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Brief report

Serum leptin and cholesterol values in violent and non-violent suicide attempters

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Abstract

Earlier studies have linked lipid metabolism to suicide and impulsive-aggressive behaviors. We previously reported that suicide attempters had significantly lower leptin and cholesterol levels than controls. Since lower cholesterol levels have been related to violence alone, we decided to evaluate serum total cholesterol and leptin levels in violent and non-violent suicide attempters. In the present study, 19 violent, 16 non-violent suicide attempters, and 20 age- and sex-matched healthy controls were compared for serum total cholesterol and leptin levels. Violent suicide attempters had significantly lower total cholesterol and leptin levels compared with those with non-violent suicide attempts. Our results suggest that low serum cholesterol and leptin levels are related to the following two dimensions of suicide attempts: suicidality and violence.

Keywords: Leptin; Cholesterol; Suicide; Violence

1. Introduction

A growing body of research implicates an association between low cholesterol levels and a variety of psychiatric disorders related to impulsive–aggressive behaviors (Freedman et al., 1987) and suicide attempts (Golomb, 1998). However, epidemiological and clinical studies also yielded conflicting results concerning a supposed association between increased risk for suicide and violence, and low serum cholesterol levels. Modai et al. (1995) indicated no influence of cholesterol on serotonin uptake, as opposed to some investigators who suggested that the high risk of suicide and aggressiveness in hypocholesterolemic individuals could be related to impaired serotonin transport (Bocchetta et al., 2001; Kim et al., 2002). In their study, Steinart et al. (1999) reported that there was no correlation between serum cholesterol levels and measures of violence in patients with schizophrenia and non-psychotic disorders.

Leptin, an adipocyte hormone, has attracted considerable interest in psychiatric disorders recently (Kraus et al., 2001; Atmaca et al., 2002a,b,c). It has been reported that leptin affects the intracellular lipid concentration via a decrease in synthesis of fatty acid and triglycerides, and an increase in lipid oxidation (Auwerx and Steals, 1998). In our previous study, we demonstrated that suicide attempters have statistically

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significant lower leptin and cholesterol levels compared with healthy controls (Atmaca et al., 2002d). In that study, we did not take into account whether the suicide attempt was of a violent or a non-violent nature. On the other hand, the relationship between lower serum cholesterol and suicide attempts has been reported to be restricted to psychiatric patients with violent suicide attempts (Alvarez et al., 2000). In keeping with our previous report regarding lower serum cholesterol and leptin levels in suicide attempters compared with healthy controls (Atmaca et al., 2002d), the association between cholesterol and leptin, and, on the other hand, the fact that lower cholesterol levels could be associated with violence alone, we aimed to evaluate serum total cholesterol and leptin levels in violent and non-violent suicide attempters.

2. Methods

2.1. Subjects and clinical evaluation

Thirty-five patients with suicide attempts (aged 19–45 years) participated in the study. They had been consecutively admitted to the Firat University School of Medicine Emergency Unit or the Department of Psychiatry. A detailed clinical evaluation was performed by one trained psychiatrist within 2 days after admission (seven patients in general surgery unit, six patients in emergency unit, five patients in neurosurgery unit, four patients in traumatology clinic, three patients in plastic surgery clinic, and 10 patients in our clinic after referral from the emergency unit) for all patients. Each patient underwent a detailed diagnostic evaluation by a trained psychiatrist with the Structured Interview for DSM-III-R (SCID-I) (Spitzer et al., 1987) and the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II) (Spitzer et al., 1990a,b). Twenty age- and sex-matched healthy staff members were included in the control group. Controls were interviewed with the non-patient version of the SCID (SCID-NP) (Spitzer et al., 1990a,b) to exclude any axis I disorder.

Exclusion criteria for both patients and controls included the presence of a severe physical illness, the history of alcohol and substance abuse or dependence without an abstinent period of at least 4 weeks, previous history of cholesterol-lowering treatment, the presence of any endocrinological state, treatment with any medication within last 2 weeks and excessive obesity. All participants were carefully assessed to exclude autoimmune, pulmonary, infectious diseases and neoplasms. In addition, the body-mass index (BMI) was calculated by dividing the weight (in kilograms) by the squared height (in meters) (kg/m^2). After complete description of the study to the subjects, written informed consent was obtained from each subject. The study protocol was approved by the Local Ethics Committee of the Firat University School of Medicine.

According to the criteria of Träskman et al. (1981), suicide attempters were divided into two subgroups: violent ($n=19$) and non-violent ($n=16$).

