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Lipid levels in female patients with affective disorders

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ABSTRACT

The role of serum lipids [total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG)] in the pathophysiology of mood disorders is not clear. The aim of this study was to determine lipid profiles in patients with affective disorders. The study included medication-free female subjects (41 patients with bipolar disorder, 22 in a manic and 19 in a depressive phase), 34 patients with major depression, and 50 healthy controls. Serum lipid levels were determined using standard laboratory tests. All patients had significantly lower HDL-C values than control subjects. Increased TG levels were found in patients with bipolar disorder compared with healthy subjects. The changes in lipid profiles persisted when data were adjusted for age, smoking and menopausal status. The results revealed no differences in cholesterol and LDL-C levels and body mass index, but significant differences in the ratios of cholesterol/HDL-C and LDL-C/HDL-C (atherogenic index) among groups. Our results suggest that low HDL-C levels and a high atherogenic index might be a hallmark of affective disorders. Since low HDL-C levels could be a risk factor for the development of coronary heart disease, further investigation of lipid metabolism in affective disorders is warranted.

1. Introduction

A number of studies (Horsten et al., 1997; Maes et al., 1997; Ghaemi et al., 2000; Atmaca et al., 2002; Cassidy and Carroll, 2002; Pae et al., 2004) have suggested that the pathophysiology of mood disorders might be related to alterations in the lipid profile. Although in the general population, women with low levels of high-density lipoprotein cholesterol (HDL-C) (Horsten et al., 1997; Chen et al., 2001) and low cholesterol levels (Horsten et al., 1997) had more depressive symptoms than women with normal lipid levels, the association between total cholesterol, HDL-C, low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels and affective disorders is still unclear. Namely, clinical studies evaluating the relationship between cholesterol levels and affective disorders have yielded inconsistent results. Decreased cholesterol levels were found in patients with mania (Ghaemi et al., 2000; Atmaca et al., 2002; Cassidy and Carroll, 2002; Pae et al., 2004; Sagud et al., 2007), while lower (Maes et al., 1997) or unaltered (Oxenkrug et al., 1983; Huang et al., 2003) serum cholesterol levels were found in female patients with major depression.

Relatively few data have been presented on the entire lipid profile (i.e. cholesterol, HDL-C, LDL-C, and TG) in affective disorders. It was reported that patients with affective disorders had hypocholesterolemia with lower LDL-C and higher HDL-C and TG levels than healthy controls (Glueck et al., 1994), while first degree relatives of bipolar patients had lower HDL-C levels than corresponding healthy controls (Sobczak et al., 2004). Since studies investigating the lipid profile in affective disorders, particularly in bipolar disorder in a manic or a depressed phase, are scarce and inconsistent, the aim of the present study was to determine serum levels of total cholesterol, TG, HDL-C and LDL-C in medication-free female patients with major depression and bipolar disorder (in a manic or a depressive episode), and to compare these values with the values in healthy control women.

2. Methods

2.1. Subjects

The study population comprised 41 female, medication-free inpatients with bipolar I disorders (22 in manic and 19 in depressive episodes), 34 female patients with major depression, and 50 healthy female subjects. Patients were diagnosed using the Structured Clinical Interview for DSM-IV disorders (American Psychiatric Association, 1994). Manic patients scored at least 18 on the Young Mania Rating Scale (YMRS) (Young et al., 1978) and 7 or less on the 17-item Hamilton Depression Rating Scale HAMD-17 (Hamilton, 1960). Patients with bipolar depression or major depressive disorder scored at least 18 on the HAMD-17, and 5 or less on the YMRS. Exclusion criteria were as follows: diagnoses of schizophrenia, dementia, schizoaffective disorder, alcohol abuse in the previous month, serious medical disease (including cardiovascular disease), no change ± 5% of their body weight in the previous 3 months, elevated (>7.0 mmol/l) cholesterol levels, use of cholesterol-lowering drugs, pregnancy, lactation and suicidal behavior (patients who scored 2 or more on item 3 on the HAMD-17). All patients had been free of psychotropic medication for at least 2 weeks (washout period ranged from 14 days to 5 years) before study entry, except for a benzodiazepine-equivalent dose of 2 mg of lorazepam daily. The control group consisted of medication-free healthy women, recruited mostly from medical staff, with no personal history of any psychiatric disorder. Nine patients with mania, seven

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patients in the depressive phase of bipolar disorder, 13 patients with major depression and 17 healthy controls were in menopause.

