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Suicidal Behavior in Schizophrenia may be Related to Low Lipid Levels

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Background: Lifetime suicide mortality in people with schizophrenia is approximately 4–5%, which is higher than in the general population. In mood disorders, many studies and meta-analyses have shown a link between suicidal behavior and low lipid levels, especially that of cholesterol, and some studies have also suggested such a relationship in schizophrenia. Therefore, the aim of the present study was to investigate a possible correlation between suicidal behavior and lipid levels in schizophrenia patients recently admitted to a psychiatric hospital.

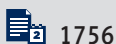
Material/Methods: Our study included 148 (69 males, 79 females) schizophrenia patients with a mean age of 32 ± 10 years, all recently admitted due to acute exacerbation of their mental illness. Psychometric and laboratory assessments were made within 24–72 hours after hospital admission. The main purpose of the interview was to assess occurrence of any suicidal thoughts, suicidal tendencies, and/or suicide attempts during the 3 months prior to admission. Serum total, LDL and HDL cholesterol, as well as triglycerides and total lipids were measured.

Results: A significant association was found between suicidal thoughts and attempts and low total cholesterol, LDL cholesterol, triglycerides, and total lipids, in both male and female patients. In male patients with suicidal tendencies, correlation with low LDL cholesterol and triglycerides did not reach statistical significance. No association with suicidality was found with HDL cholesterol in subjects studied.

Conclusions: The results obtained suggest that, similar to depressed patients, low total and LDL cholesterol, triglycerides, and total lipids can be state-dependent risk factors for suicidal behavior in Polish patients with schizophrenia.

MeSH Keywords: **Cholesterol • Lipids • Schizophrenia • Suicide**

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Background

Suicide is an important public health problem and in some countries its contribution to total deaths has been increasing [1]. Suicide is a major cause of death in people with schizophrenia and lifetime suicide mortality in this illness amounts to 4–5% [2]. A number of clinical and neurobiological risk factors have been postulated to explain the increased tendency to suicidal behavior in schizophrenia patients [2–4], and low lipid levels may also play a role.

The evidence for a possible association between low levels of lipids (particularly cholesterol) and increased suicidality dates back to 3 decades ago when the issue of lowering cholesterol levels became a popular topic in cardiology. Results from such projects as the Lipid Research Clinics and Helsinki Heart Study suggested that a reduction of cholesterol level due to low-fat diet and drugs did not decrease total mortality, because in experimental (interventional) groups, a significant increase of mortality was observed due to suicide and violent behavior, compared to control groups.

In the first meta-analysis of this issue, covering 6 randomized studies of primary prevention of ischemic heart disease, including nearly 25 000 men, Muldoon et al. [5] showed that in the group of subjects with 10% lower total cholesterol there were 28 fewer deaths due to ischemic heart disease and 29 more deaths due to suicide, violence, and accidents. Overall, the reduction caused a 2-fold increase of death risk due to suicide, violence, and accidents. Many subsequent meta-analyses performed in patients with depression demonstrated that, in most studies (including various study designs) a relationship between low serum cholesterol and suicide has been suggested [6–8]. Such a relationship was also observed in a Polish population of depressed patients [9,10].

The lower serum cholesterol levels associated with suicidal behavior may also pertain to schizophrenia. The first observation of this phenomenon was made 20 years ago when schizophrenia patients were a part of a larger psychiatric population studied [11]. This was confirmed by Gallerani et al. [12] in a subsample ($n=23$) of patients with schizophrenia who committed parasuicide and also by Tripodanakis et al. [13] in a subsample of schizophrenia patients ($n=16$) with a violent suicidal attempt. Similarly, Atmaca et al. [14] found significantly lower cholesterol levels in schizophrenia patients who attempted a violent suicide. In recent decades, a number of studies performed by Croatian researchers demonstrated an association between lower cholesterol and suicidality, especially using violent methods, in male patients with a first episode of psychosis and in those with schizophrenia [15–18].

On the other hand, Huang et al. [19], in Taiwanese patients with schizophrenia, found no difference in serum cholesterol level between patients who had and had not made a suicidal attempt.

Kim et al. [20] found a correlation between low cholesterol and suicidality in a Korean sample, but the relationship held true for depression but not for schizophrenia and bipolar disorder. Recently, Korean investigators were not able to find differences in cholesterol level between patients hospitalized for schizophrenia who subsequently died of suicide and those who did not [21].

The aim of the present study was to investigate whether lipid levels (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and total lipids) can serve as state-dependent markers of suicidal behavior in Polish patients with schizophrenia recently admitted to a psychiatric hospital due to an acute exacerbation of their illness.

