

Serum Cholesterol and Leptin Levels in Patients with Borderline Personality Disorder

Murad Atmaca^a Murat Kuloglu^a Ertan Tezcan^a Omer Gecici^a
Bilal Ustundag^b

Departments of ^aPsychiatry and ^bBiochemistry, Firat University, School of Medicine, Elazig, Turkey

Key Words

Cholesterol · Leptin · Suicide · Borderline personality disorder · Impulsivity

Abstract

The association between low or lowered cholesterol and impulsivity, aggressive behaviours and suicide remains controversial. In the present study, cholesterol and leptin levels of patients with borderline personality disorder in whom impulsivity, aggressive behaviours and suicide attempts are clearly established have been compared with those of healthy controls. The study group consisted of 16 patients with borderline personality disorder and 16 healthy controls. All patients were assessed with the Barratt Impulsivity Scale (BIS), Buss-Durkee Hostility Inventory (BDHI) and Hamilton Depression Rating Scale (HDRS). Fasting serum cholesterol and leptin levels were measured. The mean cholesterol and leptin levels of the patient group were significantly lower than those of the controls. Likewise, the patients with current suicidal thoughts and a history of suicide attempt had statistically significantly lower cholesterol and leptin levels compared with the patients without those features. There was an inverse correlation between both cholesterol and

leptin levels, and impulsivity as determined by the BIS or aggression as determined by the BDHI, but no correlation between both cholesterol and leptin levels and the HDRS was found in the patients. In conclusion, the present study demonstrates that the patients with borderline personality disorder have lower cholesterol and leptin levels than healthy controls. Low serum cholesterol and leptin levels are associated with all dimensions of the disorder – impulsivity, aggression and suicidality – but are not associated with the presence and the severity of comorbid depression.

Copyright © 2002 S. Karger AG, Basel

Introduction

Low or pharmacologically lowered serum cholesterol has been associated with impulsivity, aggressive behaviours and suicide for a long time [1, 2]. A relationship between low cholesterol levels and violence has been found in persons not undergoing cholesterol-lowering procedures, such as criminals with antisocial personality disorder [3] and aggressive conduct disorder [4]. In contrast, Stewart and Stewart [5] reported that cholesterol and aggressive behaviours are not related.

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2002 S. Karger AG, Basel
0302-282X/02/0454-0167\$18.50/0

Accessible online at:
www.karger.com/journals/nps

Dr. Murad Atmaca
Firat (Euphrates) Üniversitesi, Firat Tıp Merkezi
Psikiyatri Anabilim Dalı, 23119 Elazığ (Turkey)
Tel. +90 424 2333555/2282 2300, Fax +90 424 2387688
E-Mail matmaca_p@yahoo.com

Leptin is a fat cell-derived hormone that signals nutritional status to the hypothalamus, regulates weight and sexual behaviour [6] and has been discovered by Zhang et al. [7] as the product of the *ob* gene. It has been reported that leptin affects the intracellular lipid concentration by diminishing the synthesis of fatty acid and triglycerides and increasing the lipid oxidation [8].

Suicide and impulsive-aggressive behaviours have been observed in patients with deficient serotonergic neurotransmission. This association has motivated researchers to evaluate whether there is a relationship between serotonin indices (prolactin and cortisol responses to *d*-fenfluramine) and serum cholesterol [2]. An interaction between leptinergic and serotonergic systems was demonstrated in the central nervous system [9] and a positive correlation was found between serum leptin concentration and total cholesterol, LDL-cholesterol, triglyceride and percentage of body fat [10–12]. This has prompted us to assess the relationship between leptin and suicide, impulsivity and aggressive behaviour. Therefore, we decided to measure total serum cholesterol and leptin levels in patients with borderline personality disorder characterized by aggressive behaviour, impulsivity and suicide attempts and hypothesized that those patients might have lower serum cholesterol and leptin levels compared with healthy controls.

