Low-Density lipoproteins and suicidal behaviour in a large sample of first episode psychosis patients.

Summary

Increased risk of death by suicide has been reported in First Episode Psychosis (FEP) patients. Low concentrations of lipids have been associated with suicidality and violent suicide methods. The aims were to analyse the relationship between lipid profile at baseline with suicidality and suicide methods in a sample of 332 antipsychotic-naïve FEP patients. Depressive symptomatology (OR=1.15, 95% CI=1.06-1.24) and low Low-Density lipoproteins (LDL) (OR=0.99, 95% CI= 0.98-1.00) were significantly related with suicidal behaviour. Patients who used violent suicide methods did not show significant low levels of lipoproteins. Low LDL could be considered in the assessment of suicide risk.

KEY WORDS: lipoproteins, first episode psychosis, schizophrenia, suicide, LDL, HDL.

Introduction

Suicide represents the single most important cause of premature death in First Episode Psychosis (FEP) patients [1]. Earlier stages have been associated with higher risk periods. During last decades, there has been a growing interest in the role of the low lipids concentrations in suicidal behaviours from observation of the increased number of mortality for suicides, accidents or violence after the use of cholesterol-lowering drugs[2].

Lipid profile disturbances have been also reported in antipsychotic-naïve patients [3]. Moreover, lower Total Cholesterol (TC) and Low-Density lipoproteins (LDL) levels have been found in patients diagnosed by schizophrenia with history of suicidal behaviours[4]. In addition, leptin, an adipocyte hormone involved in energy homeostasis, has been shown to be reduced in such patients[5]. Significant low TC was also found in FEP patients with history of suicidal behaviour[6].

On the other hand, Kavoor et al. (2017) found that schizophrenic patients with lower TC, and LDL tended to act impulsively and that low lipid profile increased the risk of self-harming behaviours [7]. In a sample of 332 medication-free psychotic patients, low TC and leptin levels were also associated with violent suicide attempts[5].

The aims of our study were to confirm the association between lipid profile at baseline and suicidal behaviour occurred during a 3-year follow-up period in a large sample of antipsychotic-naïve FEP patients. Based on previous publications we hypothesized that 1) lower levels of TC, LDL and leptin will be associated with the presence of suicidal behaviours and 2) lower TC and leptin levels would correlate with more lethal method of suicide attempt.

Method

Data from this study came from a large epidemiological and 3-year longitudinal study of FEP program of Cantabria, Spain, (PAFIP) at the University Hospital Marqués de Valdecilla [8]. The study was approved by the Marqués de Valdecilla University Hospital review board, and written informed consent was obtained from all subjects after complete description of the study. The present study represents a secondary analysis drawn from a subset sample included in Ayesa-Arriola et al. (2015)[9], to specifically test the association between lipid profile and suicide risk. A complete description of the sociodemographic and clinical data as well as the differences between suicide attempters and non-attempters have been described in elsewhere[9]. No patient included in the study was under statin treatment.

Laboratory assessments

TC, High-Density lipoproteins-cholesterol (HDL-c) and LDL levels were measured. To minimize the effects of diet and lab technique, blood samples were obtained between 8 and 10 am after overnight fasting by the same personnel, in the same setting. Samples were measured by automated methods on an Advia Centaur (SIEMENS, Erlangen, Germany). Serum cholesterol levels were measured by means of immunonephelometry in a Nephelometer Analyzer II (SIEMENS) using the reagents manufactured by SIEMENS. Intra- and inter-assay reproducibility were <5% and <7%, respectively.

Statistical analyses

The Statistical Package for Social Science, version 19.0 [10], was used for statistical analyses. All statistical tests were two-tailed, and significance was set at the 0.05 level.

To test if FEP patients with suicidal behaviours presented different lipid profile ANCOVAs analyses were performed adjusted for age, sex and body mass index (BMI). To test if lower lipid profile correlated with high lethal method ANCOVAs analyses were performed controlled also for age, sex and BMI.

