

Total serum cholesterol levels and suicide attempts in child and adolescent psychiatric inpatients

Plana, Teresa; Gracia, R.; Méndez, I.; Pintor, L.; Lazaro, L.; Castro-Fornieles, J.

Postprint / Postprint

Zeitschriftenartikel / journal article

Zur Verfügung gestellt in Kooperation mit / provided in cooperation with:

www.peerproject.eu

Empfohlene Zitierung / Suggested Citation:

Plana, T., Gracia, R., Méndez, I., Pintor, L., Lazaro, L., & Castro-Fornieles, J. (2010). Total serum cholesterol levels and suicide attempts in child and adolescent psychiatric inpatients. *European Child & Adolescent Psychiatry*, 19(7), 615-619. <https://doi.org/10.1007/s00787-009-0084-x>

Nutzungsbedingungen:

Dieser Text wird unter dem "PEER Licence Agreement zur Verfügung" gestellt. Nähere Auskünfte zum PEER-Projekt finden Sie hier: <http://www.peerproject.eu>. Gewährt wird ein nicht exklusives, nicht übertragbares, persönliches und beschränktes Recht auf Nutzung dieses Dokuments. Dieses Dokument ist ausschließlich für den persönlichen, nicht-kommerziellen Gebrauch bestimmt. Auf sämtlichen Kopien dieses Dokuments müssen alle Urheberrechtshinweise und sonstigen Hinweise auf gesetzlichen Schutz beibehalten werden. Sie dürfen dieses Dokument nicht in irgendeiner Weise abändern, noch dürfen Sie dieses Dokument für öffentliche oder kommerzielle Zwecke vervielfältigen, öffentlich ausstellen, aufführen, vertreiben oder anderweitig nutzen.

Mit der Verwendung dieses Dokuments erkennen Sie die Nutzungsbedingungen an.

gesis
Leibniz-Institut
für Sozialwissenschaften

Terms of use:

This document is made available under the "PEER Licence Agreement". For more information regarding the PEER-project see: <http://www.peerproject.eu>. This document is solely intended for your personal, non-commercial use. All of the copies of this documents must retain all copyright information and other information regarding legal protection. You are not allowed to alter this document in any way, to copy it for public or commercial purposes, to exhibit the document in public, to perform, distribute or otherwise use the document in public.

By using this particular document, you accept the above-stated conditions of use.

Mitglied der

Leibniz-Gemeinschaft

Total serum cholesterol levels and suicide attempts in child and adolescent psychiatric inpatients

Teresa Plana · R. Gracia · I. Méndez · L. Pintor ·
L. Lazaro · J. Castro-Fornieles

Received: 4 February 2009 / Accepted: 4 December 2009 / Published online: 3 January 2010
© Springer-Verlag 2010

Abstract Associations between cholesterol and suicidal behavior in adolescent patients have not been explored in depth. In this study, 66 patients consecutively admitted to a psychiatric inpatient unit following attempted suicide were compared with a control group of 54 patients with no history of suicide attempts. The age range of the sample was from 8 to 18 years old. Cholesterol levels were significantly lower in attempted suicide patients than in controls ($p < 0.02$), supporting the hypothesis that lower cholesterol levels might be associated with suicidal

behavior in patients with similar acute phase of their disorder.

Keywords Suicide · Cholesterol · Adolescents · Child · Inpatients

Abbreviations

CSF Cerebrospinal fluid
5-HIAA 5-Hydroxyindolacetic acid
HVA Homovanillic acid

T. Plana (✉) · L. Lazaro · J. Castro-Fornieles
Child and Adolescent Psychiatry and Psychology Department,
Neurosciences Institute, Hospital Clinic Barcelona,
Centro Investigación Biomédica en Red de Salud Mental
(CIBER-SAM), C/Villarroel 170, 08036 Barcelona, Spain
e-mail: mtplana@clinic.ub.es

R. Gracia
Child and Adolescent Psychiatry Department,
Hospital Parc Taulí, Sabadell, Spain

I. Méndez
Alicia Koplowitz Foundation Fellowship, Department of Child
Psychiatry, University of Pittsburgh School of Medicine,
Pittsburgh, PA, USA

