The influence of metabolic syndrome in major depressive disorder outcome

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Abstract: - Major depressive disorder is the most prevalent psychiatric illness, affecting more than 12% of men and more than 21% of women in their lifetime [1]. Previous studies indicate that prevalence of major depression has increased during the past century, although these trends may, in part, be explained by methodological problems. Depression has been associated with a variety of diseases; specifically it has been implicated in the development of cardiovascular disease (CVD) and all-cause mortality. However, little is understood about mechanisms that may account for poor health outcomes associated with depression [2]. Previous reports have speculated that depression may be linked to adverse health outcomes through an association with the metabolic syndrome. The metabolic syndrome, characterized by elevated abdominal obesity, triglycerides, blood pressure, fasting glucose, and low high-density lipoprotein (HDL) cholesterol, has an estimated prevalence of more than 21% in the US population.

Key-Words: - depression, metabolic syndrome, outcome

1. Introduction

Comorbid metabolic syndrome is common in depressive disorders, both in middle and in later life. In community samples of younger adults with depression, the point prevalence of comorbid metabolic syndrome disorders ranged from 10-30%. In community samples of older adults with late life depression, the point prevalence of co-morbid metabolic syndrome disorders ranged from 26% to 48.

Beyond the high rates of coexistence, comorbid metabolic syndrome has been often cited as a clinically relevant problem owing to its impact on acute treatment response in depression. Thus, several studies have found that metabolic syndrome is associated with an increased risk of withdrawal from treatment, a decreased response to acute antidepressant treatment and a longer time to both response and remission [3].

Although the impact of metabolic syndrome on response and recurrence of major depression has been previously studied extensively in general adult populations, its relevance to long-term treatment response in depression has received much less attention. Maintenance outcomes in depression and the factors that moderate those outcomes are critical, given the brittle nature of response in this age [4].

Thus, given the high recurrence rate of late-life depression [5] and the increased morbidity and mortality risks associated with this disorder [6] as well as the lack of controlled data regarding the impact of metabolic syndrome on its long-term treatment, further examination of metabolic syndrome as a predictor not only of response but of recurrence would greatly benefit clinicians in planning treatment.

Accordingly, we conducted an analysis to assess whether comorbid metabolic syndrome predicts treatment outcomes during both acute and maintenance treatment of major depression.

Our hypothesis was that metabolic syndrome would predict poor treatment outcome, including both a longer time to response during acute treatment, and an increased rate of recurrence and shorter time to recurrence during maintenance treatment.

2. METHOD

Participants were aged between 18 to 65 years or older, with a diagnosis per Structured Clinical Interview for DSM–IV of non-bipolar major depressive disorder (single episode or recurrent), a score on the 21-item Hamilton Rating Scale for Depression (HRSD).

In the acute phase and than in the maintenance phase, patients received open pharmacotherapy until they achieved response (defined as a HRSD score of 10 or less for three consecutive weeks). Pharmacotherapy consisted of SSRI or TCA.

Patients entered in a 24 months of continuation treatment to evaluate commorbidity with metabolic syndrome and their response.

All patients were allowed to remain on a stable dosage of antidepressants and if it had been required during the acute or continuation treatment the medication were changed. Patients remained in maintenance therapy for 2 years or until recurrence of a major depressive episode.

Recurrence required a HRSD score of 15 or over, meeting DSM–IV criteria for a major depressive episode during a SCID interview.

All patients provided written informed consent.

Metabolic syndrome were measured using the operational definition outlined in the ATP III report [7], and was defined as having 3 or more of the following: (1) High blood pressure: ≧130/85 mm Hg or antihypertensive medication use; (2) High triglycerides: ≧150 mg/dL; (3) Low HDL cholesterol: <40 mg/dL in men or <50 mg/dL in women; (4) High fasting glucose: ≧110 mg/dL or antidiabetic medication use; or (5) Abdominal obesity: waist circumference >102 cm in men or >88 cm in women [8].

The analyses included data on 89 persons who participated in the acute treatment phase.

