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Depression and anxiety are associated with reduced antiepileptic drug adherence in Chinese patients

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ABSTRACT

Objective: The aim of this study was to investigate the association of depression and anxiety with adherence to antiepileptic drugs (AEDs) in Chinese patients with epilepsy.
Methods: A total of 184 Chinese patients with epilepsy, and without cognitive impairment, underwent psychometric tests: the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI). Adherence to antiepileptic drugs was measured by the eight-item Morisky Medication Adherence Scale (MMAS-8). Data on patients' demographic characteristics, disease characteristics, and treatment characteristics were also collected.
Results: The MMAS-8 indicated that 39.7% of the patients had low adherence, 34.2% had moderate adherence, and 26.1% had high adherence. Demographic, disease, and treatment characteristics were not significantly different between the low adherence group and the moderate-to-high adherence group. Thirty-six (19.6%) patients had moderate-to-severe depression according to the BDI, and 47 (25.5%) patients were considered anxious according to the BAI. A significant difference in depression scores was found between the low adherence group and the moderate-to-high adherence group ($\chi^2 = 13.625$, $P < 0.001$). We also found a significant difference in anxiety scores between the two groups ($\chi^2 = 8.331$, $P = 0.004$). Pearson's correlations indicated that depression scores ($r = -0.281$, $P < 0.001$) and anxiety scores ($r = -0.255$, $P < 0.001$) were negatively correlated with adherence. Negative correlations were found between BDI scores and items 2, 7, and 8 of the MMAS-8 ($P < 0.05$); negative correlations were also found between BAI scores and items 3 and 6–8 ($P < 0.05$).
Conclusion: Depression and anxiety were associated with reduced antiepileptic drug adherence in Chinese patients. Addressing depression and anxiety among patients with epilepsy may help improve adherence to AEDs.

1. Introduction

Long-term therapy with antiepileptic drugs (AEDs) is the mainstay of treatment for patients with epilepsy (PWE), and these drugs reduce seizure frequency in up to 67% of patients [1]. However, nonadherence to AEDs is common, with the average rate of nonadherence ranging from 20% to 50% [2]. People who fail to take their medication will visit the emergency room more often because of lack of seizure control and seizure-related injuries [3]. Moreover, nonadherence to AEDs is reported to increase the cost of treatment [4] and increase the mortality risk threefold [5].

Treatment adherence is affected by individual patient factors (demographic and socioeconomic characteristics, as well as perceptions and beliefs about epilepsy), disease characteristics (seizure frequency and severity), medication use (number of daily doses and side effects), and factors related to the patient–provider relationship [6]. Psychological factors, such as depression and anxiety, have been studied in many nonepileptic diseases [7,8], and a meta-analysis by DiMatteo et al. reported that patients with depression have a three times greater rate of nonadherence compared with patients without depression, but the relationship between anxiety and nonadherence is variable [9]. Depression and anxiety are two common psychological disorders that are comorbid with epilepsy, and they have been reported to affect the quality of life negatively [10]. In spite of the high prevalence of depression and anxiety in patients with epilepsy, only a few studies have examined the effect of depression on AED adherence [11,12], and little is known about the Chinese population, in which there were 9 million patients with epilepsy in 2007 [13]. Moreover, the relationship between anxiety and adherence to AEDs remains unclear.

Many methods have been established to measure AED adherence, including blood-level monitoring, pill counts, and medication refills; however, all of these methods have their limitations [14]. Patient self-reports can be a simple and effective measure of adherence [15]. One self-report questionnaire, the 8-item Morisky Medication Adherence Scale (MMAS-8), is widely used because it is easy to administer and simple, and it has a good relationships with other measures of adherence [16]. The Chinese version of MMAS-8 has been recently validated in Chinese PWE [17].

The primary purpose of this study, therefore, was to investigate the association of depression and anxiety with AED adherence in Chinese

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patients with epilepsy. The study also examined the relationships between the disease characteristics, treatment characteristics, and adherence to AEDs.

2. Methods

2.1. Participants

This prospective, cross-sectional study was approved by the Ethics Committee of the Second Affiliated Hospital, School of Medicine, Zhejiang University. Outpatients with epilepsy were recruited from July 2014 to March 2015. The inclusion criteria were as follows: (1) diagnosis of epilepsy according to the International League Against Epilepsy (ILAE) [18]; (2) age of ≥18 years and ≤60 years; (3) >6 months from the first seizure; (4) AED treatment for at least 3 months; (5) absence of major cognitive impairment; and (6) the ability to read and write. The exclusion criteria were as follows: (1) presence of nonepileptic psychogenic seizures; (2) any surgery related to epilepsy; and (3) without AED administration.

Patients meeting the inclusion and exclusion criteria were enrolled to undergo a clinical evaluation. These patients' demographic data and disease information were also collected. The Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) were used to evaluate depression and anxiety. Self-reported adherence was measured by the MMAS-8.