L. Pintor
Psychiatry Department, Neurosciences Institute,
Hospital Clínic Barcelona, Barcelona, Spain

L. Lazaro · J. Castro-Fornieles
Institut d'Investigacions Biomèdiques August Pi Sunyer
(IDIBAPS), Barcelona, Spain

L. Lazaro · J. Castro-Fornieles
Health Sciences Division, Psychiatry and Clinical Psychobiology
Department, University of Barcelona, Barcelona, Spain

Introduction

Suicide attempts occur in various psychiatric disorders, almost half of them (60%) in the context of depression [6]. For decades, psychiatrists have sought biological parameters to help them to determine and predict suicidal risk among their patients. Studies of cerebrospinal fluid (CSF) of depressed suicide attempters has identified lower 5-hydroxyindolacetic acid (5-HIAA) and homovanillic acid (HVA) levels in CSF and reduced HVA/5-HIAA ratio as useful biomarkers [7, 13, 16, 17, 28, 31]. Altered function of serotonin transporters and the 5HT₂ serotonin receptor also suggest a higher risk of suicidality [24, 29]. Although several studies have assessed the association between lower levels of cholesterol and suicide, the link between peripheral cholesterol and suicidal behavior remains unclear. One of the functions of serotonin in the central nervous system is to avoid harmful behavioral impulses. Engelberg's [10] theory related alterations in membrane microviscosity of cells with dysfunctions in serotonin neurotransmission, and Vevera et al. [34]

reported that lower cholesterol levels induced viscosity alterations in the cell membrane, with secondary serotonergic receptor alterations. Lower gray-matter cholesterol in some cortical brain areas has also been related with violent suicide completers [22].

This research generated a conceptual framework for molecular genetic studies on the association between genes encoding for lipid metabolism and those related to suicidality. However, a genetic study by Lalovic et al. [20] failed to report significant differences in allele or genotype frequencies of proteins involved in cholesterol biosynthesis and transport between suicide cases and controls. A recent study found that the ABCG1 transporter may influence aggression-related traits [14]. At all events, most research has focused on cholesterol serum levels and the findings have been inconsistent. Differences in the criteria used to classify patients as “suicidal” (only attempters, or subjects with suicidal ideation), and differences in criteria used to define the comparison group make results difficult to compare. Some studies have confirmed the association between lower levels of cholesterol and suicidality [2, 4, 9, 15, 19, 21, 23, 25, 27, 30, 35], while others find only a trend [32]. However, Tanskanen et al. [33] demonstrated the positive relationship of high serum total cholesterol concentration with increased risk of violent suicide. Deisenhammer et al. [8] found no significant differences in lipid levels between patients with and without suicide attempts, but noted a trend toward lower total cholesterol levels in patients who had used a violent method; Fiedorowicz and Coryell [12] reported no association between low cholesterol and subsequent suicide. Some of the studies compared suicidal psychiatric patients with the general population [3, 27, 30], while others compared suicidal and non-suicidal patients with the same psychiatric diagnosis [4, 11, 15, 18, 19, 25, 26]. To date, we have found no studies in adult patients that assess this relationship in composite samples with different psychiatric diagnoses, or that consider lower levels of cholesterol in association with suicide attempts independently of specific psychiatric disorders.

Focusing on adolescent psychiatric patients, only two studies have included adolescent psychiatric samples. Favaro et al. [11] reported an association between lower cholesterol levels and suicidality in anorexic patients. However, these results should be regarded with caution because of influences of nutritional variables on cholesterol levels in these patients. Apter et al. [1] found higher serum cholesterol levels in a group of patients with suicidal behavior in an adolescent inpatient sample with different psychiatric diagnoses. In this study, the group of patients with suicidal behavior included: patients with suicidal ideation without suicide attempts, patients with suicidal

tendencies and patients with suicide attempts. These authors also included eating disorder patients, who presented the highest serum cholesterol levels. In the suicidal behavior group, serum cholesterol correlated negatively with the degree of suicide behavior, suggesting perhaps that cholesterol levels could be inversely related with “acting”, that is, with the step from suicide ideation to suicide attempt. Following on from this research, the present study focuses only on adolescent suicide attempters and excludes patients with suicidal ideation only, to study a specific suicidality outcome group. The objective is to provide further information about the potential role of serum cholesterol levels in suicide attempters in a general sample of psychiatric adolescent patients admitted to a hospital unit.

