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Are There Differences in Serum Cholesterol and Cortisol Concentrations between Violent and Non-Violent Schizophrenic Male Suicide Attempters?

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A B S T R A C T

Previous studies have shown an association between low concentration of serum cholesterol, as well as high concentration of serum cortisol, in suicide behavior. The aim of this study was to evaluate whether men after a violent suicide attempts have different serum cholesterol and cortisol concentrations than those who attempted suicide by non-violent methods. Venous blood samples were collected within 24 hours of admission, to study concentrations of serum cholesterol and cortisol. The sample consisted of 31 male subjects suffering from schizophrenia, admitted in a general hospital after suicide attempt, and was compared with 15 schizophrenic nonsuicidal male controls. Patients with a violent suicidal attempt were found to have significantly lower cholesterol levels and significantly higher cortisol level than patients with non-violent attempts and the control subjects. Our findings suggest that suicide attempts should not be considered a homogenous group. The hypothesis of an association of violent suicidal attempts and peripheral biological markers (cholesterol and cortisol) was supported by our findings.

Key words: *suicide attempt, schizophrenia, serum cholesterol, serum cortisol*

Introduction

Individuals with schizophrenia are at increased risk for suicide attempts and completed suicide[1–2]. Suicide is the most common cause of death in schizophrenia, there is a 10% lifetime risk[3–4]. Various studies aimed at identifying possible peripheral markers that may be helpful in the early detection of suicidal behavior have been carried out. Among the most recent hypotheses[5–6], low blood cholesterol level has been extensively explored. Indeed, since the first report of an unexplained rise in suicides and other violent deaths observed in several clinical trials in coronary heart disease designed to lower plasma cholesterol[7–8], a number of studies have been convergent in observing an association between low cholesterol and heightened rates of death from suicide and violence. Atmaca[9], found that patients with suicide attempts had significantly lower cholesterol levels than controls. Patients admitted to an emergency room following a suicide attempt were found to have lower cholesterol levels than controls[10], while in a separate study[11], the severity of a suicide attempt was inversely correlated with serum cholesterol levels. Modai[12], found that patients who had attempted suicide had lower serum cholesterol level than non-suicidal patients. Patients with low serum cholesterol levels found to be twice as likely to have ever made a medically serious suicide attempt than men with levels above 25th percentile[13], while patients who survived a violent suicide attempts were found to have lower cholesterol lev-

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els than patients who survived a non-violent suicide attempts[14] or controls[15]. A number of reports also suggest a relationship between the degree of suicidal ideation and the degree of hypocholesterolemia. Papassotiropoulos[16] reported that degree of suicidal ideation in psychiatric inpatients was inversely related to their cholesterol levels, while Sullivan[17] reported a similar finding in outpatients with major depressive disorder. There are also reports of low cholesterol levels among parasuicidal patients[18–20].

The investigation of biological correlates of suicidal behavior is important to identifing high-risk subjects and developing strategies of prophylaxis. Preventing suicide is one of the main targets of care.

A role of the stress hormone (as cortisol) in the etiology of suicide is evident[21], although the mechanisms are uncertain. Functional interactions of CRH with serotonergic neurons in the midline raphe are suggested experimentally[22] but have not been established in humans. Still in question is the neuroanatomical basis for presumed humoral and neural mechanisms of interaction.

The aim of the present study is to provide whether there are any differences in serum concentration of cholesterol and cortisol between violent and non-violent suicide attempters, suffered from schizophrenia.

Subjects and Methods

The study used a case-control design to compare the cholesterol and cortisol levels of men who had a non-violent (N = 15) and violent (N = 16) suicide attempts and nonsuicidal male subjects (N = 15). All included subjects (N = 46) met diagnosis of schizophrenia (ICD-10, International Statistical Classification of Diseases and Related Health Problems = F 20). Table 1 summarizes the demographic data of the studied subjects and controls.

Inclusion and exclusion criteria

We included in the study only those individuals whose biochemical analyses from the time of admission were available (during the period between January 1st 2003 and July 1st 2003). None of the subjects and controls included in the study had used cholesterol-lowering drugs before blood drawing. Patients suffering from hypertension, hypothyroidism, diabetes mellitus, disorders of lipoprotein metabolism, diagnosis of substance abuse, including alcoholism, eating disorders and organic brain syndrome were also excluded from the study.

