The effect of cigarette smoking on vitamin D level and depression in male patients with acute ischemic stroke

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Abstract

Objective: The association between low vitamin D levels and depression has been well documented in nonstroke subjects. Accumulating evidence shows that low vitamin D levels may be also associated with depression post stroke. Cigarette smoking was associated with lower vitamin D levels. The purposes of this study were to compare vitamin D levels in smokers to nonsmokers and examine the association between vitamin D levels and depression symptoms in patients with acute ischemic stroke.

Materials and methods: Serum levels of 25-hydroxyvitamin D [25(OH)D] were measured in 194 males within 24 h after admission: 116 smokers and 78 nonsmokers. Depression symptoms were assessed with the 17-item Hamilton Depression Scale (HAMD-17). Patients with the HAMD-17 score >7 were identified to have depression symptoms.

Results: The chi-square test showed that the frequency of depression in the smoker group was 23.3% (27/116), which was significantly higher than that in the nonsmoker group (11.5% = 9/78), with an odds ratios (OR) of 2.33 (95% CI: 1.03–5.27; χ^2 = 4.25, df = 1, p = 0.039, φ = 0.15). Vitamin D levels were significantly lower in smokers than in nonsmokers (52.4 ± 20.8 vs 61.7 ± 19.2; F = 9.88, p = 0.002), with an effect size of 0.05 (η_p^2). Patients with depression symptoms showed lower vitamin D levels than those with no depression symptoms (49.2 ± 19.6 vs 57.7 ± 20.6; F = 5.03, p = 0.03), with an effect size of 0.03 (η_p^2).

Conclusion: Higher rates of depression in smokers with acute ischemic stroke may be associated with lower vitamin D levels induced by smoking.

1. Introduction

Depression is a quite prevalent issue among stroke survivors, affecting approximately one-third of individuals [1]. Patients with depression experience worse stroke-related outcomes in the form of greater functional disability and higher mortality [2]. Therefore, it will be beneficial to learn more about the risk factors for depression, which may help us to develop a better intervention to improve the outcomes of stroke survivors.

Cigarette smoking has been well established to be a risk factor for stroke [3,4]. Besides, smoking is also tightly associated with mental illness. Previous studies have demonstrated that smoking is associated with an increased risk of depression, suicide, and other mental illnesses [5–11]. In the National Comorbidity Survey, about 59% of individuals with a life-time history of depression were past or current smokers, compared to less than 39% of those without a life-time history of depression [9,12]. Considering the link between smoking and depression, it will be interesting to see whether smoking was associated with the mental health of patients with acute ischemic stroke (AIS), which has not been studied yet. Moreover, we would also like to explore an underlying mechanism which may explain for this relationship.

Vitamin D is a neurosteroid, with the vitamin D receptors widely expressed in the cerebrum, in glial and neuronal cells. Vitamin D may play a part in neuroprotection through different mechanisms such as antioxidation/anti-inflammatory mechanisms, inhibition of inducible nitric oxide synthase, neuronal calcium regulation, detoxification pathways, or enhanced nerve conduction [13]. Besides, vitamin D is also associated with depression. Previous studies have demonstrated a strong relationship between vitamin D and depression [14,15]. A study by Przybelski *et al.* found that patients suffering from mood disorders showed lower

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vitamin D concentrations [16]. Moreover, recent researches have demonstrated a strong relationship between low vitamin D level and depression in acute ischemic stroke patients [17,18].

Vitamin D deficiency is associated with various factors such as bad dietary habit and reduced sun exposure. Meanwhile, more and more studies have observed a strong association between smoking and vitamin D deficiency [19–21]. A study by Jaaskelainen *et al.* including 5714 subjects (47% men) aged 30–79 years found that smokers had lower vitamin D concentrations than nonsmokers [21]. Moreover, Thuesen *et al.* in a recent study including 6146 subjects demonstrated that the odds ratios of vitamin D severe deficiency (25(OH)D <10 ng/ml)/vitamin D deficiency (25(OH)D <20 ng/ml) associated with smoking were 1.47 and 1.36, respectively [22].

