonin was significantly lower in the group of depressed patients with no suicide attempt (F32.2), compared to the same diagnosis in the group of depressed patients with suicide attempt (MW-test, $p=0.018$).
Conclusion: In the group of depressed patients with attempted suicide, statistically significant lower serum cholesterol values have been confirmed. In the group of depressed patients with no suicide attempt, statistically significant lower values of thrombocyte serotonin have been confirmed, presumably as the response to the psychopharmacological therapy.

1. Introduction

Suicidal behavior is a complex phenomenon that requires biological, psychological, psycho-pathological, sociocultural and evolutionary factors to be included while conducting research in this field. Within this scope, the relation between cholesterol and behavior can be explained by behavioral adaptation, in terms of famine during the course of evolution. Such hypothesis does include three features: 1. low cholesterol level leads to impulsive and aggressive behavior, 2. low cholesterol level, cholesterol effect is occurring as a result of disturbed serotonin neurotransmitter system activity, and 3. the relation between cholesterol level and behavior, becomes evident in relation to the changes of conditions and quality of nutrition (Kaplan et al., 1991, 1997; Wallner and Machatschake, 2009).

Cholesterol is present in the central nervous system (23% of the total body pool, 450 mg/kg), as an important structural component of neurons and glia cell plasma membranes and in the membranes of myelin (Dietschy and Turley, 2004). Engelberg (1992) linked low

Abbreviations: ANOVA, one-way variance analysis; ELISA, enzyme-immune-chemical method; F32.2, severe depressive episode without psychotic symptoms; F33.2, recurrent depressive disorder, current episode severe without psychotic symptoms; GHQ12, General Health Questionnaire; GLMM, generalized linear mix model; ICD-10, International Classification of Diseases and Related Health Problems, Tenth Revision; SNK, Student Newman Keuls; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin, noradrenalin reuptake inhibitor; PRP, platelet rich plasma.

* Corresponding author. Tel.: +385 13430059; fax: +385 1 3794116.
E-mail addresses: n_ruljancic@yahoo.com (N. Ruljancic), pbsvi@pbsvi.hr (M. Mihanovic), icepelak@yahoo.com (I. Cepelak).

0278-5846/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.pnpbp.2011.02.007

cholesterol level to decreased central serotonergic activity. It is assumed that low cholesterol concentration reduces the activity of serotonin receptors and the serotonin transporter, due to weaker micro-viscosity of the lipid membrane of the neurons, as it increases the fluidity of the neuron cell membrane (Heron et al., 1980; Engelberg, 1992). Previous studies has shown that reduced cholesterol concentration, whether innately such or induced by drugs, is related to increased mortality or suicidality (Muldoon et al., 1990, 1993). Another meta-analysis (Mulldoon et al., 2001), has revealed only modest non-significant mortality increase, due to suicide among patients on dietary intervention and non-statin drug. Association of low or lowered cholesterol with aggressive and violent behavior has been reported in several studies (Virkkunnen and Penttinen, 1984; Golomb, 1998; Golomb et al., 2000). In a number of studies, the association between low serum cholesterol and depressive symptoms, both in general population (Lindberg et al., 1992; Neaton et al., 1992; Zureik et al., 1996; Partonen et al., 1999; Ellison and Morrison, 2001) and in various types of psychiatric inpatients with depressive symptoms, has been documented (Rabe-Jablonska and Poprawska, 2000; Steegmans et al., 2000; Ghaemi et al., 2000; Rafter, 2001). In addition to depression, low serum cholesterol has been associated with suicide attempts (Modai et al., 1994; Golier et al., 1995; Kunugi et al., 1997; Sarchiapone et al., 2000, 2001; Lee and Kim, 2003; Kim and Myint, 2004; Perez-Rodriguez et al., 2008). However, not all studies suggest a relationship between low serum cholesterol, depressive symptoms (Ledochowski et al., 2003; van Reedt Dortland et al., 2009; Sagud et al., 2009) and suicide attempt (Almeida-Montes et al., 2000; Deisenhammer et al., 2004; Huang, 2005; Fiedorowicz and Coryell, 2007; Pompili et al., 2010). Considering that both elevated and lowered serum cholesterol might contribute to the membrane structure changes, it is possible that patients with elevated cholesterol concentration (>5.17 mmol/L) are resistant to therapy, while the concentration below 4.14 mmol/L, might be connected with higher suicide risk in patients with depression (Papakostas et al., 2003, 2004). The hypothesis of relation between low serum cholesterol, depression and suicide, does include serotonin. Studies of possible association between major depression and thrombocyte serotonin, have been discrepant, reporting all kinds of results: either no changes (Jakovljevic et al., 1997; Franke et al., 2000; Muck-Seler et al., 2002), a decrease (Quintana, 1992; Pivac et al., 2003; Muck-Seler et al., 2004; Maurer-Spurej et al, 2004), or an increase (Roggenbach et al., 2007) of thrombocyte serotonin compared to healthy control subjects. Only a few studies have examined thrombocyte serotonin in patients with depression and attempted suicide, compared to thrombocyte serotonin of non-suicidal patients with depression. In these studies, thrombocyte serotonin has been lower in patients with depression and attempted suicide, compared to patients with depression and no suicide attempt (Mann et al., 1992; Muck-Seler et al., 1996; Roggenbach et al., 2007), compared to the healthy control subjects (Alvarez et al., 1999; Spreux-Varoquaux et al., 2001). With regard to the considerable interest to investigate the connection between the serum cholesterol concentration, thrombocyte serotonin and suicidal behavior, on one hand and the incongruent results that have been published until now, on the other hand, this research has been conducted. The intention of this research is to examine potential difference of the serum cholesterol and thrombocyte serotonin in groups of patients with depressive episode, (F32.2 severe depressive episode without psychotic symptoms and F33.2 recurrent depressive disorder, current episode severe without psychotic symptoms), with and without suicidal behavior and the control group of the phenotypically healthy subjects.