Subjects

We identified all men, admitted to the Department of Psychiatry, Clinical Hospital Center Zagreb, during the period of six months, following a suicide attempt and suffering from schizophrenia (N=31). Only self-destructive acts with lethal intent were classified as suicide attempts.

Violent suicidal attempts (N=16) were cutting wounds (N=8), hanging (N=4), drowning (N=2) and jumping from heights (N=2).

Overdoses by medicaments (mostly benzodiazepines, N=14) were considered non-violent (N=15).

The control group consisted of 15 randomly selected men suffering from schizophrenia (ICD-10, F 20) with no history of suicide. They met the same criteria as the study subjects.

All together, 46 patients had enough data to be included in the study. The psychiatric diagnoses of the all included patients were schizophrenia, F 20 – according to ICD 10.

Statistical analysis

Analysis of covariance (ANCOVA) with age and BMI as covariates was used to analyze differences in cholesterol levels between 3 observed groups. Analysis of variance (ANOVA) were used to analyze differences in cortisol levels between 3 observed groups, also age and body mass indeks (BMI) differences between groups.

A p value of <0.01 was considered to denote the presence of a statistically significant difference. We used Chi square test and Fisher's exact test to analyze differences in sociodemographic variables between groups. The Scheffé test was used as a post-hoc test to compare violence suicide subjects, non-violence suicide subjects and the control group. All statistical analyses were performed with SPSS version 10 for Windows.

Measures

We included in the study those patients whose following biochemical analyses from the time of admission were available: serum cortisol (at the morning) and total cholesterol concentration. Body mass index (BMI) was a marker of dietary habits. Blood samples were collected from all subjects at 7 am after overnight fasting. Serum concentrations for cholesterol were determined enzymatically, immediately after blood collection. The assays were done with commercial kits (Olympus Diagnostic GmbH, Hamburg, Germany) on Olympus AU 600 automatic analyzer. For the in vitro quantitative measurement of cortisol in human serum was used vitros immunodiagnostic products – cortisol reagent pack (Johnson-Johnson company).

Results

The sixteen violent suicide attempters, 15 non-violent suicide attempters and 15 control subjects were included in the study. There were no significant differences across the three analyzed groups of schizophrenics for age, body mass index, marital, family and employment status (Table 1).

Table 2 summarizes the mean±SD serum cholesterol concentrations and morning cortisol concentrations in non-violent, violent suicide atempters, and in control group of schizophrenic patients (without suicide attempts).

TABLE 1
DEMOGRAPHIC DATA OF THE SUBJECTS STUDIED

	Non-violent suicidal (N=15)	Violent suicidal (N=16)	Control group (N=15)
Age (years; mean±SD)*	26.53 ± 4.29	26.56 ± 4.72	26.33 ± 4.64
BMI (kg/m^2; mean±SD)**	25.01 ± 1.10	25.13 ± 1.87	25.19 ± 1.13
Marital status, N (%)^H			
Single	9 (60)	10 (62.5)	8 (53.3)
Married	6 (40)	6 (37.5)	5 (53.3)
Divorced	0 (0)	0 (0)	2 (13.3)
Family status, N (%)^I			
Living alone	5 (33.3)	8 (50)	7 (46.7)
Living with family	10 (66.7)	8 (50)	8 (53.3)
Employment status, N (%)$^{'}$			
Employed	4 (26.7)	4 (25)	4 (26.7)
Unemployed	5 (33.3)	6 (37.5)	5 (33.3)
Retired	1 (6.7)	1 (6.3)	1 (6.7)
High school	1 (6.7)	1 (6.3)	0 (0)
Student	4 (26.7)	4 (25)	5 (33.3)

*F=0.01, p=0.99; **F=0.06, p=0.94; ^{H}Fisher's exact test=3.01, p=0.58; $^I x^2$=0.97, df=2, p=0.62; $^{'}$Fisher's exact test=2.15, p=1.00

TABLE 2
CONCENTRATIONS OF SERUM CHOLESTEROL (MEAN±SD) AND MORNING CORTISOL (MEAN±SD) IN NON-VIOLENT, VIOLENT SUICIDE ATEMPTERS, AND IN CONTROL GROUP OF SCHIZOPHRENIC PATIENTS

