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Low serum prealbumin levels in post-stroke depression

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ABSTRACT

Previous studies have shown that prealbumin is associated with depression. However, the association between prealbumin and post-stroke depression remains unelucidated. This observational cohort study determined whether low baseline serum prealbumin could predict post-stroke depression at 1 month in patients admitted with acute stroke. The study, conducted from October 2013 to September 2014, included 307 patients with acute stroke who were followed-up for 1 month. Serum prealbumin was measured within 24 h after admission using an immunoturbidimetric method. The17-item Hamilton Depression Scale was used to evaluate depression symptoms. Patients with a depression score of ≥ 7 were evaluated using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th edition, for diagnosing post-stroke depression at 1 month. Binary logistic regression analysis was used to evaluate possible predictors of post-stroke depression. Overall, 93 (30.3%) patients were diagnosed with post-stroke depression. Serum prealbumin was significantly lower in patients with versus those without post-stroke depression, and was a significant predictor of post-stroke depression after adjusting for confounding risk factors. In conclusion, baseline serum prealbumin level was associated with post-stroke depression at 1 month, suggesting that prealbumin might be a useful biomarker for post-stroke depression.

1. Introduction

Depression is a common mood disorder that is recognized as an important complication of stroke. It is particularly prevalent among stroke survivors, with an incidence rate of 30% (Hackett et al., 2005; Whyte and Mulsant, 2002). Depression not only affects the quality of life (Ayerbe et al., 2013) but also reduces functional ability (Linden et al., 2007), worsens rehabilitation outcomes (Masskulpan et al., 2008), and increases mortality after stroke (Whyte and Mulsant, 2002). Factors associated with post-stroke depression include history of depression before stroke, history of a previous stroke, stroke severity, and disability after stroke (Ayerbe et al., 2013). Patients with depression are unable or are less likely to participate in the rehabilitation process or to engage in necessary behavioral changes and cognitive therapies, leading to a vicious cycle between depression and functional impairment (Hama et al., 2011).

In patients who develop depression symptoms after stroke, early intervention can effectively reduce stroke-related complications and mortality (Paolucci, 2008; Schmid et al., 2011). However, the lack of clarity on the underlying pathophysiological mechanisms is a hurdle to the effective prevention and management of post-stroke depression.

Prealbumin, also known as transthyretin, is a 54-kDa protein that is mainly synthesized by the liver and choroid plexus and participates in the transport of thyroxin and retinol. Recently, serum prealbumin has been widely studied in clinical trials. Serum prealbumin level is decreased in various conditions such as inflammation, protein malnutrition, end-stage liver disease, or malignancy (Ingenbleek and Young, 1994). Prealbumin is a negative acute-phase reactant; acute phase cytokines downregulate prealbumin mRNA expression and cause a rapid decrease in serum prealbumin concentrations (Myron Johnson et al., 2007). Further, a negative association has been reported between serum prealbumin levels and inflammation.

Low prealbumin levels have been noted in several neurological conditions such as Parkinson's disease, Alzheimer's disease, and stroke (Fleming et al., 2009). Serum prealbumin levels were found to negatively correlate with stroke severity in the young (Gao et al., 2011), and were significantly decreased in patients with recurrent ischemic stroke (Zhang et al., 2011). The relationship

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between prealbumin and depression remains controversial. A majority of studies have shown low prealbumin levels in the cerebrospinal fluid (CSF) of patients with major depressive disorder (Hatterer et al., 1993; Sullivan et al., 1999; Sullivan et al., 2006). Hatterer et al. (1993) observed that CSF prealbumin levels were significantly lower in patients with depression than in patients with other neurological conditions. Furthermore, Sullivan et al. (1999) made similar observations in two studies comparing CSF prealbumin levels between patients with major depression and healthy controls. They also found that decreased prealbumin production in depression was associated with serotonergic hypofunction.

Thus, it is plausible that serum prealbumin levels may have a predictive role in post-stroke depression; however, no study to date has evaluated this relationship. Hence, we aimed to explore if low serum prealbumin levels contributed to the development of post-stroke depression at 1 month.

