

Serum Leptin and Cholesterol Values in Suicide Attempters

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

Departments of ^aPsychiatry and ^bBiochemistry, Medical Faculty, Firat University, Elazig, Turkey

Key Words

Leptin · Cholesterol · Suicide

Abstract

The growing number of studies examining the relationship between suicide and lipid metabolism are based upon studies suggesting that cholesterol-lowering procedures may increase the risk of death due to suicide or impulsive-aggressive behavior. Leptin seems to be strongly associated with lipid metabolism. In the present study, serum total cholesterol and leptin levels were compared in 24 suicide attempters and 24 healthy controls. The patients with suicide attempts had significantly lower serum cholesterol and leptin levels than controls. There was a positive correlation between cholesterol and leptin levels in both groups. Our results suggest that suicide attempts seem to be associated with decreased serum cholesterol and leptin levels.

Copyright © 2002 S. Karger AG, Basel

Introduction

The growing number of studies examining the relationship between suicide and lipid metabolism are based upon studies suggesting that cholesterol-lowering proce-

dures may increase the risk of death due to suicide or impulsive-aggressive behavior [1–3]. Low cholesterol values have been associated with a variety of psychiatric-disorder-related suicide and impulsive-aggressive behaviors, e.g. intermittent explosive disorder [4], attention deficit disorder [5] and antisocial personality disorder [6]. In a study by Stewart and Stewart [7] no relationship between cholesterol and aggressive behaviors was found. Maes et al. [8] however revealed a relationship between decreased serum cholesterol and suicide attempts only in psychiatric patients with violent suicide attempts.

Leptin is an adipocyte hormone regulating food intake and energy balance, providing the hypothalamus with information on the amount of body fat [9], and was discovered by Zhang et al. [10] as the product of the *ob* gene. Leptin is released from white adipose tissue and some other tissues including brown adipose tissue, adipose cells of the bone marrow, the human placenta and epithelial cells of the stomach and breast tissue [11]. Plasma levels of leptin are considerably correlated with body mass index (BMI) and percent body fat. It has been reported that leptin affects the intracellular lipid concentration via a decrease in the synthesis of fatty acid and triglycerides and an increase in lipid oxidation [12]. On the other hand, a positive correlation has been shown between serum leptin concentration and total and LDL cholesterol, triglycerides and percent body fat [13–15]. Therefore, leptin may

KARGER

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

© 2002 S. Karger AG, Basel
0302-282X/02/0453-0124\$18.50/0

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

Yrd. Doç. Dr. Murad Atmaca
Firat (Euphrates) Üniversitesi, Firat Tıp Merkezi
Psikiyatri Anabilim Dalı
TR-23119 Elazig (Turkey)
Tel. +90 424 233 3555/2282 2300, Fax +90 424 2387688, E-Mail matmaca_p@yahoo.com

Table 1. Mean leptin and cholesterol levels and characteristics of the patients and controls

	Patients (n = 24)	Controls (n = 24)	p value
Age	28.6 ± 14.2	29.1 ± 13.3	p > 0.05
Sex, females/males	14/10	13/11	p > 0.05
Psychiatric diagnosis			
Borderline personality disorder	4	–	p < 0.05
Major depressive disorder	11	–	p < 0.001
Alcohol dependence	2	–	p > 0.05
Schizophrenia	4	–	p < 0.05
Bipolar disorder-manic episode	3	–	p > 0.05
Leptin, ng/ml	10.18 ± 5.28	25.54 ± 6.87	p < 0.001
Total serum cholesterol, mg/dl	152.26 ± 14.39	186.44 ± 32.56	p < 0.05
BMI, kg/m ²	23.6 ± 3.8	24.2 ± 3.6	p > 0.05

be associated with suicidal intention and attempts. For this reason, we decided to measure serum total cholesterol and leptin levels in suicidal patients.

Patients and Methods

Patients

The study consisted of 24 patients with suicide attempts (aged 18–58 years) who had consecutively been admitted to the Emergency Unit of the Firat University School of Medicine and then referred to the Department of Psychiatry by a psychiatrist (O.G.) between March and September 2001. All patients were subsequently admitted to a psychiatry clinic. After complete description of the study to the subjects, informed consent was obtained from each patient. The study was approved by a local ethics committee of the Firat University Medical School. In all the patients, clinical evaluation was performed by one trained psychiatrist within 2 days after admission. A semi-structured interview was carried out in order to establish DSM-IV diagnosis. Exclusion criteria included the presence of a severe physical illness, the history of alcohol and substance abuse or dependence, a previous history of cholesterol-lowering treatment, the presence of any endocrinological state and treatment with any psychotropic medication within the last 2 weeks. All subjects were evaluated by a semi-structured questionnaire form which was arranged by us in accordance with clinical experience and available information sources. In addition, BMI was calculated by dividing the weight by the squared height ($BMI = kg/m^2$).

