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Cholesterol and the "Cycle of Violence" in attempted suicide ☆

Peter Asellus, Peter Nordström, Anna-Lena Nordström, Jussi Jokinen *

Department of Clinical Neuroscience/Psychiatry, Karolinska Institutet, Karolinska University Hospital, Solna, SE-171 76 Stockholm, Sweden

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ABSTRACT

An association between low levels of serum cholesterol and violent or suicidal behaviour has frequently been reported. However the role of serum cholesterol in the cycle of violence (Widom, 1989) has not been studied. The aim of this study was to investigate association between exposure to violence during childhood and used adult violence in suicide attempters with low and high serum cholesterol levels. 81 suicide attempters were assessed with the Karolinska Interpersonal Violence Scale (KIVS) measuring exposure to violence and expressed violent behaviour in childhood (between 6 and 14 years of age) and during adult life (15 years or older). We used median split to dichotomise groups below and above median serum cholesterol. In patients with serum cholesterol below median, the correlation between exposure to violence as a child and used adult violence was significant (rho=0.52, p=0.002), while in patients with serum cholesterol above median, the correlation between exposure to violence as a child and expressed violent behaviour as an adult was not significant (rho=0.25, p=0.2). Comorbid substance abuse predicted violent behaviour as an adult only in patients with serum cholesterol above median. Serum cholesterol may modify the effect of the "Cycle of Violence".

1. Introduction

The old adage that "violence begets violence", conceptualised in the "Cycle of Violence" (Widom, 1989), states that children exposed to violence have higher risk to become violent adults. Early traumatisation could be regarded as a causal factor of aggressive and violent behaviour in adults, leading to the conclusion that preventing mistreatment of children might reduce aggression overall (Jaffee et al., 2004). Abused children do present an increased risk of later suicide attempts, suicide, aggressive behaviour and development of personality disorders (Klomek et al., 2009, Ball and Links, 2009, Jokinen et al., 2010).

It is matter of debate how much of the Cycle of Violence is due to maltreatment in itself (Sarchiapone et al., 2009) and what is due to genetics/structural changes representing an inherited vulnerability. Several systems where genetic vulnerability may matter have been identified, especially genes connected to serotonergic metabolism and signalling (Caspi et al., 2002, 2010, Kiser et al., 2012), but even many neuroendocrine systems may be affected by maltreatment during childhood (Veenema, 2009). Most likely genetics, environment and learned behaviour all matter, since far from every child exposed to violence grows up to be a violent adult as demonstrated by a recent twin-study which reported that the causal link was weaker than expected and that other mediating factors must be examined (Forsman and Långström, 2012).

Serum cholesterol levels have been found to be significantly correlated to aggressivity and violence (Golomb, 1998), and violent crime in general (Golomb et al., 2000). A recent prospective study reported that total serum cholesterol predicted violent behaviour during the follow-up in patients released after treatment at a psychiatric ward (Roaldset et al., 2011).

The link between cholesterol and violence is hypothesised to be mainly mediated through alteration of serotonergic activity. Low cholesterol is related to low serotonin and, in turn, linked to violence, suicidal behaviour and impulsivity (Wallner and Machatschke, 2009).

The role of serum cholesterol in the cycle of violence (Widom, 1989) has not been studied. Childhood trauma may affect serum cholesterol levels perhaps through the accumulated epigenetic modification of multiple genes regulating cholesterol levels (Ferrari et al., 2012; Ehlert, 2013). People with a history of sexual abuse had lower HDL cholesterol levels in the Netherlands Study of Depression and Anxiety (NESDA) (van Reedt Dortland et al., 2012). Since serum cholesterol is associated with both childhood trauma and adult violent behaviour, we hypothesised that serum cholesterol levels would modify the association between childhood trauma and adult violent behaviour and that association (Cycle of Violence) could be detected only in patients with low serum cholesterol (below the median).

The purpose of this study was to assess the relationship between serum cholesterol levels and expressed interpersonal

* Corresponding author. Tel.: +46 8 51776759; fax: +46 8 303706.
E-mail address: jussi.jokinen@ki.se (J. Jokinen).

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violence in suicide attempters. The hypothesis was that low cholesterol would be related to violent behaviour towards others. We further hypothesised that the connection between exposure to violence as a child and expressed violent behaviour as an adult (cycle of violence) may be more pronounced in suicide attempters with low serum cholesterol.

2. Methods

2.1. Study setting

The study participants were recruited among patients having recently committed a suicide attempt and having their clinical follow-up at the Karolinska University Hospital. The patients were asked to take part in a study of psychological and biological risk factors for suicidal behaviour and were recruited as inpatients, outpatients, and from emergency setting. The study protocols (Dnr 93-211) were approved by the Regional Ethical Review Board in Stockholm, and all patients gave their written informed consent before inclusion in the study.

