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A comparison of inpatients with anxious depression to those with nonanxious depression

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ABSTRACT

Anxiety symptoms are common for patients with major depressive disorder (MDD). Anxious depression has been considered MDD with high levels of anxiety symptoms. The objective of this study was to investigate the factors associated with anxious depression for Chinese inpatients with MDD. A total of 174 acutely ill patients were enrolled. Baseline demographic variables, suicide risk, depression severity, quality of life (QOL), and daily functional impairment were assessed. Those MDD patients with a 17-item Hamilton Depression Rating Scale (HAMD-17) anxiety/somatization factor score ≥ 7 were defined as anxious depression. Logistic regression was employed to examine the factors associated with anxious depression. One hundred and forty-one (81.0%) of the subjects reported anxious depression. Patients with anxious depression were more likely to have melancholic features, to be older, to experience more severe depression, to be at greater risk of suicide, to have more pain, poorer quality of life, and more severe functional impairment. Anxious depression is common in inpatients with MDD. These findings suggest that anxious depression significantly differs from nonanxious depression on several clinically relevant variables. These data add to a growing body of evidence that anxious depression is a more complex presentation of depression.

1. Introduction

Anxiety and depression are the most common coexisting psychological problems (Baldwin et al., 2002). There are several approaches to conceptualize the relationship between major depressive disorder (MDD) and anxiety (i.e., anxious depression) (Fava et al., 2004). A dimensional approach, advocated by DSM-5, would conceptualize anxiety as a single dimension of a multidimensional syndrome categorized together as MDD. Alternatively, anxiety can be conceptualized in MDD as a comorbid disorder. The dimensional approach is commonly regarded to be more applicable to clinical practice, since many depressed patients with prominent anxiety syndromes are not assessed clearly as having a distinct anxiety disorder, or do not fully meet criteria for a DSM-IV or ICD-10 diagnosis (Sanderson et al., 1990; Wiethoff et al., 2010). To date, many studies of anxious depression have used the dimensional approach to define this subtype (Fava et al., 2004, 2006, 2008; Wiethoff et al., 2010; Chan et al., 2012). Moreover, it has been proposed that when compared to the comorbid approach, the dimensional approach has been reported to provide more clinically relevant data on differences between those subjects with anxious depression and those without (Ionescu et al., 2013). In psychosocial theory, feeling of defeat and entrapment is associated with increased anxiety and depression (Griffiths et al., 2014). According to current neurobiological knowledge, anxious depression (dimensional) may have a distinct neurobiological profile compared to non-anxious depression (Ionescu et al., 2013). In STAR*D, anxious depression is considered major depressive disorder (MDD) with high level of anxiety and is defined as depressed patients with a baseline 17-item Hamilton Depression Rating Scale (HAMD-17) (Hamilton, 1960) anxiety/somatization factor score ≥ 7. Results indicate that 46.0–53.2% of patients have anxious depression (Fava et al., 2004, 2008).

Several differences between adults with anxious and nonanxious depression have been reported. For example, individuals with anxious depression have been reported as being more likely to be older (Fava et al., 2004, 2006; Wiethoff et al., 2010), to have lower educational attainment (Fava et al., 2004, 2006; Wiethoff et al., 2010), to manifest melancholic features (Fava et al., 2004, 2006;

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Wiethoff et al., 2010), to endorse suicidal ideation (Fawcett, 1990; Tollefson et al., 1994; Fava et al., 2004, 2006), to have greater baseline depression severity ratings (Joffe et al., 1993; Wiethoff et al., 2010), to have greater functional impairment (Joffe et al., 1993; Sartorius et al., 1996), and poorer quality of life (QOL) (Fava et al., 2004, 2006). Studies also have found that patients with anxious depression were less likely to respond or remit with antidepressants or to adhere to treatment than patients with nonanxious depression (Fawcett and Kravitz, 1983; Fava et al., 1997, 2008; Wiethoff et al., 2010; Chan et al., 2012; Wu et al., 2013). These findings imply that depression with high levels of anxiety may have important qualitative differences from depression with low levels of anxiety. Therefore, monitoring and treatment of anxiety symptoms could enhance clinical practice by optimizing antidepressant treatment (Zimmerman and McGlinchey, 2008).

