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Severe insomnia is associated with hypertriglyceridemia in women with major depression treated in psychiatry settings

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ABSTRACT

Background: Hypertriglyceridemia (HTG) is a cardiovascular risk factor. In the general population, elevated fasting triglyceridemia (TG) is associated with insomnia. Since insomnia is a core symptom of Major Depressive Episodes (MDE), we studied the association of severe insomnia with HTG in major depression.

Methods: We used the baseline data of the METADAP cohort, comprising 624 patients with a current MDE in a context of Major Depressive Disorder treated in psychiatry settings, without current alcohol use disorders. Patients were screened for severe insomnia, defined by a score of four or more on the three Hamilton Depression Rating Scale (HDRS) sleep items, and for HTG characterised by TG ≥ 200 mg/dL.

Results: Severe insomnia was observed in 335(54%) patients with a current MDE, of whom 234(70%) were women; 49(8%) patients had HTG, of whom 25(51%) were women. 69(11%) patients were treated with lipid-lowering drugs.

Severe insomnia was associated with a higher frequency of HTG in the whole sample (9.9% vs 5.6%, p = 0.046) and in the subgroup of women (9.0% vs 2.0%, p = 0.002). Multivariate logistic regression analyses adjusted for age, education levels, BMI and total HDRS scores confirmed the association between severe insomnia and HTG in the whole sample (OR = 2.02, 95%CI [1.00–4.08], p = 0.05) as well as in the subgroup of women (OR = 4.82, 95%CI [1.5–15.5], p = 0.008). No association was shown in men.

Perspectives: HTG should be systematically investigated in depressed patients with severe insomnia and particularly in women. Further studies are needed to explain the association we observed between severe insomnia and HTG.

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1. Introduction

Hypertriglyceridemia (HTG) defined as fasting triglyceridemia (TG) greater than or equal to 200 mg/dL is a cardiovascular risk factor and a biological marker linked to insulin resistance (Miller et al., 2011). Its frequency is 7.8% in the French general population (Ferrières et al., 2009) and 16.2% in the United States population (Miller et al., 2011). Studies in general population showed gender differences with a higher prevalence in men, though a higher cardiovascular risk was reported for women with HTG (Miller et al., 2011).

In the general population, there was no evidence from the NHANES study of a higher prevalence of HTG among the 4757 participants who declared having insomnia (Vozoris, 2016). Whereas, in the Hordaland study an inverse association was shown between sleep duration and fasting TG in 8860 subjects, aged 40–45 years (Bjorvatn et al., 2007). In this study, a sleep duration < 5 h was a risk factor for high fasting TG. Moreover, results from a population-based study of 3430 middle-aged Chinese subjects suggested that insomnia severity might be linked to higher fasting TG (Chien et al., 2010).

Major Depressive Disorder (MDD) is a main public health issue. By 2020, major depression will be the second leading cause of world disability and it is estimated by the World Health Organization that depression would take the first place in the global burden of disease by 2030 (WHO, 2012). Furthermore, MDD is associated with an increased risk for cardiovascular disease (Penninx, 2016). Insomnia is a core symptom of MDE: it is found in 80 to 90% of patients with MDE (Srisurapanont et al., 2015). Severe insomnia is identified in 25 to 50% of patients with MDE (Srisurapanont et al., 2015) and could lead to a worsening of health-related quality of life to a similar extent as chronic physical conditions (Srisurapanont et al., 2015).

Since MDE are associated with insomnia and an increased risk of cardiovascular disease, we investigated whether insomnia is associated with HTG in patients with a current MDE. We hypothesized that insomnia in MDE could be associated with a higher frequency of HTG. Moreover, since men and women in general population have differential HTG-related cardiovascular risks (Miller et al., 2011), we studied this association in men and women separately.

2. Methods

This study used the baseline data at inclusion time point from the METADAP cohort (Corruble et al., 2015).

