Psychiatry Research 255 (2017) 1–7

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Low cholesterol level as a risk marker of inpatient and post-discharge violence in acute psychiatry – A prospective study with a focus on gender differences

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ARTICLE INFO

Keywords:
HDL
Total cholesterol
Violence
Risk assessment
Emergency psychiatry
Biomarkers

ABSTRACT

Several studies indicate an association between low levels of serum cholesterol and aggressive behaviour, but prospective studies are scarce. In this naturalistic prospective inpatient and post-discharge study from an acute psychiatric ward, we investigated total cholesterol (TC) and high-density lipoprotein (HDL) as risk markers of violence. From March 21, 2012, to March 20, 2013, 158 men and 204 women were included. TC and HDL were measured at admission. Violence was recorded during hospital stay and for the first 3 months post-discharge. Univariate and multivariate binary logistic regression were used to estimate associations between low TC and low HDL and violence. Results showed that HDL level was significantly inversely associated with violence during hospital stay for all patients. For men, but not for women, HDL level was significantly inversely associated with violence the first 3 months post-discharge. Results indicate that low HDL is a risk marker for inpatient and post-discharge violence in acute psychiatry and also suggest gender differences in HDL as a risk marker for violence.

1. Introduction

Potential biological markers associated with psychiatric disorders, like mood disorders or psychotic disorders, or different types of aggressive behaviours (like violence or self-harm) have been identified during the last couple of decades (Kalia and Costa, 2015; Siever, 2008). Two examples of potential risk markers associated with violence are low levels of total cholesterol (TC) and high-density lipoprotein cholesterol (HDL). TC is a measure of all the cholesterol transported in the blood stream and consists of cholesterol particles like HDL, low-density lipoproteins (LDL), very low density lipoproteins (VLDL) and chylomicrons (Fielding and Fielding, 2008).

A positive association between low levels of TC and violence has been found in most previous studies, e.g. in a meta-analysis of 32 studies with different design (Golomb, 1998), in a large community cohort study (Golomb et al., 2000), and in studies from different areas of psychiatry (Asellus et al., 2014; Paavola et al., 2002; Roaldset et al., 2011a). When it comes to HDL, results have been more conflicting. In a study on personality disordered male cocaine addicts, significantly lower levels of HDL were found in patients with a history of aggression (Buydens-Branchey et al., 2000). In another study on 20 young adult males with a history of aggression and 40 controls, correlations between lower levels of antiatherogenic lipoproteins (HDL and Apo A-I) and aggression were found in the aggressive subjects, and between atherogenic lipoproteins (LDL and Apo-B) and aggression in the controls (Troisi and D'Argenio, 2006). In two of the studies mentioned earlier, Roaldset et al. (2011a) found a significant association between low HDL and post-discharge violence in acute psychiatry, while Paavola et al. (2002) found higher HDL in violent patients compared to controls in a study from forensic psychiatry. A recent study on schizophrenia inpatients found no significant associations between HDL and violence (Chen et al., 2015). Our literature search on studies on TC, HDL and other cholesterol particles as risk markers for violence showed that prospective studies were rare.

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http://dx.doi.org/10.1016/j.psychres.2017.05.010
Received 7 January 2017; Received in revised form 30 March 2017; Accepted 7 May 2017
Available online 08 May 2017
0165-1781/

Mechanisms of a possible connection between low levels of TC or other cholesterol particles and violence are not fully known. One main hypothesis of a possible biological mechanism which might explain the association is that low cholesterol levels in the central nervous system (CNS) may contribute to reduced transportation of serotonin through cholesterol-containing cell membranes. This may result in low levels of serotonin in the CNS and insufficient top-down control from the prefrontal cortex to the limbic structures of the brain, resulting in increased risk of affective and impulsive aggression (Engelberg, 1992; Siever, 2008; Wallner and Machatschke, 2009). Associations between low cholesterol levels and impulsivity in patients with mood symptoms were found in a recent study (Troisi, 2011). Buydens-Branchey et al. (2000), who found an association between low HDL and a history of aggression, identified a significant association between low HDL and impulsivity in the same investigation.

Methods for violence risk assessments among psychiatric patients in use today consist solely of psychosocial risk factors and do not take knowledge of potential biological markers of aggression into account. Examples of psychosocial risk factors are psychotic disorders and symptoms, personality disorders, psychopathic traits, previous violence, low education level, violence-prone living conditions and unemployment. Two examples of existing methods in violence risk assessments are the Historical Clinical Risk Management-20 (HCR-20) Version 3 (Douglas et al., 2013), mainly used in forensic and long-term settings, and the Violence risk screening - 10 (V-RISK-10) (Hartvig et al., 2011; Roaldset et al., 2011b) used in acute and general settings. Singh et al. (2011) emphasized the need for research on alternative risk factors and risk markers for violence, including the use of potential biological markers of violence like TC and HDL, to improve existing risk assessment methods (Singh et al., 2011).