	Non-violent suicidal (N=15)	Violent suicidal (N=16)	Control group (N=15)	F value	p value
Cholesterol (mmol/L)	4.79 ± 0.67	3.87 ± 0.63*	5.55 ± 1.06	17.35**	<0.01
Cortisol (nmol/L)	402.33 ±153.32	682.12 ±161.30*	326.66 ± 96.77	26.49	<0.01

* significantly different from non-violent and control group (post-hoc Scheffe test, p<0.01);
** ANCOVA (after adjusted for BMI and Age as covariates)

In analyses controlling for age and BMI, the serum cholesterol concentration was found to be significantly lower (F –17.35; p<0.01) in the group of violent suicide attempters (3.87 ± 0.63 mmol/L, N=16) than in the groups of non-violent suicide attempters (4.79 ± 0.67 mmol/L, N=15) or control subjects (5.55 ± 1.06 mmol/L, N=15).

For post-hoc testing, we used the Scheffé test and a significant difference (p<0.01) in cholesterol levels was revealed between the group of violent and non-violent suicide attempters. A significant difference (p<0.01) between the group of violent suicide attempters and controls was found, while no significant difference (p<0.01) was found between the non-violent suicide attempters group and controls.

The adjusted means of cholesterol levels for the violent, non-violent and control groups are shown in Figure 1.

Using analyses of variances, the serum cortisol concentration (morning values) was found to be signifi-

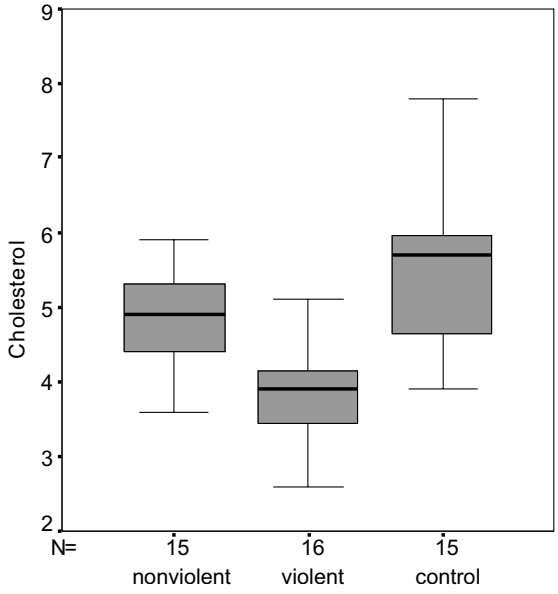

Fig. 1. Adjusted means of cholesterol (mmol/l).

cantly higher (F –26.49; p<0.01) in the group of violent suicide attempters (682.12 ±161.30 nmol/L, N=16) than in the groups of non-violent suicide attempters (402.33 ±153.32 nmol/L, N=15) or control subjects (326.66 ± 96.77 nmol/L, N=15). No significant difference (p<0.01) was found between the non-violent suicide attempters group and controls.

Boxplots of serum morning cortisol levels (nmol/l) in three observed groups are shown in Figure 2.

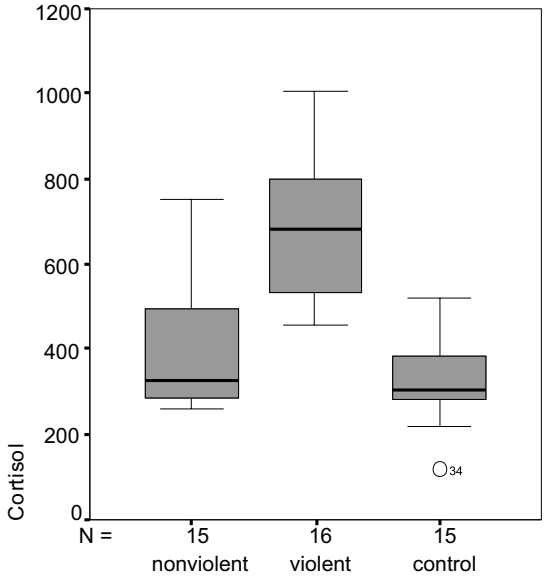

Fig. 2. Boxplots of serum morning cortisol (nmol/l) concentrations in three observed groups.