2.2. Blood sampling and biochemical determination

To determine serum levels of leptin and total cholesterol, venous blood samples were obtained at 08.00 a.m. In the patients, blood was collected within 24 h after the suicide attempt. The leptin levels were measured using the DRG Diagnostics kit (DRG Instruments GmbH, Germany) with the enzyme-linked immunoassay (ELISA) method. The limit of detection was 0.2 ng/ml. Total cholesterol levels were measured with the Olympus AU 600 autoanalyzer (Olympus, Japan) using the Randox kit (RANDOX Laboratories, UK).

2.3. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS/PC 9.05 version, 1998). Analysis of variance (ANOVA) and chi-square tests were used for the comparisons, whenever appropriate. The General Linear Model command of the SPSS was used when controlling for covariates. Correlation analysis was performed by Pearson correlations and the Spearman Rank correlation test, whenever appropriate. Differences were considered significant at the $P<0.05$ level for all these tests.

3. Results

Violent, non-violent suicide attempters and healthy controls did not differ with respect to age or sex. Of the patients, 19 (54.3%) were violent suicide attempters (deep knife wound in 10 patients, jumping from a high place in six patients and firearm in three patients) whereas 16 (45.7%) were non-violent suicide attempters (benzodiazepine ingestion in 11 patients, vitamin B1 capsules in four patients, and analgesic ingestion in one patient). General characteristics of the patients and controls are summarized in Table 1.

The mean cholesterol levels for violent suicide attempters, non-violent suicide attempters, and controls were 140.2±24.1, 164.5±28.4 and 193.7±27.9 mg/dl, respectively ($P<0.05$ for violent vs. non-violent suicide attempters; $P<0.01$ for non-violent suicide attempters vs.

Table 1
The mean leptin and cholesterol levels and some characteristics of the patients and controls

	I Violent suicide attempters (n=19)	II Non-violent suicide attempters (n=16)	III Controls (n=20)	P
Age (years)	32.6±6.2	34.1±6.7	31.8±5.8	>0.05
Sex (F/M)	12/7	10/6	12/8	>0.05
Psychiatric diagnoses				
Major depressive disorder	8	7		
Schizophrenia	5	3		
Alcohol dependence	2	1		
Histrionic personality disorder	3	2		
Bipolar disorder–manic episode	3	3		
BMI (kg/m^2)	23.8±2.1	24.6±2.9	24.4±3.2	>0.05
Total cholesterol (mg/dl)	140.2±24.1	164.5±28.4	193.7±27.9	<0.05 I–II <0.01 II–III <0.001 I–III
Leptin (ng/ml)	5.6±3.1	8.6±4.9	18.1±7.6	<0.05 I–II <0.01 II–III <0.01 I–III

controls; and $P<0.001$ for violent suicide attempters vs. controls). A significant difference in mean serum cholesterol levels among groups was found after controlling for BMI or age ($F=4.78$, $P<0.05$ adjusted for BMI; $F=4.22$, $P<0.05$ adjusted for age). In addition, when comparing the mean cholesterol level between sexes within each group, no statistically significant difference was found ($P>0.05$).

Leptin levels were lower in 11 (57.9%) violent suicide attempters, in five (31.3%) non-violent suicide attempters and in one (5.0%) control, when individually compared with normal leptin levels adjusted for BMI and sex. The mean leptin levels for violent suicide attempters, non-violent suicide attempters, and controls were 5.6±3.1, 8.6±4.9 and 18.1±7.6 mg/dl, respectively ($P<0.05$ for violent vs. non-violent suicide attempters; $P<0.01$ for non-violent suicide attempters vs. controls; and $P<0.01$ for violent suicide attempters vs. controls). A significant difference in mean leptin levels among groups was found after controlling for BMI or sex ($F=14.72$, $P<0.001$ adjusted for BMI; $F=4.84$, $P<0.05$ adjusted for sex). In addition, when comparing the mean leptin level between sexes within each group, no statistically significant difference was found ($P>0.05$).