2.2. Subjects

The cohort study consists of 81 patients with a recent suicide attempt. There were 35 men, with a mean age of 39 years (S.D.=11.8, range 20–69) and 46 women, mean age 35 years (S.D.=12.1, range 18–68). To be included in the study, all participants must have a recent suicide attempt, exhibit a fair capacity to communicate verbally and in writing the Swedish language and be 18 years or older. Suicide attempt was defined as non-fatal, self-injurious behaviour with some intent to cause death and with a time limit of one month prior to inclusion to the study. Exclusion criteria were intravenous drug abuse, dementia, mental retardation and schizophrenia spectrum psychosis. Participants were interviewed by a trained psychiatrist using the SCID-I interview and diagnosis was established according to DSM-III criteria. A SCID-2 interview was conducted in order to establish Axis II diagnosis.

In this study 94% of the patients fulfilled criteria for at least one Axis 1 diagnosis; 80% having a mood disorder, 5% adjustment disorder and 4% anxiety disorder. Of the participants 21% fulfilled criteria for a co-morbid substance disorder, the majority of those being alcohol related. Axis II diagnosis: 39% of the patients fulfilled criteria for a personality disorder. Concerning the method of suicide attempt, 17% had used a method considered to be violent according to criteria of Träskman et al. (1981). Fifty-one patients (78%) were drug naïve previous to the suicide attempt (antidepressants). The part of the study population with cerebrospinal fluid data (42 patients) has earlier been described (Asellus et al., 2010; Moberg et al., 2011).

The subjects were generally somatically healthy. The somatic diagnoses of the patients at study inclusion were: cardiovascular disease ($n=2$), diabetes ($n=4$), Morbus Crohn ($n=1$) migraine ($n=1$/), pain NOS ($n=6$), celiaki ($n=1$), kidney stone (2) and asthma (2).

2.3. Serum cholesterol assays

Blood samples were collected in a controlled setting from the antecubital vein, after the participants had been fasting overnight. The resulting samples were analysed for total serum cholesterol, using standard procedures, at the Laboratory of Clinical Chemistry at the Karolinska University Hospital.

2.4. Assessments

The Karolinska Interpersonal Violence scale (KIVS) consists of four subscales, designed to assess the exposure to and expression of interpersonal violence as a child (between 6 and 14 years of age), and as an adult (15 and older), (Jokinen et al., 2010). The ratings are based on a semi-structured interview and items refer to serious events during your lifetime. The scoring is between 0 and 5 for all four subscales. The KIVS scale is presented in Supplementary material. In this study, trained clinicians performed and assessed all interviews and ratings.

2.5. Data analysis

Of the 81 patients, 16 had not left fasting blood samples. Initial analyses were carried out to evaluate skewness and kurtosis of the distributions with Shapiro Wilks test. One patient was identified using Mahalanobis distance as multivariate outliers. The exclusion of this individual affected the results, and was therefore excluded in all analyses. Two patients had no KIVS scores. Group differences were computed with one-way ANOVA or with Wilcoxon test in continuous variables. Tests of parametric correlations were performed using Pearson's r and non-parametric correlations using Spearman's rho. A linear regression was performed to control for age, gender and co-morbid substance abuse diagnosis. We used a median split to dichotomise groups below and above median serum cholesterol.

The cut-off for significance of p values was set at 0.05. The Statistical Package JMP VI software, SAS Institute inc., Cary, NC, USA was used for all statistical analyses.

3. Results

3.1. Cholesterol and exposure to and expression of violence

The mean serum- total cholesterol was 5.0 mmol/l, (S.D.=0.9, range 2.8–7.5, median 4.9 mmol/l). There was no significant gender difference in cholesterol levels. The mean value of KIVS exposure to violence as a child was 2.2, (S.D.=1.3, range 0–5, median=2). The mean value of KIVS expressed violence as an adult was 1.4, (S.D.=1.1, range 0–5, median=2).

Unadjusted correlation between serum cholesterol and expressed interpersonal violence as an adult was significant (rho=−0.26, $p=0.04$) and correlation between serum cholesterol and exposure to interpersonal violence as a child showed a trend to be significant (rho=−0.23, $p=0.07$).

Standard regression analysis was conducted with KIVS subscales as the dependent variable and serum cholesterol, age and co-morbid substance abuse as independent variables. The correlations between serum cholesterol and KIVS subscales did not remain significant in adjusted models ($p=0.27$, $p=0.80$).

In the whole group the correlation between exposure to violence as a child and violent behaviour as an adult was significant (rho=0.39, $p=0.002$).

Table 1
Depicts demographic variables, cholesterol levels and KIVS ratings in low versus high cholesterol groups.

	Suicide attempters								p-Value
	Low cholesterol, $n=32$				High cholesterol, $n=32$				
	Mean	Median	S.D.	Range	Mean	Median	S.D.	Range	
Gender % F	20/32				17/32				0.4
	62.5%				53.1%				
Age	31.2	28	10.7	18–55	42.4	42	10.8	24–68	0.0001
Serum cholesterol	4.3	4.5	0.5	2.8–4.9	5.7	5.6	0.6	4.9–7.6	0.0001
Exposure to violence during childhood	2.7	3	1.1	1–5	2.3	2	1.5	0–5	0.2
Used violence as adult	1.7	2	1.2	0–5	1.5	2	1.1	0–4	0.3
Mood disorder	28/32				24/32				0.2
	87.5%				75%				
Substance abuse yes %	10/32				3/32				0.03
	31.3%				9.4%				
Personality disorder %	16/31				11/31				0.2
	51.6%				35.5%				