Based on the close relationship between smoking and vitamin D insufficiency, as well as the link between depression and vitamin D deficiency, we hypothesize that smoking may play a role in the altered vitamin D levels of stroke patients, which was associated with the depression. Because smoking is substantially more common among Chinese men than in women, we included only male subjects. The purposes of this study were to determine (1) differences in vitamin D levels between smokers and nonsmokers and (2) any associations between vitamin D levels and depression symptoms in smokers and nonsmokers with acute ischemic stroke.

2. Materials and methods

2.1. Participants

One hundred and ninety four patients with first-ever or recurrent acute ischaemic stroke were recruited from the Stroke Unit of The First Affiliated Hospital of Wenzhou Medical University between October 2013 and May 2014. The inclusion criteria were (1) Chinese; (2) age 18–80 years; (3) acute stroke occurring within 7 days before admission; (4) confirmed by computerized tomography (CT) or magnetic resonance imaging (MRI). The exclusion criteria were (1) transient ischemic attack; (2) patients with a history of central nervous system diseases such as Parkinson's disease, dementia, trauma, tumor or hydrocephalus; (3) patients who had a history of mental illness and had recently accepted antidepressant, antipsychotics and participated in any psychological treatment; (4) patients who were unconscious and showed serious cognitive impairment; (5) patients with severe visual or auditory impairments; (6) active alcohol or drug abuse; and (7) patients with osteoporosis or taking vitamin D supplementation.

All the patients in the research had signed an informed consent and the study was approved by the ethics committee of The First Affiliated Hospital of Wenzhou Medical University.

2.2. Measures

Demographic data was obtained through the patients' self-reports. Clinical data was abstracted from the medical records as well as the self-reports. All the scales were measured at admission. Depression symptoms were measured using the 17-item Hamilton Depression Scale (HAMD-17) at admission [23]. Subjects with the HAMD-17 score >7 were identified to have depression symptoms. Stroke severity was assessed by experienced neurologists using the National Institutes of Health Stroke Scale (NIHSS) at admission. Sleep quality of the patients was evaluated by the Pittsburgh Sleep Quality Index (PSQI) questionnaire [24]. Cognition function was assessed by the Mini-Mental State Examination.

In addition, we adopted a cigarette smoking questionnaire to record the smoking behavior, smoking history, as well as family history of smoking. Smokers were defined as individuals who smoked more than one cigarette per day and had smoked for more than one year. Nonsmokers were defined as those who had smoked less than 100 cigarettes during their lifetime. If the subject identified themselves as a smoker, then further questions were asked: (1) the average number of cigarettes per day in the week before admission and (2) the total years of smoking. If the subject currently was a nonsmoker, further questions were asked including whether or not they had quit smoking, regarding previous smoking behavior. Quitters were excluded from our study. According to the questionnaire responses, 116 (59.8%) were identified as "smokers", whereas 78 (40.2%) were identified as "nonsmokers". The baseline characteristics of the two groups are displayed in Table 1.

The cranial computerized tomography was performed on patients within 24 h after admission. The cranial magnetic resonance imaging was performed on patients within 72 h after admission. The lesion locations of acute stroke were also recorded.

Blood samples were collected within 24 h after admission. Serum 25-hydroxyvitamin D [25(OH)D] was selected as the measure of vitamin D status for its widespread clinical application, testing protocol and standardized ranges. Serum 25(OH)D level was measured by a competitive protein binding assay in our hospital's laboratory. The intraassay coefficient of variation was 7%–10%.

2.3. Statistical analysis

Baseline characteristics of the smoker and nonsmoker groups were compared using the chi-square test, analysis of variance, student t test, Mann–Whitney U test and Fisher's exact test, as appropriate. As vitamin D levels were normally distributed in smoker and nonsmoker groups (Kolmogorov–Smirnov one sample test), the principal analysis was one-way ANOVA. Similarly, vitamin D levels were also compared between the depression group (HAMD-17 > 7) and normal group (HAMD-17 ≤ 7) by one-way ANOVA. The difference of smoke time and number of cigarettes between the depression group and normal group was analyzed by analysis of covariance, with the age being included as the covariate. Correlation among vitamin D and clinical ratings (e.g. smoke time, number of cigarettes smoked) was examined by Pearson