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Serotonin biomarkers and brain-derived neurotrophic factors in heart failure: a prospective cohort

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ABSTRACT

Aim: To analyze the prognostic of serotonin biomarkers and brain-derived neurotrophic factors (BDNF) on depression in patients with systolic heart failure. **Method:** An observational, multicenter, prospective cohort study in three specialized centers, from April 2014 to November 2016. **Study protocol:** multidisciplinary medical consultation, depression inventory, quality of life questionnaire and blood test to measure serotonin and BDNF, with analysis via high performance liquid chromatography and ELISA, respectively. In order to study the association of these markers with the analytical methods used, a statistical evaluation will be carried out using the chi-square test and the Pearson correlation coefficient. For the analysis of mortality and hospitalization, logistic regression and analysis of mortality risk will be used. The statistical significance is 5%. **Expected results:** biological markers are more effective than conventional tests (questionnaires) when used to identify the degree of depression.

Descriptors: Serotonin; Brain-Derived Neurotrophic Factor; Heart Failure; Depression.

INTRODUCTION

Heart failure (HF) is a disease that is highly prevalent worldwide⁽¹⁾. One study has demonstrated that depressed subjects have lower levels of the Brain-Derived Neurotrophic Factor (BDNF) than a control group. After antidepressant treatment, serum levels rose due to the increase of serotonin which regulates the synthesis of BDNF⁽²⁾.

Nevertheless, the author is now aware of any studies that have been developed in multicenter cohorts aimed at correlating the prognostic impact of these markers on depression in systolic HF.

To assess the symptoms of depression, the Beck Depression Inventory (BDI) is currently used to discriminate between healthy individuals and the depressed or anxious⁽¹⁾.

Since this disorder is a predictor of the quality of life⁽¹⁾, we suggest that a longitudinal follow-up may indicate the likelihood of the occurrence of depression in HF patients. This study's hypothesis is that serotonin and BDNF, when evaluated prospectively, may be, in heart failure, markers of depression or risk factors.

AIM

To correlate the prognostic of serotonin, biomarkers and BDNF with depression in patients with systolic HF.

METHOD

Study design and participants:

Multicenter observational study, prospective cohort⁽³⁾ type, involving 12 months of follow up in the form of quarterly checks in three outpatient specialist clinics: the Antônio Pedro

University-Hospital (center 1, Niterói, RJ); the Laranjeiras National Institute of Cardiology (center 2, Rio de Janeiro, RJ) and the Porto Alegre General Hospital (center 3, Porto Alegre, RS). The research will be carried out from April 2014 to January 2016.

Participants:

Adult patients diagnosed with systolic HF (Boston criteria) whose communication skills have been preserved will be invited to participate in the study. Patients who use medication with selective serotonin reuptake inhibitors, who are illiterate, who have limited movement and/or have medical records of cognitive impairment, will be excluded.

Definition of Variables:

- Dependent variable: depression
- Independent variable: sociodemographic and clinical levels of serotonin and BDNF.

Sample calculation:

The sample was calculated based on moderate and/or severe BDI scores (BDI>18) of 51% in a previous study (1). Considering the population served in centers 1 (120 patients), 2 (150 patients) and 3 (700 patients), with a 95% confidence level and a margin of error of 5%, we will include 276 patients in this study. Assuming a 20% discontinuity in the patients being monitored, the estimated sample will be 332 individuals. The calculation was done using WinPepi v.11.43 software.

Study protocol:

In the three centers, after training, the multidisciplinary team will work with standardized

questionnaires. Patients will be monitored for 12 months. Blood samples for determining the markers shall be taken by a single lab (also in charge of transport and storage). The researchers will have no access to the test results in order to minimize errors that might interfere with the study. Investigator 1 will conduct the query and investigator 2 will be in charge of storing the examined material.

- Stage 1: Training of research protocols in the centers. Selection of patients from the database, applying the protocol to the ones considered eligible. In the first query procedure: history, quality of life questionnaire, questionnaire on depression, anthropometry, physical capacity and blood test.
- Stage 2: Medical visit (3rd to 9th month). The group will be monitored in terms of general health guidelines.
- Stage 3: Medical visit (6th to 12th months). The patients will participate in the consultation with the protocol described in Stage 1.

Data Analysis

The organization of data will be carried out using the Microsoft Excel 2007 program, and the analysis will be done using the SPSS (Statistical Package for the Social Sciences) v.17.0 program. Categorical variables are expressed by the distribution of absolute and relative n (%) frequencies and percentages. Continuous variables were analyzed in terms of the calculation of mean, median, standard deviation, coefficient of variation (CV) and percentiles. In terms of inferential analysis, the Student "T" and the Mann-Whitney tests will be used, and the Cronbach's alpha will be used to determine data reliability. To determine the association between serotonin and BDNF and the biopsychosocial variables, the chi-square test will be used. For categorical

variables, comparisons between groups will use the Pearson correlation coefficient. A *p* bivariate value <0.05 will be considered statistically significant for all analyzes⁽³⁾.

EXPECTED RESULTS

Biological markers are more effective than conventional tests (questionnaires) for identifying the degree of depression.

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