2. Subjects and methods

2.1. Subjects

Case–control study has been carried out, with two separate control groups used for comparison.

2.1.1. Case — subjects with medical history of attempted suicide

First group consisted of 55 patients who attempted suicide, and have been admitted to the Psychiatric Hospital "St. Ivan" shortly after suicide attempt. Data was collected for the period August 2005 to January 2007. The initial psychiatric interviews have been conducted within the period of 1 to 24 h upon admission. The evaluation consisted of psychiatric and medical history review, data on current and previous medications and alcohol intake. This has been followed by a semi-structured interview, with the purpose of establishing an ICD-10 (International Classification of Diseases and Related Health Problems, Tenth Revision, 2004) criteria for diagnosis F32.2 and F33.2, with Intentional self-harm (X60–X84).

2.1.2. Psychiatric controls — subjects without history of suicide attempt

Another group consisted of 77 patients who have been consecutively admitted to the same hospital during the same period. Upon admission, ICD-10 diagnosis (F32.2 and F33.2) has been established and it has been confirmed that there was no history of suicide attempt in this group of patients. In terms of age and gender, the patients in this study group were closely matched with the individual patients from the previously described patient group, with reported suicide attempt.

2.1.3. Phenotypically healthy control group

The phenotypically healthy control group consisted of voluntary blood donors from the Croatian Institute for Blood Transfusion. Voluntary blood donation in Croatia is a non-profit and altruistic act. The criteria for blood donation exclude numerous somatic diseases and pharmacological therapy. A General Health Questionnaire (GHQ12 test) has been used as a screening test for possible psychopathology in the control group.

In Table 1, the features of the study subjects according to diagnosis, age and gender have been presented. Tested by Chi-square test, no difference has been reported in all 3 groups, with respect to gender ($\chi^2 = 2.174$, DF = 2, $p = 0.337$). One-way variance analysis (ANOVA test) presented lower age of phenotypically healthy control subjects ($p < 0.001$, $F = 7.78$) to be statistically significant. The correlation of thrombocyte serotonin and age, serum cholesterol and age, for the group of patients with depression, with and without suicide attempt, has shown not to be significant. We have found positive correlation between serum cholesterol and age ($r = 0.421$, $p < 0.001$) and negative correlation between thrombocyte serotonin and age, for the healthy control group ($r = -0.210$, $p = 0.038$).

Ongoing and previous antidepressant therapy status and dosage have been determined for all patients. It was found that 84% of patients were currently receiving the therapy, in accordance with the current algorithms for depression treatment (Rush, 2004; Schatzberg et al., 2008; Cipriani et al., 2009). The psychiatric pharmacological therapy has been presented in Table 2. Fisher's exact test, found no differences in psychiatric pharmacological therapy between patients groups. Using generalized linear mix model (GLMM), we have analyzed the influence of age, gender and psychopharmacological therapy (independent variable) in the group of patients with depression, with/without suicide (dependent variable). Psychopharmacological therapy has been found as significant predictor for belonging to the group of depressive suicide attempters in this model ($\chi^2 = 6.004$, DF = 1, $p = 0.014$).

In all 3 groups, the exclusion criteria have been the same, including: BMI > 30 kg/m^2, usage of lipid cholesterol-lowering drugs, pregnancy, lactation, alcohol and reported substance abuse or dependence, cardiovascular disease and hypertension.

2.2. Blood collection and biochemical measurements

The sample of patient blood for analysis has been taken in all cases on the second fasting day upon patient's hospitalization in the