Method

Subjects

The study included 16 patients (aged 18–49 years) who had applied to the Firat University, School of Medicine, Department of Psychiatry, Elazig, Turkey and had been diagnosed with borderline personality disorder according to the DSM-III-R criteria. The research protocol was approved by the ethics committee of the Firat University. Written consent to participate in the study was obtained from the subjects after they had been thoroughly informed about the research details.

Each patient underwent diagnostic evaluation by a trained psychiatrist using a structured interview for the DSM-III-R outpatient form (SCID-OP) [13] and a structured clinical interview for the DSM-III-R personality disorders (SCID-II) [14]. Patients with any kind of axis I or II comorbidity were excluded. However, patients with a current or past history of major depressive disorder, such as axis I disorder, were not excluded from the study because such disorders are frequently associated with borderline personality disorder. Additionally, all patients were assessed by the 21-item Hamilton Depression Rating Scale (HDRS) [15], Barratt Impulsivity Scale (BIS) [16] and Buss-Durkee Hostility Inventory (BDHI) [17]. All subjects were drug free for 2 weeks. Exclusion criteria were as follows: the presence of a severe physical illness, a history of alcohol and substance abuse or dependence, a previous history of cholesterol-lowering treatment, the presence of any endocrinological disorder or the

absorption of any psychotropic medication within the last 2 weeks. All participants were carefully assessed to rule out autoimmune, pulmonary, infectious diseases and neoplasms. The body mass index (BMI) was calculated by dividing the patients' weight (in kilograms) by the squared height (in meters) ($BMI = kg/m^2$).

Sixteen healthy control subjects were chosen among the hospital staff. They did not take any psychotropic medication, nor did they have any history of psychiatric disorder or suicide attempt. The controls were interviewed with the non-patient version of the SCID (SCID-NP) [18] and SCID-II to exclude any axis I and II disorder. After providing a complete description of the study to the subjects, written informed consent was obtained from each control.

Determination of Serum Leptin and Total Cholesterol

The patients and controls fasted overnight. Venous blood samples were drawn from the antecubital vein at 08.00 a.m. to determine the serum levels of leptin and cholesterol. The leptin levels were measured with the Linco rat leptin kit (Linco Corp., St. Charles, Mo., USA) radioimmunoassay in an LKB Wallac Multigamma counter 1261 (Wallac Corp., Turku, Finland). Total cholesterol levels were assayed using a Randox total cholesterol kit (Randox Laboratories Ltd., UK) and an Olympus AU 600 autoanalyzer (Olympus Corp., Japan).

Statistical Analysis

Statistical analysis was performed with the statistical package for social sciences (SPSS/PC 9.05 version, 1998). In the statistical analysis, the Student *t* test, analysis of covariance and Pearson's correlation test were used. Differences were considered significant at the $p < 0.05$ level for all these tests.

Results

The patients and controls did not differ with respect to sociodemographic characteristics ($p > 0.05$). Of the patients, 6 (37.5%) had comorbid major depressive disorder and 7 (43.8%) a history of suicide attempt and current suicidal thought. The mean HDRS score was 16.9 ± 5.4 for the patients and 5.6 ± 2.3 for the controls ($p < 0.05$). The mean BMIs were 23.6 ± 3.8 and 24.2 ± 3.6 for the patients and controls, respectively ($p > 0.05$).

The cholesterol levels were decreased in 9 (56.3%) of the patients and in 1 (6.3%) of the controls, when individually compared with normal cholesterol levels adjusted for BMI and sex. The mean cholesterol levels in the patient group and controls were 155.88 ± 11.45 and 182.01 ± 17.42 mg/dl, respectively. A significant difference in mean serum cholesterol levels between the patients and controls was found in the analysis of covariance after BMI or age adjustment ($F = 3.29$, $p < 0.05$ adjusted for BMI; $F = 3.08$, $p < 0.05$ adjusted for age). In addition, when comparing the mean cholesterol levels between sexes within each group, no statistically significant difference was found ($p = 0.5$). The mean cholesterol levels in