Method

Subjects

This case–control retrospective study was conducted in the inpatient unit of a Child and Adolescent Psychiatry and Psychology Department (Hospital Clinic of Barcelona). Over a 4-year period (2004–2007), 66 patients (49 females and 17 males) were consecutively admitted following attempted suicide. For being included in the attempted suicide group, patients must have committed an attempt to kill themselves (a suicide attempt with suicide ideation). Patients presenting self harm behavior without suicidal intention were not included in this group. The control group included 54 patients (39 females and 15 males) who were also admitted to the inpatient unit during the same period but who had no history of suicide attempts. Control subjects (non-suicide attempts) were paired with case subjects (suicide attempts) according to psychiatric diagnosis, age and gender. If no control subject with the same psychiatric diagnosis was enrolled during the same year of study, the corresponding case subject was left without a control pair. We failed to control 11 depressive cases, because we found only 35 patients with depressive symptoms without a history of suicide attempts in previous admissions. Exclusion criteria for both groups included taking medication known to alter lipid metabolism, dyslipemia, eating disorders and body mass index <19 or current eating binges, to avoid cholesterol and nutritional alterations due to these disorders. Exclusion criteria for control group included any suicide attempt in the past or recently. Patients with suicide ideation or tanatic ideation without lifetime history of suicide attempts were not excluded. All attempted suicide patients did not have control pairs because of the exclusion criteria.

Procedures

Levels of cholesterol were obtained from the blood samples collected upon admission, after overnight fasting. All blood samples were measured by the same laboratory, using milligrams/deciliter (mg/dl). The normal range of total cholesterol at our hospital is defined as 148–247 mg/dl. The American Heart Association endorsed with guidelines of the National Cholesterol Education Program's Expert Panel on Blood Cholesterol in children and adolescents (from 2 to 19 years) and determines as correct total cholesterol levels as less than 170 mg/dl, borderline from 170 to 199 mg/dl and high from 200 mg/dl or greater. We did not find patients clearly outside the normal cholesterol range. Socio-demographic data, clinical diagnoses, psychotropic medication at admission in both groups and suicide methods used by the suicidal group were recorded. This study was approved by the Ethical Committee of Hospital Clinic of Barcelona. This study was retrospective and we did not have informed consent of the patients and their families. However, Ethical Committee approved the study because it did not imply any experimental procedure. The blood samples were obtained from the usual screening laboratory tests, carried out in all patients admitted at the hospitalization unit.

Data analysis

Results were analyzed using descriptive statistics. A Kolmogorov–Smirnov test was used to test for the normality of variables and then parametric tests were used, Student's *t* test for quantitative variables and χ^2 test for qualitative variables. Statistical analyses were performed using SPSS (14.0).

Results

Clinical characteristics and serum cholesterol levels in both groups of patients are listed and compared in the Table 1. There were no significant differences between the two groups with respect to gender, age or psychiatric diagnosis or in terms of antidepressant or antipsychotic medication at admission; nor were there significant differences between cholesterol levels in patients who were taking antipsychotic medication at admission and those who were not ($t = 0.8$, $df = 23.3$, $p = 0.37$), nor with respect to gender ($t = 1.7$, $df = 118$, $p = 0.08$). Levels of cholesterol were significantly lower in attempted suicide patients than in controls. When only patients with a diagnosis of depression were included, lower cholesterol levels were found in attempted suicide patients, though the difference was not statistically significant. If we focused on method of suicide attempts

and divide the suicide sample in two big groups, overdose-suicide attempt (more frequent method) and non-overdose suicide attempts, the differences in cholesterol levels were not statistically significant (overdose-suicide attempt: mean = 144.51, SD = 24.08; non-overdose suicide attempts: mean = 152.42, SD = 27.21; $t = 1.16$, $p = 0.249$). We do not find patients clearly outside the normal cholesterol range.