A generalizability limitation of the existing studies is that they have almost exclusively been conducted in western countries, and to our knowledge, few studies (Wu et al., 2013) investigate anxious depression in Chinese patients, who have been reported to express depression somatically (Parker et al., 2001). The aim of this study herein was to compare a well characterized group of Chinese adults with MDD with and without high baseline anxiety on demographic, clinical, functional, and quality of life outcomes to provide a comparison with results obtained in western populations.

2. Methods

2.1. Subjects

This study, approved by Kai-Syuan Psychiatric Hospital's institutional review board, was conducted in accordance with Good Clinical Practice procedures and followed the most recent revision of the Declaration of Helsinki.

Patients were recruited from Kai-Syuan Psychiatric Hospital, a major psychiatric center in Taiwan, from April 2007 to September 2010. The board-certified psychiatrists (1st, 2nd, and 3rd authors) used the Structured Clinical Interview for DSM-IV (SCID) (APA, 1994) to screen and evaluate all MDD patients newly hospitalized for acute treatment to ensure the accuracy of the diagnosis. The psychiatrists also rated the patients' total scores of the HAMD-17 (Hamilton, 1960). The intraclass correlation coefficient (ICC) of reliability between the raters (i.e., the 1st, 2nd, and 3rd authors) was 0.95 for HAMD-17. Each rater has at least 10-year clinical experiences in MDD and 3-year experiences in using HAMD-17 for clinical trials. To maintain high interrater reliability and prevent rater drift, raters met at least once a month for training and reliability re-testing. Han Chinese patients in Taiwan were enrolled in this study if they: 1) were physically healthy and had all laboratory parameters within normal limits (including electrocardiography, electroencephalograph, and chest X-ray), 2) were aged 18–70 years old, 3) satisfied DSM-IV criteria for MDD, 4) had no DSM-IV diagnosis of substance abuse or dependence (including alcohol) within the past 6 months, and 5) gave written informed consent to participate in the study after a full explanation of the study's aims and procedures. Patients excluded from this study were those: 1) with a history of epilepsy or organic mental disorders, 2) with psychotic depression, bipolar I disorder or bipolar II disorder, 3) with schizophrenia or any other psychotic disorder, and 4) with severe cognitive impairment.

2.2. Procedures and assessments

The possible variables related to anxious depression included: gender, marital status (married or not married), family history, melancholic features of MDD, age, age at onset, educational level (years), number of previous major depressive episodes, current length of depressive episode (month), duration of hospital stay (day), depression severity, suicide risk, pain, daily functioning, and quality of life.

Anxious depression was defined as depressed patients with HAMD-17 anxiety/somatization factor score ≥ 7 (Fava et al., 2004, 2008). The HAMD-17 anxiety/somatization factor, derived from a factor analysis of the HAMD-17 scale (Cleary and Guy, 1977), includes six items from the HAMD-17: the items for psychic anxiety (Item 10), somatic anxiety (Item 11), gastrointestinal somatic symptoms (Item 12), general somatic symptoms (Item 13), hypochondriasis (Item 15), and insight (Item 17). Higher scores indicate more severe levels of anxiety. A recent study (McClintock et al., 2011) has proven that anxiety/somatization factor has acceptable psychometric properties and can reliably identify anxious features in depressed patients. Thus, it can also be used to identify anxious features for clinical or research purposes.

Each subject's family history was taken to determine whether first-degree relatives had histories of depressive disorders. Melancholic features were assessed according to DSM-IV criteria. The presence of melancholic features of MDD according to DSM-IV criteria was determined using results from the SCID. Age at onset was regarded as the age at which the first major depressive episode occurred. The educational level was measured by total years of formal schooling. Depression severity was measured with the HAMD-17 subtotal score (not including the items used to identify anxious depression) (Tollefson et al., 1994; Fava et al., 2004; Wiethoff et al., 2010), and the Zung Self-Rating Depression Scale (ZDS) (Zung, 1965). ZDS is a 20-item self-rated measure of adults' depressive symptoms over the past week. It is rated on a 1–4 spectrum (1=none, 4=severe). The scale has a score range of 20–80, with higher scores indicating more severe depression. We did not only use the HAMD-17 total score to assess depression severity, as the measures of anxiety are included in this score. Suicide risk was determined from the suicide item (Item 3) score of the HAMD-17; a higher score indicates a higher suicide risk.