There was a positive correlation between the mean cholesterol and leptin levels in violent and non-violent suicide attempters ($r=0.56$, $P<0.05$; $r=0.58$, $P<0.05$ for violent and non-violent suicide attempters, respectively), but not in controls ($r=0.12$, $P>0.05$). Between total cholesterol levels and BMI, there was a positive correlation in all groups ($r=0.62$, $P<0.05$ for violent suicide attempters; $r=0.60$, $P<0.05$ for non-violent suicide attempters; and $r=0.54$, $P<0.05$ for controls). The leptin levels correlated to BMI in suicide attempters ($r=0.82$, $P<0.01$) and non-violent suicide attempters ($r=0.63$, $P<0.05$), whereas there was a tendency toward such a correlation in controls ($r=0.42$, $P>0.05$). There was no statistically significant relation between the type of psychiatric disorder and serum total cholesterol ($r=0.14$, $P>0.05$ for violent and $r=0.08$, $P>0.05$ for non-violent suicide attempters) or leptin levels ($r=0.24$, $P>0.05$ for violent and $r=0.16$, $P>0.05$ for non-violent suicide attempters) in violent and non-violent suicide attempters.

4. Discussion

The principal finding of the present study is that suicide attempters have lower serum total cholesterol and leptin levels compared with healthy controls. Moreover, there were significantly lower total cholesterol and leptin levels in patients with violent suicide attempts than in those with non-violent suicide attempts.

Earlier studies performed in psychiatric patients found an association between low cholesterol levels and suicide attempts (Golomb, 1998). However, some authors reported that this relation existed only in patients with violent suicide attempts (Alvarez et al., 2000). Alvarez et al. (1999) suggested that low serum cholesterol levels might be more a reflection of the dimensions of suicidality and violence than of impulsivity. In our previous study, we demonstrated that suicide attempters have statistically significantly lower leptin and cholesterol levels compared

with healthy controls (Atmaca et al., 2002d). However, in that study, we did not evaluate the association between violence and cholesterol or leptin levels. Kaplan et al. (1997) reported low serum cholesterol levels and cerebrospinal fluid (CSF) concentrations of 5-hydroxy-indolacetic acid (5-HIAA) in primates which were given low fat diet and proposed that serum cholesterol could affect serotonin metabolism. In addition, impulsive aggression has been found to be negatively correlated with CSF levels of 5-HIAA (Higley et al., 1996; Higley and Linnoila, 1997; Schalling and Åsberg, 1997). Different hypothetic explanations have been proposed to account for the association between cholesterol and aggression, violence and suicidal behaviors. It has been suggested that reduced plasma cholesterol could suppress the cholesterol/phospholipid ratio in neuronal membranes with consequent alterations in membrane fluidity, viscosity and function, including serotonin (5-HT) receptors and serotonergic neurotransmission (Hawton et al., 1993). Moreover, phospholipase A_2 (PLA_2) and fatty acid coenzyme A ligase-4 (FACLs-4), which are involved in lipid metabolism, are two key enzymes in the signal transduction processes following the activation of various receptors, e.g. 5-HT_2, which may be involved in the pathophysiology of both violence and suicide attempts (Horrobin, 1999). In another study (Atmaca et al., 2002a), we demonstrated that patients with borderline personality disorder had lower cholesterol and leptin levels than healthy controls and speculated that low serum cholesterol and leptin levels might be associated with all dimensions of the disorder, impulsivity, aggression and suicidality, but were not associated with the presence and the severity of comorbid depression. Therefore, the explanations mentioned above confirm our important finding in the present study that low serum cholesterol levels are related to two dimensions of suicide attempts, suicidality and violence, in contrast to Alvarez et al. (2000), who found serum cholesterol levels are associated with the violence of the suicide attempt and not the suicide attempt itself. A positive correlation between serum leptin concentration and total cholesterol was found by (Kaplan, 1998), in agreement with the present study. There has been shown to be an interaction between leptinergic and serotonergic systems in the central nervous system (Leibowitz and Alexander, 1998), and leptin administration has been observed to stimulate serotonin turnover (Calapai et al., 1999). In addition, low serotonin activity has been implicated in impulsivity and aggressive and suicidal behavior (Roy and Linnoila, 1988). Therefore, these relationships have allowed us to consider that leptin may be associated with violent and non-violent suicide attempts, although, in suicide attempts, the exact roles of cholesterol, leptin and serotonin, which appear to be related to one another, have yet to be determined.

The main limitations of the present study include the small sample size, differences in economic and dietary status that might affect the serum total cholesterol and leptin levels, and our failure to use a structured scale to assess violence. It should be noted that we are not aware of, for example, the effect of the menstrual cycle on the biological parameters studied.

In summary, our results suggest that suicide attempters have significantly lower total serum cholesterol and leptin levels compared to healthy controls, and that the difference appears to be more obvious in violent suicide attempters compared to non-violent suicide attempters, suggesting low serum cholesterol and leptin levels are related to two dimensions of suicide attempts, suicidality and violence. However, further studies with larger numbers of patients are required.

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