Discussion

This is the first study to point out an association between suicide attempts and low levels of cholesterol in a psychiatric adolescent inpatient sample with a range of psychiatric disorders. Psychometric measures of suicidality were not used in the study; however, confirmed and substantiated reports of suicide attempts were used as dependent variables rather than potentially biased self-reports or unsubstantiated verbal reports of suicidal behaviors.

This finding is similar to those of most adult studies that have reported this association. Mean serum total cholesterol level obtained in our subjects with suicide attempts was similar with those reported by Kim et al. [19], and was near the lower end of the range defined as normal at our hospital. The study was not designed to identify a cutoff point for cholesterol.

Although suicide risk is known to increase in the presence of a history of personal or family psychiatric disorders, it has been shown that liability to suicidal behavior—specifically, suicide attempts and completions—might be familial transmitted as a trait independent of psychiatric disorders [5]. As all subjects in our inpatient groups were in the acute period of their illness, our findings support the hypothesis that low levels of cholesterol might be associated with suicidal behavior. However, if lower blood cholesterol levels help to predict suicide, we may wonder whether this is the case in any psychiatric diagnosis. More studies are needed with larger samples, in which all psychiatric disorders are represented, to explore this issue further. The serotonin–suicide–cholesterol relationship might suggest that affective disorders involving serotonin system dysfunction would be the psychiatric illnesses with the highest rates of suicidality. However, studies with other psychiatric disorders have also found this association, raising the possibility that altered serotonin neurotransmission may also be linked with cholesterol and suicide with non-affective disorders. The findings are limited to psychiatric child and adolescent patients and may not be generalizable to other psychiatric patients.

Our study is limited due to the small sample size, which reduces the statistical power required to establish subgroups and to confirm the association between suicidal

Table 1 Clinical characteristics and serum cholesterol levels in both groups

	Suicide attempts group		No suicide attempts group		χ^2	<i>p</i>	
	<i>N</i>	%	<i>N</i>	%			
Gender: female	49	74.2	39	72.2	0.06	0.803	
Psychotropic medication at admission							
Antipsychotic	9	13.6	11	20.4	2.7	0.425	
Antidepressant	16	24.2	18	33.3	2.1	0.545	
Psychiatric diagnoses							
Depression	35	53	25	46.3	1.6	0.978	
Conduct disorder	20	30.4	20	37.1			
Bipolar disorder	4	6.1	3	5.6			
Schizophrenia	2	3	2	3.7			
Obsessive–compulsive disorder	2	3	2	3.7			
Personality disorders	1	1.5	1	1.8			
Eating disorders	1	1.5	1	1.8			
Mental retardation	1	1.5	0	0			
Method							
Drug overdose	47	71.2					
Fall from a height	9	13.7					
Wrist phlebotomy	4	6.1					
Hanging	2	3					
Caustic ingestion	1	1.5					
Electrocution	1	1.5					
Throwing oneself under a car	1	1.5					
Endovenous air injection	1	1.5					
		Mean	SD	Mean	SD	<i>t</i>	<i>p</i>
Age (years)		15.44	1.99	15.19	1.68	0.7	0.458
Cholesterol levels in total patients (mg/dL)		146.79	25.07	159.37	33.21	−2.3	0.02
Cholesterol levels in depressed patients (mg/dL)		148.43	26.7	164.6	41.25	−1.7	0.094

behavior and lower cholesterol levels in all psychiatric diagnoses separately. Other limitations are the fact that we did not monitor body mass index; patients were not assessed with structured psychometric tests for suicidality, and inferring causal relations with retrospective studies is also problematic. If this association is replicated from future studies with bigger samples and methodological designs for studying cholesterol levels as a risk factor, this parameter could help to add more information to the clinicians to evaluate suicidal risk of our patients, in a similar way as we asked for psychopathology and familiar variables. Further studies assessing the relationship between cholesterol-related biological and genetic factors and suicide-related clinical factors are required to establish the role of cholesterol in this complex human behavior.