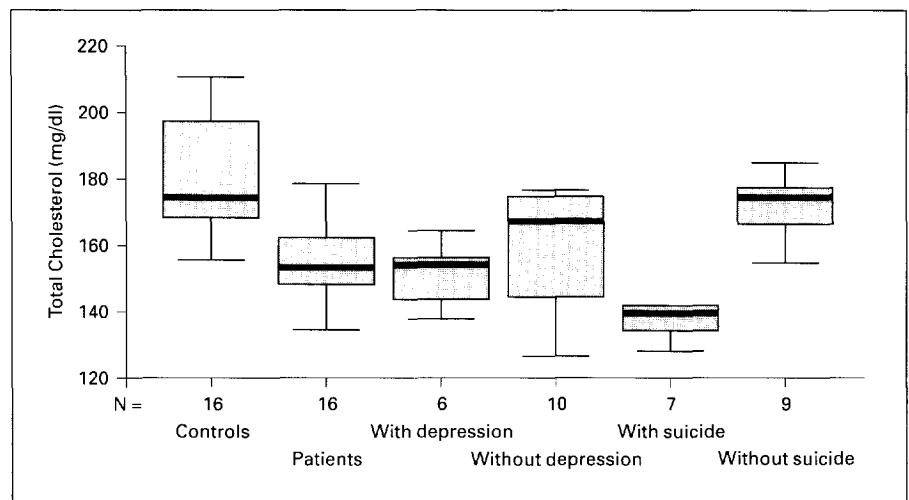


Fig. 1. Distribution of cholesterol levels in the groups as box plot.

patients with ($n = 7$) and without ($n = 9$) a history of suicide attempt and current suicidal thought were 141.29 ± 12.82 and 170.56 ± 13.83 mg/dl, respectively. A significant difference in mean serum cholesterol levels between patients with and without a history of suicide attempt and current suicidal thought was found in the analysis of covariance after BMI or age adjustment ($F = 3.92$, $p < 0.05$ adjusted for BMI; $F = 3.79$, $p < 0.05$ adjusted for age). The mean cholesterol levels in patients with ($n = 6$) and without ($n = 9$) major depression were 152.17 ± 9.66 and 159.50 ± 19.33 mg/dl, respectively. Analysis of covariance after age or BMI adjustment revealed no differences in mean serum cholesterol levels between patients with and without major depression ($F = 0.06$, $p > 0.05$ adjusted for BMI; $F = 0.28$, $p > 0.05$ adjusted for age).

The leptin levels were decreased in 11 (45.8%) of the patients and in 1 (8.3%) of the controls, when individually compared with normal leptin levels adjusted for BMI and sex. The mean leptin levels in the patient group and controls were 10.56 ± 3.05 and 26.13 ± 5.06 ng/ml, respectively. A significant difference in mean serum leptin levels between the patients and controls was found in the analysis of covariance after BMI or age adjustment ($F = 8.78$, $p < 0.001$ adjusted for BMI; $F = 7.02$, $p < 0.001$ adjusted for age). In addition, when comparing the mean leptin levels between sexes and within each group, no statistically significant difference was found despite a higher level in females in both groups ($p = 0.6$). The mean leptin levels in patients with and without a history of suicide attempt and current suicidal thought were 7.43 ± 3.87 and 14.56 ± 4.53 ng/ml, respectively. A significant difference in mean leptin levels between the patients with and without a his-

tory of suicide attempt and current suicidal thought was found in the analysis of covariance after BMI or age adjustment ($F = 3.92$, $p < 0.05$ adjusted for BMI; $F = 3.78$, $p < 0.05$ adjusted for age). The mean leptin levels in patients with and without major depression were 10.29 ± 3.12 and 10.80 ± 3.46 ng/ml, respectively. Analysis of covariance after age or BMI adjustment revealed no differences in mean serum cholesterol levels between patients with and without current major depression ($F = 0.03$, $p > 0.05$ adjusted for BMI; $F = 0.12$, $p > 0.05$ adjusted for age).