Material and Methods

Patients

We recruited 148 schizophrenia patients consecutively admitted to an inpatient clinic at the Department of Adult Psychiatry, Poznan University of Medical Sciences, from September 2005 to June 2006. The reason for admission was an acute exacerbation of the illness. They were 69 male patients (mean age 30 ± 10 years, duration of illness 7 ± 8 years), and 79 female patients (mean age 33 ± 10 years, duration of illness 7 ± 7 years). Exclusion criteria for the study included severe somatic illness, drug and/or alcohol abuse/dependence, comorbid eating disorder, and using low-fat diet, lipid-lowering drugs, or hormonal therapy. Consensus diagnosis by at least two psychiatrists was made for each patient, according to DSM-IV criteria (SCID) [22].

Methods

Clinical assessment

A semi-structured questionnaire was used for demographic data, duration of illness, and psychiatric and suicidal family history, as well as psychiatric and somatic treatment during the 3 months prior to admission. The main purpose of the interview was to establish an occurrence of any suicidal thoughts, suicidal tendencies, and/or suicide attempts during the 3 months prior to admission.

Laboratory measures

Fasting blood was drawn at 8:00 A.M. within 24–72 hours of admission to the outpatient clinic. Laboratory measures included concentrations of the following lipids: total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and total lipids.

The study was approved by the Bioethics Committee, Poznan University of Medical Sciences and all patients gave their informed consent after the procedures had been fully explained to them.

Table 1. Lipid levels in schizophrenia patients with (+) and without (-) suicidal thoughts in recent 3 months. Values are expressed as mg/dl (mean \pm SD).

Group		Total cholesterol	LDL cholesterol	HDL cholesterol	Tri-glycerides	Total lipids
Male	(+)	175 \pm 45**	112 \pm 42**	45 \pm 15	91 \pm 48*	554 \pm 129**
	(-)	220 \pm 47	143 \pm 42	45 \pm 10	145 \pm 84	706 \pm 168
Female	(+)	174 \pm 24**	109 \pm 25**	52 \pm 14	70 \pm 44**	530 \pm 69**
	(-)	235 \pm 55	155 \pm 49	55 \pm 14	117 \pm 71	706 \pm 168

Concentrations significantly lower in patients with suicidal thoughts. ** $p < 0.001$; * $p < 0.01$.

Table 2. Lipid levels in schizophrenia patients with (+) and without (-) suicidal tendencies in recent 3 months. Values are expressed as mg/dl (mean \pm SD).

Group		Total cholesterol	LDL cholesterol	HDL cholesterol	Tri-glycerides	Total lipids
Male	(+)	179 \pm 45*	113 \pm 41	47 \pm 16	95 \pm 51	567 \pm 174*
	(-)	206 \pm 52	133 \pm 45	44 \pm 11	129 \pm 79	659 \pm 174
Female	(+)	174 \pm 27*	111 \pm 28*	50 \pm 12	65 \pm 39**	526 \pm 73**
	(-)	222 \pm 55	144 \pm 49	55 \pm 14	108 \pm 69	668 \pm 166

Concentrations significantly lower in patients with suicidal tendencies. ** $p < 0.01$; * $p < 0.05$.

Table 3. Lipid levels in depressive patients with (+) and without (-) suicide attempt in recent 3 months. Values are expressed as mg/dl (mean \pm SD).

Group		Total cholesterol	LDL cholesterol	HDL cholesterol	Tri-glycerides	Total lipids
Male	(+)	161 \pm 22*	93 \pm 21*	54 \pm 16	64 \pm 20**	495 \pm 55**
	(-)	204 \pm 51	132 \pm 45	44 \pm 11	126 \pm 76	651 \pm 170
Female	(+)	163 \pm 16**	101 \pm 18**	49 \pm 13	69 \pm 51*	505 \pm 61**
	(-)	215 \pm 54	140 \pm 47	54 \pm 14	100 \pm 66	646 \pm 161

Concentrations significantly lower in patients with suicide attempt. ** $p < 0.01$; * $p < 0.05$.

Statistical methods

Calculations were performed using the Statistica version 7.1 statistical package. Distribution of the results was tested with the Shapiro-Wilk test. Since the results were normally distributed, parametric statistical tests were employed. Comparisons of the 2 groups (with and without suicidal behavior) were performed by the use of the non-paired t-test. Statistical significance was set at $p < 0.05$.

Results

Suicidal thoughts were reported by 45% of men and by 44% of women with schizophrenia. In Table 1, concentrations of lipids studied in patients with and without suicidal thoughts are shown.

As seen in Table 1, concentrations of total cholesterol, LDL cholesterol, triglycerides, and total lipids were significantly lower in patients with suicidal thoughts compared with the remaining ones. This was demonstrated both in male and in female patients. No relationship with HDL cholesterol was found.