Acknowledgments All the authors of the article state that there is no actual or potential conflict of interest for this publication. The authors would like to thank Child and Adolescent Psychiatry and Psychology Department of Hospital Clínic of Barcelona for their collaboration.

References

1. Apter A, Laufer N, Bar-Sever M, Har-Even D, Ofek H, Weizman A (1999) Serum cholesterol, suicidal tendencies, impulsivity, aggression, and depression in adolescent psychiatric inpatients. *Biol Psychiatry* 46(4):532–541
2. Atmaca M, Kuloglu M, Tezcan E, Ustundag B, Gecici O, Firidin B (2002) Serum leptin and cholesterol values in suicide attempters. *Neuropsychobiology* 45(3):124–127
3. Atmaca M, Kuloglu M, Tezcan E, Gecici O, Ustundag B (2002) Serum cholesterol and leptin levels in patients with borderline personality disorder. *Neuropsychobiology* 45(4):167–171
4. Atmaca M, Kuloglu M, Tezcan E, Ustundag B (2003) Serum leptin and cholesterol levels in schizophrenic patients with and without suicide attempts. *Acta Psychiatr Scand* 108:208–214
5. Brent DA, Bridge J, Johnson BA, Connolly J (1996) Suicidal behaviour runs in families. A controlled family study of adolescent suicide victims. *Arch Gen Psychiatry* 53(12):1145–1152
6. Carlson GA, Rich CL, Grayson P, Fowler RC (1991) Secular trends in psychiatric diagnoses of suicide victims. *J Affect Disord* 21(2):127–132
7. Cremniter D, Jamain S, Kollenbach K, Alvarez JC, Lecrubier Y, Gilton A et al (1999) CSF 5-HIAA levels are lower in impulsive