2.1. Participants

Patients were aged 18–65 years. They had a current MDE in a context of MDD and were followed in psychiatry settings. This diagnosis was ascertained by the MINI International Neuropsychiatric Interview and a minimum score of 18 on the Hamilton Depression Rating Scale-17 items (HDRS-17). Patients with psychotic symptoms, bipolar disorders, psychotic disorders, eating disorders, current substance abuse or dependence (including alcohol use disorder) (DSMIV-TR), those currently taking psychostimulant or antipsychotic drugs, those with pregnancy, organic brain syndromes or severe unstable medical conditions were not included. All of them provided written informed consent.

2.2. Measures

2.2.1. Insomnia

Insomnia was assessed based on the 3 items of the HDRS-17 scale: difficulty falling asleep, difficulty staying asleep, and early morning awakenings. Each item was rated from 0 to 2 depending on the symptom presence and severity. The total insomnia score was the sum of the 3 item scores (0 − 6) (Manber et al., 2005). Severe insomnia was defined based on a total insomnia score ≥4, corresponding to a maximum rating on 2 out of 3 insomnia items. Severe insomnia (yes/no) was the main independent variable.

2.2.2. Hypertriglyceridemia

After an overnight fast, blood samples were obtained to measure the blood levels of fasting TG (mg/dL) using routine standardized laboratory methods.

HTG was defined according to the international standard TG ≥ 200 mg/dL, which is considered as the most relevant cut-off value to predict cardiovascular risks (Miller et al., 2011). HTG (yes/no) was the main dependent variable. Elevated TG was defined as TG ≥ 150 mg/dL, which cut-off is not a cardiovascular risk in itself but is rather considered as a marker of a metabolic dysregulation or syndrome (Miller et al., 2011).

2.3. Statistical analyses

After complete description of the data (means(standard deviation) or n(%)), bivariate analyses comparing patients with and without severe insomnia were performed using Chi2 tests for categorical variables and *t*-tests for continuous variables. Afterwards, multivariate linear and logistic regression analyses were used to control for potential confounders. Potential confounders were variables statistically significant in bivariate analyses. Age and sex were chosen as a priori confounders in all multivariate analyses. P values < 0.05 were accepted as statistically significant.

3. Results

3.1. Whole sample

Among the 624 participants, 433(69%) were women and 191(31%) men. Mean(sd) age was 46.1(13), HDRS score was 24.3(4.6) and Body Mass Index (BMI) was 23.6(5.1) kg/m^2.

The mean(sd) insomnia score was 3.5(1.9), with a median of 4 (IQR:3). Patients with severe insomnia were 335(54%), of whom 234(70%) were women.

The mean(sd) fasting TG level was 116(64) mg/dL. Its median was 108 (IQR:72). Elevated TG (≥150 mg/dL) was found in 134(21.5%) patients.

HTG were found in 49 (7.9%) patients, of whom 25(51.0%) were women. 69(11.0%) were treated with lipid-lowering drugs.

Bivariate analyses (Table 1) showed that patients with severe insomnia had both higher TG levels (p = 0.01) and higher rates of HTG (p = 0.04) than those without severe insomnia. Patients with severe insomnia had also a lower educational level (p = 0.02) and higher depression levels (p < 0.0005) compared to those without. There was no difference between the two groups in terms of number of prescriptions for lipid-lowering drugs.

Multivariate analyses controlled for age, sex, educational level, BMI and HDRS total score confirmed the results of bivariate analyses. TG levels were positively associated with severe insomnia (Hazard Ratio (HR) = 1.14, 95%CI[1.0–1.27], p = 0.02), independently from other variables. HTG was independently associated with sex (OR = 0.36, 95%CI[0.19–0.68], p = 0.001) with HTG being less frequent in women, BMI (OR = 1.13, 95%CI[1.07–1.2], p < 0.0005) and with severe insomnia (OR = 2.02, 95%CI[1.00–4.08], p = 0.05) (Table 2).

3.2. Men and women

Bivariate analyses (Table 1) showed that women with severe insomnia had higher TG levels (p = 0.001) and more frequent HTG (9.0%(sd = 1.4) vs 2.0%, p = 0.002). They also had a lower educational level (p = 0.003), a higher depression score (p < 0.0005) and a higher BMI (p = 0.002). No difference was shown in the number of prescriptions for lipid-lowering drugs.

Multivariate analyses controlled for age, educational level, BMI and