Controls

Twenty-four staff members were included in the control group. They were free of any psychotropic medication, without any history of psychiatric disorder and suicide attempt. In addition, none of them had ever undergone a cholesterol-lowering treatment.

Determination of Total Cholesterol and Leptin

To determine serum levels of leptin and cholesterol, venous blood samples were obtained at 08.00 a.m. Leptin levels were measured

using the Linco rat leptin kit (Linco, St. Charles, Mo., USA) radioimmunoassay method using an LKB Wallac Multi gamma counter 1261 (Wallac, Turku, Finland). Total cholesterol levels were measured using an Olympus AU 600 autoanalyzer (Olympus, Japan) Randox total cholesterol kit (RANDOX Laboratories, UK).

Statistical Analysis

Statistical analysis was performed using the statistical package for social sciences (SPSS/PC 9.05 version, 1998). Student's test was used for the mean leptin and cholesterol levels and some characteristics of the patients and controls. The χ^2 test was used to compare the diagnoses between groups. Correlation analysis was performed by Pearson's correlation test. Differences were considered significant at $p < 0.05$ for all these tests.

Results

General characteristics of the patients and controls are summarized in table 1. There were no significant differences between groups regarding age, sex and the frequency of psychiatric disorders. Thirteen patients (54.2%) were violent suicide attempters whereas 11 (45.8%) were non-violent suicide attempters.

Cholesterol levels were decreased in 13 (54.2%) patients and in 1 (4.2%) control, when individually compared with normal cholesterol levels adjusted for BMI and gender. The mean cholesterol levels in suicidal patients and controls were 152.26 ± 14.39 and 186.44 ± 32.56 mg/dl, respectively. The mean level of the patients was significantly lower than that of the controls ($p < 0.05$). Likewise, when comparing the mean cholesterol level between sexes within each group, no statistically significant difference was found ($p = 0.04$).

The leptin levels were decreased in 11 (45.8%) patients and in 1 (8.3%) control, when individually compared with normal leptin levels adjusted for BMI and gender. The mean leptin levels in the patient and control groups were 10.18 ± 5.28 and 25.54 ± 6.87 ng/ml, respectively. The mean level for the patients was significantly lower than that for the controls ($p < 0.001$). Likewise, when comparing the mean leptin level between sexes and within each group, no statistically significant difference was found ($p < 0.03$).

There was a positive correlation between the mean cholesterol and leptin levels in both groups ($r = 0.41$, $p < 0.01$; $r = 0.38$, $p < 0.01$ for patients and controls, respectively).

The mean BMIs were 23.6 ± 3.8 and 24.2 ± 3.6 for the patients and controls, respectively ($p > 0.05$). There was no correlation between the mean cholesterol level and age ($r = 0.08$, $p = 0.53$), sex ($r = 0.06$, $p = 0.44$) for the entire sample, or the type of psychiatric disorder ($r = 0.07$, $p = 0.49$) for the patients. There was no correlation between the mean leptin level and age ($r = 0.12$, $p = 0.23$), sex ($r = 0.16$, $p = 0.20$) for the sample, or the type of psychiatric disorder ($r = 0.09$, $p = 0.62$) for the patient group.

Discussion

To the best of our knowledge, this is the first study on leptin levels in suicide attempters. The major findings of our study are as follows: (1) suicide attempters have a marked decrease in serum cholesterol and leptin levels compared to controls, and (2) there was a positive correlation between the mean cholesterol and leptin levels.

The studies performed in psychiatric patients implicated an association between low cholesterol levels and suicide attempts [16, 17]. With respect to diagnostic categories, the relationship was determined in personality and neurotic disorders, depressive disorders and male inpatients with serious suicide attempts [16, 17]. However, some authors reported this relationship merely occurring in patients with violent suicide attempts [8]. For this reason, the association between suicide and cholesterol remained subject to controversy.

A positive correlation between serum leptin concentration and total cholesterol has been determined [13–15], which has been supported by this study. Therefore, we hypothesize that leptin may be associated with suicidal intention and attempts. In the present study, suicide attempters have a marked decrease in serum cholesterol

and leptin levels compared to controls. An interaction between leptinergic and serotonergic systems in the central nervous system has been shown [18]. Fluoxetine, a selective serotonin reuptake inhibitor, has been reported to reduce plasma leptin levels in rats [19] and it has been noted that leptin administration stimulated serotonin turnover [20]. On the other hand, reduced serotonin activity has been implicated in impulsivity and aggressive and suicidal behavior [21, 22]. Examining the association between serotonin metabolism and serum cholesterol, low serum cholesterol levels have been found in men with lower plasma serotonin concentrations [23]. However, Alvarez et al. [24] evaluated the relationship between serum cholesterol and platelet serotonin content. They found that although both parameters were lower in suicidal patients compared to healthy controls, there was no significant correlation between these parameters. The exact roles of cholesterol, leptin and serotonin, which seem to be related with each other, have been obscured due to the lack of investigations.