There was a positive correlation between cholesterol and leptin levels in both groups ($r = 0.39$, $p < 0.01$; $r = 0.42$, $p < 0.01$ for the patient and control group, respectively). However, cholesterol and leptin levels in both groups were not correlated with severity of depression, as determined by the HDRS (patients without major depressive disorder: $r = -0.08$, $p = 0.52$; patients with major depressive disorder: $r = -0.11$, $p = 0.25$; controls: $r = 0.03$, $p = 0.68$).

There was an inverse correlation between cholesterol levels and the BIS ($r = -0.42$, $p < 0.05$) or the BDHI ($r = -0.66$, $p < 0.01$) for the patient group. Likewise, both the BIS ($r = -0.38$, $p < 0.05$) and the BDHI ($r = -0.70$, $p < 0.01$) for the patient group correlated negatively with leptin levels.

The distribution of leptin and cholesterol levels in the groups is presented in figures 1 and 2 as box plot (patients and controls, patients with and without a history of suicide attempt and patients with and without current major depression).

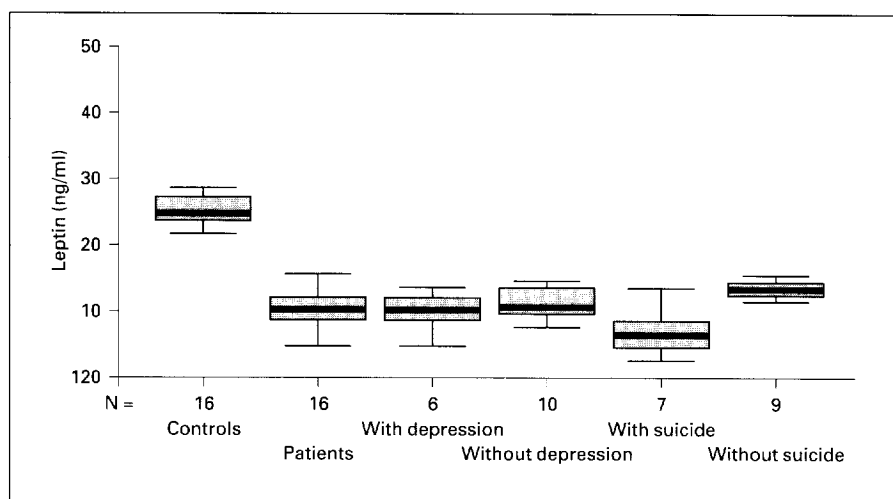


Fig. 2. Distribution of leptin levels in the groups as box plot.

Discussion

As far as we know, this is the first study regarding leptin levels in patients with borderline personality disorder. The main findings of our study are as follows: (1) patients with borderline personality disorder have statistically significantly decreased mean total serum cholesterol and leptin levels compared with controls, (2) both total serum cholesterol and leptin levels are negatively correlated with impulsivity and impulsive aggression, as determined by the BIS and BDHI, respectively, but are not correlated with the presence and the severity of comorbid depression, (3) patients with current suicidal thoughts and a past history of a suicide attempt have significantly lower mean cholesterol and leptin levels.

New et al. [19] reported that patients with borderline personality disorder had lower serum cholesterol levels compared with patients with other personality disorders although no significant relationship was found between serum cholesterol levels and impulsivity or aggression, and no significant difference with respect to the mean serum cholesterol between those with and without suicide attempt was found. In another study performed by Huang and Wu [20], it was reported that schizophrenic patients using physical violence had lower serum cholesterol levels than those not using physical violence although the difference was not statistically significant. Alvarez et al. [21] suggested that low serum cholesterol might be associated with the violence of a suicide attempt and not with the suicide attempt itself. In their previous study, Alvarez et al. [22] had suggested that low serum cholesterol levels might rather reflect the dimension of suicidality or vio-

lence than that of impulsivity. In our study, all dimensions – impulsivity, aggression and suicidal behaviour – seem to be associated with low serum cholesterol and leptin levels. However, both low cholesterol and leptin levels do not seem to be associated with the presence or the severity of depression. Different hypotheses support the association between cholesterol and aggression, violence and suicidal behaviours. It was reported that low cholesterol might influence neuronal membrane fluidity and consequently the availability of serotonergic receptors [23]. It was proposed that this relationship might result in reduced 5-HT neuronal activity by actions at both presynaptic and postsynaptic sites and that this reduced central serotonergic activity might be associated with impulsive aggression and suicidal behaviour [24, 25].