Written informed consent was obtained from all participants, under procedures approved by the Local Ethics Committee and in accordance with the Helsinki Declaration.

2.2. Blood collection and biochemical measurements

Blood samples were drawn in the morning after a 12-h overnight fast. Serum cholesterol, HDL-C and TG levels were determined by the enzymatic color test for clinical analyzers, with the linearity within concentrations in the range of 0.64–18 mmol/l, 0.05–4.65 mmol/l and 0.11–11.40 mmol/l for serum cholesterol, HDL-C and TG, respectively. Serum LDL-C levels were determined by enzymatic clearance assay, with linearity up to 22.4 mmol/l.

The body mass index (BMI) was calculated by dividing the weight (in kilograms) by squared height (in meters).

2.3. Statistical procedures

All results are expressed as mean ± S.D. Results were evaluated using one-way analysis of variance (ANOVA), followed by Tukey's Honestly Significant Difference (HSD) test for multiple comparisons. Analysis of covariance (ANCOVA) was used with age, smoking and menopause as covariates. The significance level was $P<0.05$. The statistical packages used were SigmaStat 3.1.

3. Results

Table 1 presents the demographic characteristics of patients and healthy controls. No significant difference in age ($F_{3,\ 121}=2.011$, $P=0.11$, ANOVA) and BMI ($F_{3,\ 121}=1.581$, $P=0.19$) was observed between groups.

Serum HDL-C levels were significantly ($F_{3,\ 121}=22.575$, $P=0.000$) different in healthy controls and patients with major depressive or bipolar disorder (Fig. 1). Significantly lower serum HDL-C values were observed in patients with bipolar disorder in manic ($P<0.001$; Tukey's HSD) or depressive ($P<0.001$, Tukey's test) episodes, and with major depression ($P<0.001$, Tukey's test), when compared with values for healthy controls. HDL-C levels differed significantly among groups when data were adjusted with age ($F_4=18.606$, $P<0.000$), smoking ($F_4=16.838$, $P<0.000$) and menopause ($F_4=18.968$, $P<0.000$) as covariates (ANCOVA).

There was a significant ($F_3=6.909$, $P<0.000$) difference in serum TG levels among groups (Fig. 2). Patients with bipolar disorders in manic ($P=0.007$, Tukey's HDS test) or depressive ($P<0.001$ Tukey's HDS test) episodes had significantly higher TG values than healthy controls. Serum TG values were significantly ($P<0.048$) higher in bipolar disorder patients in a depressed phase than in patients with major depression. TG levels differed significantly among groups when data were adjusted with age ($F_4=5{,}195$, $P<0.001$), smoking ($F_4=5.787$, $P<0.000$) and menopause ($F_4=5.139$, $P<0.001$), entered as covariates (ANCOVA).

Table 1
Demographic characteristics of patients with bipolar disorder (in a manic and a depressed phase), patients with major depression, and healthy controls.

	Bipolar disorder		Major Depressive Disorder (34)	Healthy Controls (50)
	Manic Episode (22)	Depressive Episode (19)		
Age (years)	48.5 ± 13.2	44.1 ± 12.9	50.1 ± 6.6	44.7 ± 12.8
BMI (kg/m^2)	24.7 ± 4.5	23.3 ± 2.4	24.3 ± 2.2	24.0 ± 4.5
YMRS (scores)	26.1 ± 6.0			
HAMD (scores)	5.7 ± 1.6	27.3 ± 4.2	26.1 ± 2.2	
Disorder duration (years)	9.4 ± 9.6	12.5 ± 9.8	12.7 ± 10.4	
Current episode duration (days)	10.4 ± 11.3	4.2 ± 3.0	3.2 ± 1.5	
Number of prior manic episodes	5.2 ± 7.5	4.6 ± 5.8		
Number of prior depressive episodes	6.7 ± 9.2	7.9 ± 7.8	3.1 ± 2.9	

Data are presented as means ± SD. The number of subjects is given in brackets.