Pain over the past 1 month was measured by the Body Pain Index (BPI) of the Medical Outcomes Study Short-Form-36 (SF-36) (Ware and Sherbourne, 1992; Bair et al., 2004; Karp et al., 2005). The BPI consisted of two items that measured: 1) pain severity (Item 7) ranging from 1 (none) to 6 (very severe), and 2) pain interference (Item 8) ranging from 1 (not at all) to 5 (extremely). The BPI was computed by summation and then transformation of raw Likert-scale scores to a 0–100 scale, with a higher score signifying less pain. This approach has been used previously (Karp et al., 2005). The Medical Outcomes Study Short-Form 36 (SF-36) (Brazier et al., 1992), which has two primary-factor analytic components, the physical component summary (PCS) and the mental component summary (MCS), was used to measure quality of life. The MCS is designed to assess mental health, while the PCS is designed to assay physical health. A lower score represents a poorer quality of life. The Taiwanese version of the SF-36 has shown good validity and reliability (Tseng et al., 2003). Functional impairment was measured by the Global Assessment of Functioning (GAF) and the Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002). The WSAS is a self-rated scale which consists of five Likert scales that measure an individual's perception of work and social functioning, with higher scores representing greater functional impairment. Each item is scored from 0 (not affected at all) to 8 (severely affected), with a maximum total score of 40.

2.3. Statistical analysis

The internal consistency of each scale (i.e., HAMD-17, ZDS, SF-36 BPI, SF-36 PCS, SF-36 MCS, and WSAS) was assessed using Cronbach's alpha coefficient (Cronbach and Warrington, 1951). Cronbach's alpha coefficient > 0.70 was considered a threshold for internal consistency by the Nunnally criterion (Nunnally and Bernstein, 1994). Logistical regression model was employed to examine the factors associated with anxious depression. The clinical variables used in these models were sex, marital status, family history of MDD, the presence of melancholic features, age, age at onset of major depressive episode, educational level, number of previous major depressive episodes, current length of depressive episode, duration of hospital stay, HAMD-17 subtotal scores, ZDS scores, HAMD-17 suicide item scores, SF-36 Body Pain Index scores, WSAS scores, SF-36 PCS scores and SF-36 MCS scores.

In the first step, Pearson's χ^2 test and the independent t-test were used to select a factor that significantly contributed to anxious depression. In the second step, if the potential predictive variables ($p < 0.05$) were identified from the first step, forward stepwise logistical regression was employed to determine the best factors for anxious depression. All tests were two-tailed, and statistical significance was set at $p < 0.05$. All data were processed by the SPSS version 17.0 for Windows (SPSS, IBM Company, Chicago, Illinois, USA).

3. Results

The participant selection process is shown in Fig. 1. A total of 190 inpatients who met the inclusion criteria agreed to participate in this study. One hundred and seventy-four (91.6%) patients completed all clinician-rated and self-rated assessments and measures. Table 1 shows the antidepressant use during the assessment period. Twenty-seven percent (48/174) of patients were admitted for self-injury or suicide attempt, 3.0% (5/174) admitted for harm to others, 33% (57/174) admitted for suicide idea without self-injury, suicide attempt, or harm to others, and 37% (64/174) admitted for severe depression without suicide, self-injury or harm to others. One hundred and forty-one (81.0%) of the subjects reported anxious depression, whereas 33 (19.0%) patients had nonanxious depression. Cronbach's alpha coefficients of the HAMD-17, ZDS, SF-36 BPI, SF-36 PCS, SF-36 MCS, and WSAS were 0.78, 0.78, 0.86, 0.86, 0.83 and 0.88, respectively. All the values