Discussion

Primary finding of this study is that male schizophrenic patients with violent suicide attempts have significantly lower cholesterol level and significantly higher cortisol level than patients with non-violent suicidal attempts. This supports the earlier hypothesis[23] that low or lowered serum cholesterol may be associated with low lipid microviscosity in the brain-cell-membrane and may decrease the exposure of serotonin receptors on the membrane surface, resulting in decreased serotonergic receptor function as a whole. Consequently, serotonergic neurotransmission may be inhibited, which may lead to poorer suppression of impulsive or aggressive behavior or to a depressive state, triggering a more violent pattern of behavior in susceptible individuals.

Our findings suggest that suicidal attempts are not a homogenous group. Men with a history of violent suicide attempts, which are associated with a higher level of impulsivity, had lower cholesterol levels. This is consistent with the postulated role of cholesterol in impulsive behavior[24].

Golier[13] reported that male patient with low cholesterol levels were mre likely to have made a serious attempt at suicide compared with those with higher cholesterol levels. Howewer, Apter[25] founded that serum cholesterol levels were significantly higher in adolescent patients who were considered to be at high risk of suicide compared with their low-risk counterparts.

Several different mechanisms have been suggested to describe the potential effect of low cholesterol levels on suicidality. Hawton[26] have speculated on the influence of decreased serotonergic transmission on suicidal behavior. Steegmans[27] described lower plasma serotonin concentrations in men with persistently low serum cholesterol concentrations.

Terao[28] have reported on the possibility that serum cholesterol levels are positively associated with serotonergic function via cortisol and prolactin responses to meta-chloro-phenylpiperazine (M-CPP) neuroendocrine challenges. It support the hypotheses that reduced cholesterol levels result in reduced central serotonin transmission. In contrast, neither prolactin nor cortisol response to d-fenfluramine was found to correlate significantly with serum cholesterol levels in another study[29]. The existence of inverse correlation between serum cholesterol level and the level of violence of suicide attempts in our study suggest strongly that low cholesterol is a risk indicator for suicidal behaviour.

The results from this study suggest furthermore that violent suicide attempts are associated with higher level of cortisol in addition to overactivity in the hypothalamic-pituitary-adrenal (HPA) axis. Our finding is in keeping the results from a previous study[30] demonstrating higher cortisol plasma levels in violent suicide attempters when compared to non-violent attempters. Hypersecretion of cortisol is strongly implicated in the pathophysiology of mental disorders and suicide[31–32] by diminished capacity of the dorsal raphe to synthesize serotonin, and excessive noradrenergic activity of the locus coeruleus[33–34].

In conclusion, the present study supports the previous reports that low serum cholesterol and also high cortisol are associated with violent suicide attempts. These results suggest that low serum cholesterol and high serum cortisol in patients with psychosis might be a useful biological markers of suicide risk. Further investigations are necessary to elucidate the biological mechanisms of these findings.

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POSTOJE LI RAZLIKE SERUMSKE KONCENTRACIJE KOLESTEROLA I KORTIZOLA MEĐU NASILNIM I NENASILNIM SHIZOFRENIM MUŠKARCIMA KOJI POKUŠAJU SAMOUBOJSTVO

SAŽETAK

Neke od ranijih studija pokazuju povezanost niskih vrijednosti serumskog kolesterola i visokih vrijednosti serumskog kortizola i suicidalnog ponašanja. Cilj ispitivanja bio je ustanoviti postoje li razlike u serumskih koncentracijama kolesterola i kortizola između pacijenata nakon nasilnih pokušaja suicida u odnosu na pacijente koji su imali nenasilni pokušaj suicida. Vađenje krvi obavljeno je unutar 24 sata od prijema, kako bi se odredile koncentracije serumskog kolesterola i kortizola. Uzorak se sastojao od 31 pacijenta sa shizofrenijom, hospitaliziranih u općoj bolnici nakon pokušaja suicida, te su uspoređeni s kontrolnom skupinom od 15 nesuicidalnih shizofrenih pacijanata. Ustanovili smo kako pacijenti nakon nasilnih pokušaja suicida imaju signifikantno niže vrijednosti kolesterola i signifikantno više vrijednosti kortizola u odnosu na skupinu nakon nenasilnih pokušaja suicida i kontrolnu skupinu. Naši rezultati ukazuju na to kako suicidalni pokušaji ne mogu biti razmatrani kao homogena skupina. Hipoteza povezanosti nasilnih suicidalnih pokušaja i perifernih bioloških pokazatelja (kolesterol i kortizol) je potvrđena u našem ispitivanju.