Our study confirms the positive correlation between serum leptin concentration and total cholesterol reported in the literature [10–12]. In our study, the patients with borderline personality disorder had decreased serum cholesterol and leptin levels compared with the controls. An interaction between leptinergic and serotonergic systems was demonstrated in the central nervous system [9]. Fluoxetine, a selective serotonin reuptake inhibitor, was reported to reduce plasma leptin levels in rats [26] and it was noted that leptin administration stimulated serotonin turnover [27]. On the other hand, reduced serotonin activity was implicated in impulsivity and aggressive and suicidal behaviour [24, 28]. Kaplan et al. [29] reported decreased serum cholesterol levels and cerebrospinal fluid (CSF) concentrations of 5-hydroxyindoleacetic acid in primates given a low-fat diet. They proposed that serum cholesterol could affect serotonin metabolism. However,

in a study in which the relationship between serum cholesterol and platelet serotonin content was evaluated, Alvarez et al. [22] found that although both parameters were lower in suicidal patients compared with healthy controls, there was no significant correlation between these parameters. Likewise, Ringo et al. [30] suggested that there was no clear relationship between serum cholesterol and CSF 5-hydroxy-indoleacetic acid concentrations. There has been a dearth of evidence concerning an association between suicide and impulsive aggressive behaviours, and cholesterol, leptin and serotonin.

Several limitations should be taken into consideration when interpreting our results. First, the relatively small sample size might not be representative of a borderline personality disorder population. Apart from this, we

could not test if poor economic status and other psychosocial factors might be related to serum total cholesterol or leptin levels.

In summary, our results suggest that patients with borderline personality disorder have statistically significantly decreased mean total serum cholesterol and leptin levels compared with healthy controls and that low serum cholesterol and leptin levels are associated with all dimensions of the disorder, i.e., impulsivity, aggression and suicidality, but are not associated with the presence and severity of comorbid depression. However, further investigations including serotonin indices are required to decipher the exact roles of leptin and cholesterol in borderline personality disorder.