Binary logistic regression (backward: conditional) was conducted to identify predictors of suicidal behaviour. Significant variables in the univariate analyses reported in Ayesa-Arriola et al.[9] as well as significant variables found in the present study were included as predictors.

Results

ANCOVAs analyses confirmed that participants with the presence of suicidal behaviour had significantly lower TC ($F=4.49$; $p<0.05$), LDL ($F=4.69$; $p<0.05$) and leptin ($F=4.04$; $p<0.05$) compared to those without suicidal behaviours adjusted for sex, age and BMI (Table 1).

The regression model contained six independent variables: sex ($p<0.03$), depression ($p<0.01$), cannabis ($p<0.04$), TC ($p<0.04$), LDL ($p<0.03$) and leptin ($p\leq0.05$)[9]. Binary regression analysis showed that high scores in Calgary Depression Scale for Schizophrenia (CDSS) (OR=1.15, 95% CI=1.06-1.24) and low levels of LDL (OR=0.99, 95% CI=0.98-1.00) were significant independent parameters associated with suicidal behaviours (Table 1).

Discussion

Our hypotheses were partially confirmed. In accordance with the first hypothesis, we found that lower baseline LDL levels were associated with increased risk of suicide behavior in a 3-year follow-up period after a FEP presentation. However, we did not find any association with TC and leptin. Regarding the second hypothesis, we failed to find significant relationship between low concentrations of lipoproteins and more violent suicide methods. Finally, not surprisingly, depression was associated with suicidal behaviour as widely shown in the previous literature[11].

Although few studies have analysed the relationship between low serum lipid concentrations and violent suicidal behaviours in schizophrenic patients, significant relationship between low levels of TC, LDL[7] and leptin[5] and violent suicide methods have been reported. Although, the results of the present study have not shown significant association between self-harming methods and the presence of lipid profile, we found a trend towards significant differences between those who used violent methods and those who used non-violent methods in the levels of TC (157.06±25.24 vs. 170.85±27.46, p=0.07) and leptin (4.87±5.70 vs. 6.39±5.34, p=0.07).

A diathesis-stress model has been proposed to explain the relationship between lipid profile and suicidal behaviour[12]. Diathesis model suggested the presence of a low lipid profile as a trait factor related to aggression/impulsivity. Serum lipids levels might influence behaviours such as impulsivity, aggression and suicide through their influences on serotonergic transmission in the brain. Serum lipids could play a role in the production of the myelin sheath, in transmembrane exchange, enzyme function, synthesis of steroid hormones and neurotransmitter receptor expression[2]. Leptin regulates dopamine responses to salient stress stimuli not directly linked to food.

On the other hand, stress model sets forth that a low lipid profile could set off the suicidal behaviour. In our study, we found that exclusively low LDL level was independently associated with suicidality, which according to the previous model mentioned could act as a trait factor associated with aggression/impulsivity or as a triggering factor of the suicidal behaviour.

Some limitations need to be considered. Firstly, the design of the study did not allow to capture the dynamics of the lipids and their influence on suicidal behaviour. Secondly, although serotoninergic transmission, depends in part on brain cholesterol, experimental animal studies have demonstrated that brain cholesterol is relatively insulated from changes in circulating cholesterol. Thus, although our results show peripheral cholesterol changes, they should be interpreted with caution.

To the best of our knowledge no previous study has assessed the association between lipid profile with suicidal behaviours and suicidal method in a such large sample of antipsychotic-naïve FEP patients.

In conclusion, the role of low LDL in suicidal behaviour is supported by the results of this study. Suicidal behaviour is far from clear and seems that it depends on different cultural, social, individual and biological factors in a complex interrelated relationship. The identification of a low lipid profile at baseline related to suicidal behaviour can contribute to improve accuracy in detecting high-risk patients as well as implementing new prevention strategies of suicidal behaviour in FEP patient during the first stages of the disorder.

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