Suicidal tendencies were reported by 23% of men and by 28% of women with schizophrenia. In Table 2, concentrations of lipids studied in patients with and without suicidal tendencies are shown.

As seen in Table 2, concentrations of total cholesterol and total lipids were significantly lower in both male and female patients with suicidal thoughts compared with the remaining ones. Significantly lower levels of LDL cholesterol and triglycerides were also found in female patients. No relationship with HDL cholesterol was observed.

Six men with schizophrenia (9%) had made a suicidal attempt during the 3 months prior to admission, as did 13% of women. In Table 3, concentrations of lipids studied in patients with and without suicidal attempt in recent 3 months are shown

As seen in Table 3, concentrations of total cholesterol, LDL cholesterol, triglycerides and total lipids were significantly lower in patients with schizophrenia who had a suicidal attempt in the 3 months prior to admission, compared with the remaining ones. No relationship with HDL cholesterol was observed.

Discussion

The main finding of our research is that elements of lipid profile (total cholesterol, LDL cholesterol, triglycerides, and total lipids) can serve as state-dependent markers of suicidal behavior in Polish schizophrenia patients recently admitted to a psychiatric hospital. This corroborates the results of a previous Polish study performed by Rabe-Jablonska and Poprawska [9] in patients with acute depressive episodes, in which lower levels of total and LDL cholesterol were observed in those with suicidal behavior. Also, in one of our own previous investigations, a significant association was found between low total cholesterol, LDL cholesterol, and total lipids and suicidal thoughts, tendencies, and attempts in both male and female patients with unipolar and bipolar depression [10]. On the other hand, no association with HDL cholesterol was observed in these patients for any suicidal parameter, which was also the case in the present study. Therefore, the results obtained here corroborate most studies in which a relationship between suicidal behavior and low cholesterol in schizophrenia patients was observed [11–18]. Additionally, our results may add the new elements of lipid profile (e.g., LDL cholesterol, total lipids and triglycerides) to this relationship.

The main neurobiological mechanism explaining an association between low cholesterol and suicidal behavior is the cholesterol-serotonin-impulsivity model [24]. Low cholesterol is associated with decreased activity of the serotonergic system, which is reflected by low levels of serotonin and its main metabolite, 5-hydroxyindolacetic acid (5-HIAA), in serum and cerebrospinal fluid (CSF). In early studies performed in people who had attempted suicide, lower concentration of 5-HIAA was observed in CSF, as well as its connection with low serum cholesterol [25,26]. However, in the largest study to date no correlation between CSF 5-HIAA and suicidal behavior was found [27]. The cholesterol-serotonin-suicide link may also have a genetic component. Subjects with the s allele of serotonin transporter

gene 5-HTTLPR polymorphism are over-represented among suicide attempters [28] and have lower LDL cholesterol [29]. An association of suicidal behavior with 5-HTTLPR polymorphism was observed in subjects with childhood trauma [30], which corresponds with the results of a study showing a significant correlation between exposure to violence as a child and adult violence in patients with low serum cholesterol [31].

Another link may exist between low cholesterol and depression, which has been demonstrated by Morgan et al. [32] in elderly men, as well as between low cholesterol and intensity of depression in a Polish study [9]. The association between cholesterol and mood disorders, also in the context of suicide, has been a subject of excellent reviews by Papacostas et al. [33] and De Bernardis et al. [34]. Recently, Freemantle et al. [35] analyzed brain oxysterol levels, which are enzymatic oxidation products of cholesterol, in the prefrontal cortex of suicide victims. Their results showed a significant increase in 24-hydroxysterol, reflecting a higher turnover of cholesterol, which suggests that this process is responsible for reduction of central and peripheral cholesterol in these subjects. Finally, lower lipid levels in people with schizophrenia may also relate to the occurrence of metabolic syndrome. In relation to this, Vuksan-Cusa et al. [35] observed that the prevalence of metabolic syndrome in people with schizophrenia was lower in suicide attempters than in non-attempters.

However, it should be stressed that an association between low cholesterol and suicidal behavior in schizophrenia was not confirmed in a number of studies [19–21]. As most of the studies yielding negative results in this respect were performed in Asian populations, it can be speculated that ethnic differences may play a role.

Conclusions

The results of our study add to a growing body of evidence showing the association between suicidal behavior and low levels of total cholesterol in people with schizophrenia. In addition, we found that this association may also apply to low total lipids, and, in most cases, to low LDL cholesterol and triglycerides. The limitation of our study may be its cross-sectional nature, and the strength may be with the large number of patients studied.

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