2. Methods

2.1. Study population

We used an observational cohort study design to explore the relationship between serum prealbumin and post-stroke depression. Patients without post-stroke depression formed the comparison group. Between October 2013 and September 2014, patients with a first-ever episode of or recurrent acute stroke who were consecutively admitted to the Stroke Unit of the First Affiliated Hospital of Wenzhou Medical University were considered for inclusion in the study. Stroke was diagnosed using computed tomography or magnetic resonance imaging. The study included Chinese patients aged 18–80 years with acute stroke, admitted to the hospital within 7 days of stroke onset, and who were able to provide informed consent. The exclusion criteria included transient ischemic attack or subarachnoid hemorrhage; history of any central nervous system condition such as Parkinson's disease, dementia, or trauma; history of depression (clinical diagnosis or previous treatment) or other psychiatric disorders; and serious diseases such as moderate-to-severe liver or renal disease, heart failure, malignancy, or severe infections. Written informed consent was obtained from all study participants or their relatives. The protocol was approved by the Medical Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University.

2.2. Clinical variables

Demographic data (age, sex, body mass index [BMI], years of education and marital status), location of stroke lesion, and vascular risk factors (current smoking and drinking status and history of hypertension, diabetes, or previous stroke) were recorded at admission (baseline).

Stroke severity at admission was assessed by trained neurologists using the National Institute of Health Stroke Scale (NIHSS) (Brott et al., 1989), a 15-item impairment scale used to assess stroke severity based on the following domains: level of consciousness, eye movements, facial movements, visual fields, neglect, sensation, muscle strength, coordination, language and speech. A higher score indicates a more severe stroke.

Post-stroke functional impairment at discharge was evaluated by trained neurologists using the modified Rankin Scale (mRS) (Bonita and Beaglehole, 1988) and the Barthel Index (BI) (Mahoney and Barthel, 1965). The mRS is a scale for measuring the degree of disability or dependence in activities-of daily living, and ranges from 0 (perfect health without symptoms) to 6 (death). The BI is a measure of activities of daily living and indicates the degree of independence over 10 domains of functioning (activities). The scale for each function ranges from 0, indicating inability or dependence, to a maximum of 5, 10, or 15, indicating full independence.

2.3. Psychological measurement

The 17-item Hamilton Depression Scale (17-HAMD) (Hamilton, 1960) is a questionnaire used to rate the severity of depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss, and somatic symptoms. A score of 0 to -7 is considered to be normal, while a score of >7 is indicative of depression. A higher score indicates more severe depression. The 17-HAMD was used to evaluate depression symptoms in this study. Patients with a HAMD score of ≥ 7 were evaluated using the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) for the diagnosis of post-stroke depression. DSM-IV is the standard classification for mental disorders used by mental health professionals in the United States (Association, 1994). Depression assessments were evaluated by psychiatrists who were blinded to the type, size, and location of the index stroke.

2.4. Blood collection and laboratory tests

Fasting blood samples were obtained from all patients within 24 h after admission. Blood was drawn from the antecubital vein and collected in anticoagulant tubes. Serum prealbumin was measured using an immunoturbidimetric method on an immunoassay analyzer (Beckman Coulter Inc., Fullerton, CA, USA). The intra-assay and inter-assay coefficients of variation were less than 2.5% and 3.0%, respectively. Serum albumin levels were measured simultaneously using the bromocresol green method. The biomarker concentrations were evaluated in a central laboratory by investigators who were blinded to the patients' clinical outcomes.

2.5. Statistical analyses

Continuous variables were summarized as mean (standard deviation [SD]) or median (interquartile range [IQR]), depending on the normality of data distribution and categorical variables were summarized as counts and proportions. Student's t test or one-way analysis of variance (ANOVA) was used to compare the differences between the two groups. The years of education and NIHSS, BI, mRS, and HAMD scores were not normally distributed, and are reported in terms of median and IQR. The non-normal variables were log-transformed. The Mann–Whitney U test was used when variables were not normally distributed even after log-transformation. Categorical data (sex, history of hypertension, and location of stroke lesion.) were compared using the chi-square test. The various statistical tests are summarized in Table 1. Pearson correlation coefficient was used for bivariate correlations analysis. A binary logistic regression analysis was used to assess variables associated with the development of post-stroke depression. The results are presented as the adjusted odds ratios (ORs) with the corresponding 95% confidence intervals (CIs). Data were managed and analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered to be statistically significant.

3. Results

Of the 552 patients with acute stroke screened, 375 met the study entry criteria and were included in the study and 307 completed follow-up (Fig. 1).