- as compared to non-impulsive violent suicide attempters and control subjects. *Biol Psychiatry* 45(12):1572–1579
8. Deisenhammer E, Karin K-R, Liensberger D, Kemmler G, Hinterhuber H, Fleischhacker W (2004) No evidence for an association between serum cholesterol and the course of depression and suicidability. *Psychiatry Res* 121:253–261
 9. Diaz-Sastre C, Baca-Garcia E, Perez-Rodriguez M, García-Resa E, Ceverino A, Saiz-Ruiz J et al (2007) Low plasma cholesterol levels in suicidal males: a gender and body mass index-matched case-control study of suicide attempters and non-attempters. *Prog Neuropsychopharmacol Biol Psychiatry* 31:901–905
 10. Engelberg H (1992) Low serum cholesterol and suicide. *Lancet* 339(8795):727–729
 11. Favaro A, Caregato L, Di Pascoli L, Brambilla F, Santonastaso P (2004) Total serum cholesterol and suicidality in anorexia nervosa. *Psychosom Med* 66(4):548–552
 12. Fiedorowicz Jess G, Coryell W (2007) Cholesterol and suicide attempts: a prospective study of depressed inpatients. *Psychiatry Res* 152:11–20
 13. Franke L, Uebelhack R, Muller-Oerlinghausen B (2002) Low CSF 5-HIAA level in high-lethality suicide attempters: fact or artifact? *Biol Psychiatry* 52(4):375–376 author reply 376–377
 14. Gietl A, Giegling I, Hartmann AM, Schneider B, Schnabel A, Maurer K et al (2007) ABCG1 gene variants in suicidal behavior and aggression-related traits. *Eur Neuropsychopharmacol* 17:410–416
 15. Guillem E, Péliissolo A, Notides C, Lépine JP (2002) Relationship between attempted suicide, serum cholesterol level, and novelty seeking in psychiatric in-patients. *Psychiatry Res* 112:83–88
 16. Jokinen J, Nordström AL, Nordström P (2007) The relationship between CSF HVA/5-HIAA ratio and suicide intent in suicide attempters. *Arch Suicide Res* 11(2):187–192
 17. Jones JS, Stanley B, Mann JJ, Frances AJ, Guido JR, Traskman-Bendz L et al (1990) CSF 5-HIAA and HVA concentrations in elderly depressed patients who attempted suicide. *Am J Psychiatry* 147(9):1225–1227
 18. Kim YK, Myint AM (2004) Clinical application of low serum cholesterol as an indicator for suicide risk in major depression. *J Affect Disord* 81:161–166
 19. Kim YK, Lee HJ, Kim JY, Yoon DK, Choi SH, Lee MS (2002) Low serum cholesterol is correlated to suicidality in a Korean sample. *Acta Psychiatr Scand* 105(2):141–148
 20. Lalovic A, Sequeira A, DeGuzman R, Chawky N, Lesage A, Seguin M, Turecki G (2004) Investigation of completed suicide and genes involved in cholesterol metabolism. *J Affect Disord* 79:25–32
 21. Lalovic A, Merckens L, Russell L, Arseneault-Lapierre G, Nowaczyk MJ, Porter FD et al (2004) Cholesterol metabolism and suicidality in Smith-Lemli-Opitz syndrome carriers. *Am J Psychiatry* 161(11):2123–2126
 22. Lalovic A, Levy E, Luheshi G, Canetti L, Grenier E, Sequeira A, Turecki G (2007) Cholesterol content in brains of suicide completers. *Int J Neuropsychopharmacol* 10(2):159–166
 23. Lester D (2002) Serum cholesterol levels and suicide: a meta-analysis. *Suicide Life Threat Behav* 32:333–346
 24. Marazziti D, Presta S, Silvestri S, Battistini A, Mosti L, Balestri C et al (1995) Platelet markers in suicide attempters. *Prog Neuropsychopharmacol Biol Psychiatry* 19(3):375–383
 25. Marcinko D, Martinac M, Karlovic D, Filipic I, Loncar C, Pivac N, Jakovljevic M (2005) Are there differences in serum cholesterol and cortisol concentrations between violent and non-violent schizophrenic male suicide attempters? *Coll Antropol* 29(1):153–157
 26. Marcinko D, Pivac N, Martinac M, Jakovljevic M, Mihaljevic-Peles A, Muck-Seler D (2007) Platelet serotonin and serum cholesterol concentrations in suicidal and non-suicidal male patients with a first episode of psychosis. *Psychiatry Res* 150:105–108
 27. Morgan RE, Palinkas LA, Barret-Connor RE, Wingard DL (1993) Plasma cholesterol and depressive symptoms in older men. *Lancet* 341(8837):75–79
 28. Nordstrom P, Samuelsson M, Asberg M, Traskman-Bendz L, Aberg-Wistedt A, Nordin C, Bertilsson L (1994) CSF 5-HIAA predicts suicide risk after attempted suicide. *Suicide Life Threat Behav* 24(1):1–9
 29. Pandey GN, Pandey SC, Janicak PG, Marks RC, Davis JM (1990) Platelet serotonin-2 receptor binding sites in depression and suicide. *Biol Psychiatry* 28(3):215–222
 30. Partonen T, Haukka J, Virtamo J, Taylor PR, Lonnqvist J (1999) Association of low serum cholesterol with major depression. *Br J Psychol* 175:259–262
 31. Roy A, Agren H, Pickar D, Linnoila M, Doran AR, Cutler NR et al (1986) Reduced CSF concentrations of homovanillic acid and homovanillic acid to 5-hydroxyindolacetic acid ratios in depressed patients: relationship to suicidal behavior and dexametason suppression. *Am J Psychiatry* 143(12):1539–1545
 32. Sullivan PF, Joyce PR, Bulik CM, Mulder RT, Oakley-Browne M (1994) Total cholesterol and suicidality in depression. *Biol Psychiatry* 36(7):472–477
 33. Tanskanen A, Vartrianinen E, Tuo-Milehto J, Viinamaeki IL, Leitonen J, Puska P (2000) High serum cholesterol and risk of suicide. *Am J Psychiatry* 157:648–650
 34. Vevera J, Zdenek F, Kvasnicka T, Zdenek H, Stárkova L, Ceska R et al (2005) Cholesterol-lowering therapy evokes time-limited changes in serotonergic transmission. *Psychiatry Res* 133:197–203
 35. Zureik M, Courbon D, Ducimetiere P (1996) Serum cholesterol concentration and death from suicide in men. *Br Med J* 313:649–652