The results of the present study suggest that suicide attempts seem to be associated with decreased serum cholesterol and leptin levels. However, more comprehensive studies dealing with leptin, cholesterol and indices of serotonin altogether in suicidal patients are needed.

References

- 1 Frick MH, Elo O, Haapa K, Heinonen OP, Heinsalmi P, Huttunen JK, Kaitaniemi P, Koskinen P, Manninen V: Helsinki heart study primary prevention trial with gemfibrozil in middle-aged men with dyslipidemia: Safety of treatment, changes in risk factors, and incidence of coronary heart disease. *N Engl J Med* 1987;317:1237-1245.
- 2 Muldoon MF, Manuck SB, Mathews KA: Lowering cholesterol concentrations and mortality: A quantitative review of primary prevention trials. *BMJ* 1990;301:309-314.
- 3 Sarchiapone M, Camardese G, Roy A, Casa SD, Satta MA, Gonzalez B, Berman J, Risio SD: Cholesterol and serotonin indices in depressed and suicidal patients. *J Affect Disord* 2001;62:217-219.
- 4 Virkkunen M, Penttinen H: Serum cholesterol in aggressive conduct disorder: A preliminary study. *Biol Psychiatry* 1984;19:435-439.
- 5 Virkkunen M: Serum cholesterol levels in homicidal offenders. A low cholesterol level is connected with a habitually violent tendency under the influence of alcohol. *Neuropsychobiology* 1983;10:65-69.
- 6 Freedman DS, Byers T, Barrett DH, Stroup NE, Eaker E, Monroe-Blum E: Plasma lipid levels and psychologic characteristics in men. *Am J Epidemiol* 1987;141:507-517.
- 7 Stewart MA, Stewart SG: Serum cholesterol in antisocial personality: A failure to replicate earlier findings. *Neuropsychobiology* 1981;7:9-11.
- 8 Maes M, Sharpe P, D'Hondt P, Pecters D, Wauters A, Neels H, Verkerk R: Biochemical metabolic and immune correlates of seasonal variation in violent suicide: A chronoepidemiologic study. *Eur Psychiatry* 1996;11:21-33.
- 9 Prolo P, Wong ML, Licinio J: Leptin. *Int J Biochem Cell Biol* 1998;30:1285-1290.
- 10 Zhang Y, Proenca R, Malfai M, Barone M, Leopold L, Friedman JM: Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994;372:425-432.
- 11 Himms-Hagen J: Psychological roles of the leptin endocrine system: Differences between mice and humans. *Crit Rev Clin Lab Sci* 1999;36:575-655.
- 12 Auwerx J, Steals B: Leptin. *Lancet* 1998;351:737-742.
- 13 Haynes WG, Sivitz WI, Morgan DA, Walsh SA, Mark AL: Sympathic and cardiorenal actions of leptin. *Hypertension* 1997;30:619-623.
- 14 Kaplan LM: Leptin, obesity, and liver disease. *Gastroenterology* 1998;115:997-1001.
- 15 Sinha M: Human leptin: The hormone of adipose tissue. *Eur J Endocrinol* 1997;136:461-464.
- 16 Kunugi H, Takei N, Aoki H, Nanko S: Low serum cholesterol in suicide attempters. *Biol Psychiatry* 1997;41:196-200.
- 17 Modai I, Valevski A, Dror S, Weizman A: Serum cholesterol levels and suicidal tendencies in psychiatric inpatients. *J Clin Psychiatry* 1994;55:252-254.
- 18 Leibowitz SF, Alexander JT: Hypothalamic serotonin in control of eating behavior, meal size, and body weight. *Biol Psychiatry* 1998;44:851-864.
- 19 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.
- 20 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.
- 21 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.
- 22 Roy A, Linnoila M: Suicidal behavior, impulsiveness and serotonin. *Acta Psychiatr Scand* 1988;78:529-535.
- 23 Steegmans P, Fekkes D, Hoes A, Bak A, Van Der Does E, Grobbee D: Low serum cholesterol concentration and serotonin metabolism in men. *BMJ* 1996;312:221.
- 24 Alvarez C, Creminter D, Lesieur P, Gregorie A, Gilton A, Macquin-Mavies L, Jarreau C, Spreux-Varoguaux O: Low blood cholesterol and low platelet serotonin levels in violent suicide attempters. *Biol Psychiatry* 1999;45:1066-1069.