2.2. Measures

2.2.1. MMAS-8

The MMAS-8 is a multi-item questionnaire that is widely used to measure self-reported adherence. The Chinese version of the MMAS-8 has been validated [17]. Items 1–7 are yes/no questions, in which a "no" answer receives a score of 1 and a "yes" answer receives a score of 0, except for item 5, which is reverse-scored. Item 8 is measured on a five-point scale. The responses "never", "once in a while", "sometimes", "usually", and "all the time" are scored, 1, 0.75, 0.50, 0.25, and 0, respectively. The total score ranges from 0 to 8. Scores of 8, 6–7, and <6 indicate high, moderate, and low adherence, respectively.

2.2.2. BDI

The Beck Depression Inventory (BDI) is a commonly used self-administered measure of depressive symptoms, which consists of 21 items reflecting subjective and vegetative symptoms of depression. Each item is rated on a 4-point scale ranging from 0 to 3. Total scores range from 0 to 63. A cutoff score is used to classify individuals who who have no-to-mild depressive symptoms or moderate-to-severe symptoms. The cutoff score for patients with epilepsy is higher than that for populations without epilepsy. The cutoff score in our study was 16, as suggested by Devinsky et al. [19].

2.2.3. BAI

The Beck Anxiety Inventory (BAI) is a commonly used self-administered measure of anxious symptoms, which consists of 21 symptoms associated with anxiety. Participants were asked to rate how much each symptom had bothered them over the last week on a 4-point scale ranging from 1 (not at all) to 4 (severely—could barely stand it). Scores range from 21 to 84. A cutoff score is used to classify patients who have no-to-mild anxiety (scores < 37) or moderate-to-severe anxiety (scores ≥ 37) [19].

2.3. Statistical analysis

The data are presented as mean (standard deviation, SD), median (interquartile range, IQR), or percentages. Continuous variables were tested for normality with the Kolmogorov–Smirnov test. For the comparison of continuous variables between groups, we used Student's *t*-test when variables were normally distributed; otherwise, the nonparametric Mann–Whitney test or Kruskal–Wallis test was used. For the comparison of categorical variables, we used Pearson's chi-square test. The relationships of the BDI scores and the BAI scores with the MMAS-8 scores were analyzed by Pearson's correlations. The relationships of the BDI scores and the BAI scores with individual items on the MMAS-8 were analyzed by Spearman's rank correlations. All of the data were analyzed using IBM SPSS software, version 20. Statistical tests were performed using a 5% significance level ($P < 0.05$).

3. Results

The descriptive statistics for the demographic, epilepsy, and treatment variables of the 184 participants (18–58 years old) are summarized in Table 1. The median MMAS-8 score was 6.76 (range = 0.50 to 8.00). Of the 184 patients, 39.7% had low adherence, 34.2% had moderate adherence, and 26.1% had high adherence. The median age of the participants was 28 years (IQR = 23–36 years), 52.7% were married, and the majority (61.4%) were employed; 42.9% were living in rural areas. The median duration of the disease was 84 months; 80.4% of the patients had partial seizures, and 41.3% were on monotherapy. Comparisons of the variables between the low adherence group and the moderate-to-high adherence group are also shown in Table 1; no significant difference was found between the two groups on any of the variables.

According to the BDI, 148 (80.4%) patients had no or mild depressive symptoms, and 36 (19.6%) patients had moderate-to-severe depressive symptoms. The median score was 8 (IQR, 2–13). Forty-seven of the 184 (25.5%) patients were considered to have anxiety as measured by the BAI; the median score was 28 (IQR, 24–37). The relationship of psychogenic factors (depression and anxiety) with adherence is shown in Table 2. A significant difference in depression scores was found between the low adherence group and the moderate-to-high adherence group ($\chi^2 = 13.625$, $P < 0.001$). We also found a significant difference in anxiety scores between the two groups ($\chi^2 = 8.331$, $P = 0.004$). Pearson's correlations indicated that the depression scores ($r = -0.281$, $P < 0.001$) and the anxiety scores ($r = -0.255$, $P < 0.001$) both were negatively correlated with adherence.

The correlations between the individual MMAS-8 items and the BDI and BAI scores were analyzed in order to identify the specific component of medication nonadherence impacted by depression and anxiety (see Table 3). Significant negative correlations were found between BDI scores and items 2, 7, and 8 ($P < 0.05$). Significant negative correlations were also found between with BAI scores and item 3 and items 6 through 8 ($P < 0.05$).

4. Discussion

This is the first study, to our knowledge, to investigate the impact of depression and anxiety on adherence to AEDs in China. We found that self-reported symptoms of depression and anxiety were associated with reduced AED adherence in Chinese PWE. Such patients were more likely to report that antiepileptic treatment was difficult and to forget to take their AEDs.

In our study, seventy-three (39.7%) patients had low adherence, consistent with Lupattelli et al.'s study [20], which included only 25 pregnant women with epilepsy. A study in the USA found that AED nonadherence among low-income, racially/ethnically diverse patients with epilepsy was 36% [21], which is comparable with our results. Nonadherence to AEDs has been reported as ranging from 20% to 50% due to different definitions of adherence and methods of measurement [2]. Another Chinese study reported that the low adherence rate for taking AEDs was 20.8%, as assessed by the MMAS-8 [17]. The discrepancy with our results could be related to different patient samples, that a much smaller sample was enrolled in that study [17], and that stricter inclusion/exclusion criteria were used in our study. The moderate-to-