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

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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

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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.

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