For statistical analysis we used Kaplan–Meier survival analysis to assess the effect of metabolic syndrome on time to response. In order to analyse the influence of gender and metabolic syndrome on time to response [9] we compared the time to response in the group without metabolic syndrome v. the group with metabolic syndrome. Further, we stratified the sample based on the value of HDRS score. In order to control for other potential confounders, we subsequently fitted Cox proportional hazards models for each outcome, stratifying on severity of depression to estimate the unique effects of metabolic syndrome on acute treatment outcomes. Logistic regression models were used to examine the relationship between depression and the metabolic syndrome by gender. In univariate analyses, lifetime prevalence of a major depressive episode was entered as an independent variable and presence of the metabolic syndrome was entered as the dependent variable. In multivariate analyses, age, race, education, smoking status, physical inactivity, percent of dietary energy from carbohydrates, and alcohol use were added as covariates. Obesity was not included in the model because it correlates with waist circumference, which is a component of the metabolic syndrome. We tested for the presence of first-order interactions between depression and gender, depression and age, depression and race, and depression and education in evaluating the relationship with the metabolic syndrome. We controlled for baseline depression severity as measured by the HRSD scores, with the metabolic syndrome items.

3. RESULTS

As anticipated, there is no differences between women and men in the prevalence of the metabolic syndrome which was in this sample 29.6%, with men and women experiencing similar rates (population weighted prevalence for women: 30,12%; men: 29.08%; $x2 = 1.02$, p = .29). However, men were more likely to have lower blood pressure, p < .31), higher triglycerides ($x2 = 40.6$, p < .05), whereas women were more likely to have low HDL ($x2 = 12.60$, p = .001) and large waist circumferences ($x2 = 45.22$, p < .001).

Severity of depression, as measured by the HRSD, had a marked effect on hazard for relapse. This effect was independent of type of treatment and increased with level of pre-treatment severity of illness. For example, a 30-point HRSD score increased the hazard for relapse by 25% compared with those with a HRSD score less than of 29.

As showed in fig. 1, in men abandoned more often treatment than women, after 80 weeks (Gehan's Wilcoxon Test p=0,033)
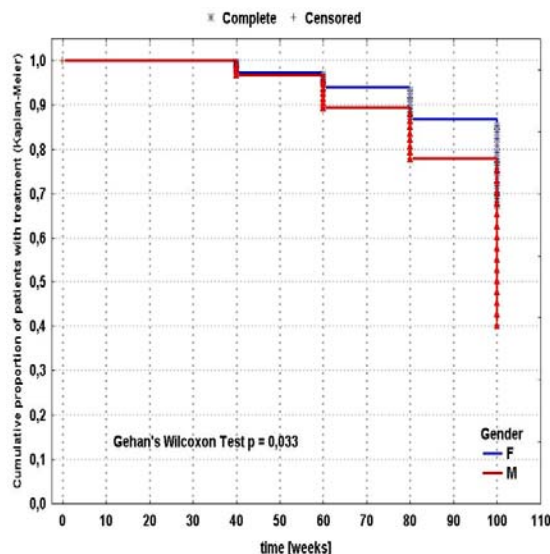

Fig.no.1.

4. CONCLUSIONS

Our study show that metabolic syndrome increase not only the risk of non-response in acute treatment of depression but also the risk of recurrence of the disorder.

In other words, patients who start treatment with metabolic syndrome have both a poorer acute response and a more brittle long-term response to pharmacotherapy [9]. These results demonstrate a strong negative impact of metabolic syndrome on short and long term outcomes of depression, even with optimal treatment [10]. These findings for acute treatment effects confirm previous reports that metabolic syndrome is associated with poorer response during acute treatment of depression [11, 12]. To our knowledge, only one previous uncontrolled follow-up study has examined the impact of comorbid metabolic syndrome on long-term outcome of depression: in this naturalistic study, metabolic syndrome did not predict time to recurrence [13].

We found that patients with higher HDRS scores had increased time to response. However, patients with lower HDRS scores had a shorter time to response than those with higher scores.

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