References

- Muldoon MF, Manuck SB, Matthews KA: Lowering cholesterol concentrations and mortality: A quantitative review of primary prevention trials. *BMJ* 1990;301:309–314.
- Sarchiapone M, Camardese G, Roy A, Della Casa S, Satta MA, Gonzalez B, Berman J, De Risio S: Cholesterol and serotonin indices in depressed and suicidal patients. *J Affect Dis* 2001;62:217–219.
- Virkkunen M: Serum cholesterol in antisocial personality disorder. *Neuropsychobiology* 1979;5:27–30.
- Virkkunen M, Penttinen H: Serum cholesterol in aggressive conduct disorder: A preliminary study. *Biol Psychiatry* 1984;19:435–439.
- Stewart MA, Stewart SG: Serum cholesterol in antisocial personality. A failure to replicate earlier findings. *Neuropsychobiology* 1981;7:9–11.
- Prolo P, Wong ML, Licinio J: Leptin. *Int J Biochem Cell Biol* 1998;30:1285–1290.
- Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM: Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994;372:425–432.
- Auwerx J, Staels B: Leptin. *Lancet* 1998;351:737–742.
- Leibowitz SF, Alexander JT: Hypothalamic serotonin in control of eating behavior, meal size, and body weight. *Biol Psychiatry* 1998;44:851–864.
- Sinha MK: Human leptin: The hormone of adipose tissue. *Eur J Endocrinol* 1997;136:461–464.
- Haynes WG, Sivitz WI, Morgan DA, Walsh SA, Mark AL: Sympathetic and cardiorenal actions of leptin. *Hypertension* 1997;30:619–623.
- Kaplan LM: Leptin, obesity, and liver disease. *Gastroenterology* 1998;115:997–1001.
- Spitzer RL, Williams JBW, Gibbon M, First MB: Structured Interview for DSM-III-R (SCID). New York, Biometrics Research, 1987.
- Spitzer RL, Williams JBW, Gibbon M, First MB: Structured Interview for DSM-III-R Personality Disorders (SCID-II). New York, Biometrics Research, 1990.
- Hamilton M: A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62.
- Barratt ES, Patton JH: Impulsivity: Cognitive, behavioral, and psychological correlates; in Zuckerman M (ed): *Biological Basis of Sensation-Seeking, Impulsivity, and Anxiety*. Hillsdale, Lawrence Erlbaum, 1983.
- Buss AH, Durkee A: An inventory for assessing different kinds of hostility. *J Consult Psychol* 1957;21:343–348.
- Spitzer RL, Williams JBW, Gibbon M, First MB: Structured Interview for DSM-III-R, Nonpatient Version (SCID-NP, Version 1.0). Washington, American Psychiatric Association, 1990.
- New AS, Sevin EM, Mitropoulou V, Reynolds D, Novotny SL, Callahan A, Trestman RL, Siever LJ: Serum cholesterol and impulsivity in personality disorders. *Psychiatry Res* 1999;85:145–150.
- Huang TL, Wu S: Serum cholesterol levels in paranoid and non-paranoid schizophrenia associated with physical violence or suicide attempts in Taiwanese. *Psychiatry Res* 2000;96:175–178.
- Alvarez J-C, Cremniter D, Gluck N, Quintin P, Leboyer M, Berlin I, Therond P, Spreux-Varoquaux O: Low serum cholesterol in violent but not in non-violent suicide attempters. *Psychiatry Res* 2000;95:103–108.
- Alvarez J-C, Cremniter D, Lesieur P, Gregoire A, Gilton A, Macquin-Mavier L, Jarreau C, Spreux-Varoquaux O: Low blood cholesterol and low platelet serotonin levels in violent suicide attempts. *Biol Psychiatry* 1999;45:1066–1069.
- Heron DS, Shinitzky M, Hershkowitz M, Samuel D: Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. *Proc Natl Acad Sci USA* 1980;77:7463–7467.
- Brown GL, Ebert MH, Goyer PF, Jimerson DC, Klein WJ, Bunney WE, Goodwin FK: Aggression, suicide, and serotonin: Relationships to CSF amine metabolites. *Am J Psychiatry* 1982;139:741–746.
- Coccaro EF, Siever LJ, Klar HM, Maurer G, Cochrane K, Cooper TB, Mohs RC, Davis KL: Serotonergic studies in patients with affective and personality disorders. Correlates with suicidal and impulsive-aggressive behavior. *Arch Gen Psychiatry* 1989;46:587–599.
- Dryden S, Brown M, King P, Williams G: Decreased plasma leptin levels in lean and obese Zucker rats after treatment with the serotonin reuptake inhibitor fluoxetine. *Horm Metab Res* 1999;31:363–366.
- Calapai G, Corica F, Corsonello A, Sautebin L, Di Rosa M, Campo GM, Buemi M, Mauro VN, Caputi AP: Leptin increases serotonin turnover by inhibition of brain nitric oxide synthesis. *J Clin Invest* 1999;104:975–982.
- Roy A, Linnoila M: Suicidal behavior, impulsiveness and serotonin. *Acta Psychiatr Scand* 1988;78:529–535.
- Kaplan J, Muldoon M, Manuck S, Mann JJ: Assessing the observed relationship between low cholesterol and violence-related mortality. Implications for suicide risk. *Ann NY Acad Sci* 1997 832:57–59.
- Ringo LD, Lindley SE, Faull KF, Faustman WO: Cholesterol and serotonin: Seeking a possible link between blood cholesterol and CSF 5-HIAA. *Biol Psychiatry* 1994;62:217–219.