Acute settings are characterised by high patient turnover, short stays and time pressure, which underlines the importance of developing simple and rapid procedures for risk assessments. Taking a blood sample is often a routine procedure at admission, and results normally appear within a day. Using potential risk markers like TC or HDL to supplement existing procedures for violence risk assessments may therefore be quite easily integrated in the clinic's work. This underlines the need for prospective studies on the possible association between low cholesterol and future violence, especially from acute settings.

Violence is more common among men than women. One possible biological explanation is that male brains are larger and therefore they have been evolutionarily more vulnerable to low levels of serum cholesterol than female brains (Wallner and Machatschke, 2009). This may strengthen the link between low cholesterol levels and violence in men. A recent study of V-RISK-10 indicated that there may be gender differences concerning psychosocial risk factors of violence in acute psychiatry (Eriksen et al., 2016). In our literature search on studies of associations between different types of cholesterol and violence among psychiatric patients, we found only two studies that addressed gender differences (Asellus et al., 2014; Chen et al., 2015). Asellus and co-workers found no gender differences with respect to low TC levels as a risk marker of violence when examining association between exposure to childhood violence and violent behaviour as an adult. Chen et al. found that low TC levels in women added significant incremental validity to a psycho-social model of risk factors for violence.

In sum, research findings indicate that there may be an association between low levels of TC, and possibly also subtypes of cholesterol like HDL, and violence. Still, there seems to be a lack of prospective studies on this topic. Studies that have investigated gender differences concerning cholesterol levels as a potential risk marker of violence are scarce. Hence, our main objectives in this study from acute psychiatry were to investigate (1) the predictive accuracy of TC and HDL recorded at admission as risk markers for violence during hospital stay and the first 3 months after discharge and (2) possible gender differences in TC and HDL recorded at admission as risk markers for violence during hospital stay and the first 3 months after discharge.

2. Methods

2.1. Design

This was a naturalistic prospective inpatient and outpatient observational study. The research was approved by the Regional Committee for Medical and Health Research Ethics. The approval granted exemption from asking for patients' informed consent to be included, but all patients could at any time withdraw from the project. Approval of access to police records for additional post-discharge recordings of violent behaviour was given by the National Police Directorate.

2.2. Setting and participants

Oslo is the capital of Norway with a total population of 650,000. The acute psychiatric ward at Oslo University Hospital has five units with a total of 45 beds for all emergency psychiatric admissions from a catchment area of about 200,000 persons older than 18 years. Patients are first admitted to the Emergency Unit (7 beds), where they stay for a maximum of 3 days. Then they are either discharged or transferred to one out of four specialized units.

All patients admitted during one year, from March 21, 2012, to March 20, 2013, were included, resulting in a total of 558 patients with 755 hospital stays. Thirty patients used their right to withdraw from participation and were excluded. Another 166 patients were excluded due to missing or incomplete serum-lipid samples. The inpatient study sample then included recordings of 362 patients, 158 men and 204 women (counted with only one hospital stay each; see 2.3. Procedure). The 3-months follow-up sample included recordings of 61 patients in outpatient clinics, 32 when readmitted to the ward, 3 from police records and 3 from hospital records: in total, 99 patients, comprising 46 men and 53 women (see 2.3. Procedure).

2.3. Procedure

All patients were informed verbally and in writing about the project. Routine blood samples (to measure TC and HDL) were taken by nurses at the ward the morning after admission, in most cases the patients had not been fasting. When patients were admitted on weekends or public holidays, the blood sample was given on the first regular working day. As part of the routine examination at admission, the physician on duty measured height and weight and performed an overall clinical judgment of the general condition ("*impaired general condition*" or "*normal general condition*").

Violent episodes during hospital stay were recorded by nursing staff using the Staff Observation Aggression Scale-Revised (SOAS-R) (Nijman et al., 1999). Additional information about inpatient violent episodes, including any use of protocols of coercive measures, was gathered from hospital records by the researchers. Violent episodes during the first 3 months after discharge were coded in a recording sheet by the patient's therapist at three collaborating outpatient clinics (see 2.5. Outcome measure). If a patient had been discharged and then admitted again to the acute ward during the project, outpatient violence for that post-discharge period was recorded in the recording sheet by the hospital staff. Additional information about episodes of post-discharge violence was collected by the researchers from out-patient hospital records and police records.

If a patient was readmitted to the ward during the project period, his or her previous post-discharge follow-up period was ended. The patient was then re-included with a new file number. Patients who had more than one hospital stay with recordings of TC and HDL during the project period were only counted once in the analyses. For patients with recorded violence in more than one hospital stay or post-discharge period, the stay with the earliest violent episode was chosen. For non-violent patients, the first stay was chosen.