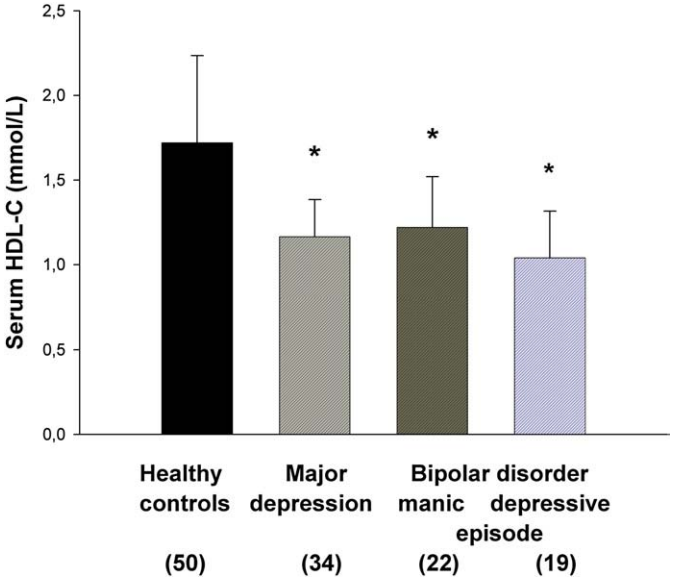

Fig. 1. Serum HDL-C levels in healthy controls, patients with major depressive disorders and patients with bipolar disorders in manic or depressive episodes. Each column represents mean ± SD. Number of subjects is given in brackets. *$P<0.001$ vs. healthy controls (ANOVA and Tukey's test).

Serum cholesterol and LDL-C concentrations did not differ significantly between healthy controls and patients with major depression or bipolar disorder (Table 2). Age ($F_4=1.416$, $P=0.218$; ANCOVA), smoking ($F_4=0.397$, $P=0.811$, ANCOVA) and menopause ($F_4=0.486$, $P=0.746$, ANCOVA) did not influence serum cholesterol levels among subjects. There was no significant effect of age ($F_4=2.071$, $P=0.089$, ANCOVA), smoking ($F_4=1.437$, $P=0.226$, ANCOVA) and menopause ($F_4=1.442$, $P=0.224$, ANCOVA) on serum LDL-C levels among subjects.

The atherogenic index differed significantly among groups (Table 2). Patients with major depression and patients in both phases

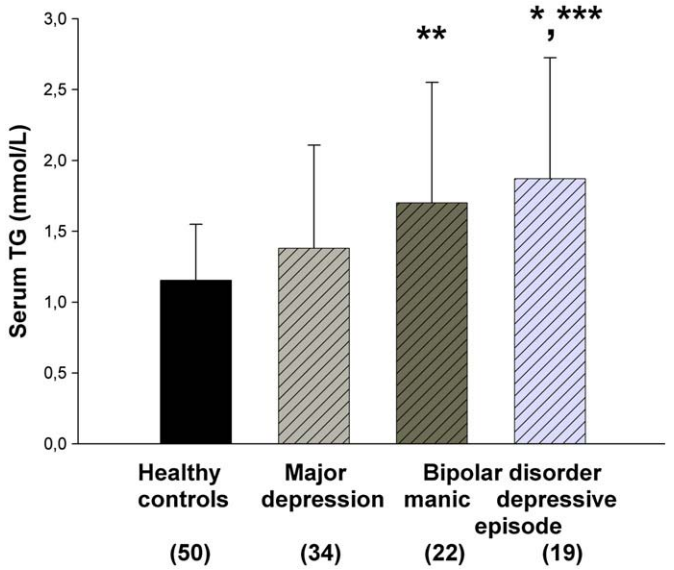

Fig. 2. Serum TG levels in healthy controls, patients with major depressive disorders and patients with bipolar disorders in manic or depressive episodes. Each column represents mean ± SD. Number of subjects is given in brackets. *$P=0.048$ vs. major depression; **$P=0.007$ vs. healthy controls; *** $P<0.001$ vs. healthy controls (ANOVA and Tukey's test).