Prevalence, demographic and clinical features of comorbid depressive symptoms in drug naïve patients with schizophrenia presenting with first episode psychosis

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ABSTRACT

Depressive symptoms are common in first episode schizophrenia. However, the prevalence and its associations of comorbid depressive symptoms with clinical variables are less well characterized in Chinese Han patients with schizophrenia. In this cross-sectional study, we recruited 240 first-episode and drug naïve (FEDN) inpatients with schizophrenia. All patients were rated on the 17-item Hamilton Depression Rating Scale (HAMD-17) to measure depressive symptoms, and also on the Positive and Negative Syndrome Scale (PANSS) for psychopathology. Our results showed that 131 patients had a total score of 8 or more points on HAMD-17, making the prevalence of comorbid depressive symptoms 54.6%. Fewer women (48.1%, 62 of 129) than men (62.2%, 69 of 111) had comorbid depressive symptoms. Compared to those patients without depressive symptoms, those with depressive symptoms showed higher PANSS total, general psychopathology, cognitive factor and negative symptom scores (all p < 0.05). Further stepwise multiple logistic regression analysis indicated that the PANSS general psychopathology, the PANSS total score and gender (all p < 0.05) remained significantly associated with depressive symptoms. In addition, correlation analysis showed significant correlations between HAMD total score and the following parameters: the PANSS general psychopathology, total score, and cognitive factor (Bonferroni corrected p's < 0.05). Our results suggest that depressive symptoms occur with high prevalence in FEND schizophrenia in a Chinese Han population, and show association with general psychopathology, as well as with cognitive impairment.

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1. Introduction

Depressive symptoms frequently occur in all stages of schizophrenia and appear to be a manifestation of the schizophrenia symptom spectrum in most patients (Buckley et al., 2009; Romm et al., 2010; Chiappelli et al., 2014). Depending on how depressive symptoms are defined, their prevalence in schizophrenia varies markedly (Hou et al., 2016). For example, a previous review paper of 36 studies showed that the depression rate in patients with schizophrenia varied between 6% and 65%, with a modal rate of approximately 25% (Siris and Bench, 2003). A recent study showed that the prevalence rate of clinical depression in chronic patients with schizophrenia was 31% (Majadas et al., 2012). This variance may be attributed to the definition of depression, the time interval under observation, the phase of the illness (Siris and Bench, 2003), and the evaluation tool used for depression identification (Lako et al., 2012). For instance, a previous study found that the frequency of depression was higher in the acute phase than in stable

patients (Mulholland and Cooper, 2000). Moreover, the highest rates of depression were found in the studies that estimated the accumulated prevalence from 3 to 5 years (Siris and Bench, 2003).

A few longitudinal studies found that 25%–40% of patients with schizophrenia remained depressed at baseline and follow-up, 35%–45% were non-depressed at both baseline and follow-up, 10%–17% became depressed over time, and 13%–19% transitioned to non-depression over time (Sands and Harrow, 1999; Conley et al., 2007; Lako et al., 2012). The most recent longitudinal study examining depression in older adults with schizophrenia after mean 54-month follow-up found that persistent depression occurred in about two-fifths of persons, 30% remain persistently non-depressed, and one-fourth may fluctuate between depression and non-depression (Cohen and Ryu, 2015). These findings suggest a core group of depressed (roughly one-third) and non-depressed (one-third to two-fifths) individuals, with the remainder fluctuating between these two states (Cohen and Ryu, 2015).

Depressive symptoms are often associated with other symptom dimensions, particularly negative symptoms (Muller et al., 2006). Depression primarily affects daily activities and social functions (Tan and Rossell, 2016). For example, it has been found that co-morbid depression in schizophrenia is associated with general reduced functioning, worse employment status, poor quality of life, a greater risk of relapse or hospitalization, and an increased risk of suicide (Akinsulore et al., 2014; Abramowitz et al., 2014; Dan et al., 2011). The presence of depressive symptoms in patients with schizophrenia has been associated with overall worse outcomes (Narvaez et al., 2008), and also with an imminent onset of a psychotic relapse (Cohen and Ryu, 2015). Antipsychotics induce a remission of both psychotic symptoms and depressive symptoms; however, the efficacy of adding antidepressants for dual therapy of psychosis and depression is equivocal (Siris et al., 2001; Addington et al., 2002a, 2002b). This indicates that this core group of depressed individuals may represent a specific subtype of schizophrenia in which there is an interrelationship between the depressive symptoms of schizophrenia and the psychosis itself.

Although it is well established that schizophrenia is often accompanied by depressive symptoms, few studies have examined comorbid depressive symptoms in the first episode and drug naïve (FEDN) patients with schizophrenia. The study of first-episode psychosis (FEP) is particularly advantageous in understanding the prevalence and the symptom patterns of depressive symptoms in schizophrenia in part because of the opportunity to minimize confounding factors such as illness duration, long-term medication effects, and the psychiatric and medical comorbidities that are associated with chronic schizophrenia. Moreover, most of the previous studies regarding the comorbid depressive symptoms in schizophrenia were carried out in Western countries. Only one study investigated the prevalence and correlates of comorbid moderate–severe depressive symptoms and their association with quality of life (QOL) in Chinese chronic schizophrenia patients, showing that depressive symptoms (defined as a total score of 9 or above on the MADRS) were present in 54.1% of patients. Moreover, comorbid depression was significantly associated with lower mental QOL (Hou et al., 2016). The aims of the present study were therefore to investigate the prevalence, socio-demographic correlates, and clinical correlates of comorbid depressive symptoms among FEND patients with schizophrenia in a Chinese Han population. We hypothesized that: (1) the rates of comorbid depressive symptoms will be high in FEDN patients, ranging approximately 30%; (2) The predictors described above will significantly correlate with depressive symptoms in FEDN patients.

2. Methods

2.1. Subjects

All patients were inpatients in Beijing Hui-Long-Guan hospital, one of the largest psychiatric hospitals in China, with about 1400 beds specializing in the treatment of all kinds of mental disorders, and with about 500 daily outpatient visits. It is a public psychiatric hospital owned by the Beijing city, located 30 km from central Beijing and serves a catchment area population of 25 million people.

240 FEND patients (male/female = 111/129; age range 16–45 years) were recruited from consecutive admissions to the inpatient unit of the hospital after 27 patients were excluded due to documented medical abnormalities (n = 7), substance dependence other than tobacco (n = 5), comorbid other psychiatric disorders (n = 6), and refusal to participate in the study/inability to provide consent (n = 9). All patients met the following criteria: (1) an acute episode at study intake that met the criteria of the fourth edition of the Diagnostic and Statistical Manual (DSM-IV) for schizophrenia; (2) maximum symptom duration of 60 months; (3) no prior treatment with antipsychotic medication; (4) between 16 and 45 years of age; (5) ethnic Han Chinese; (6) current psychotic symptoms of moderate severity or greater measured with the Clinical Global Impression Scale (CGI) ≥ 4; (7) provided written informed consent and able to take part in clinical assessment. Diagnoses were made for each patient at baseline and at a 3–6 month follow-up by two experienced psychiatrists trained to use the Chinese version of the Structured Clinical Interview for DSM-IV (SCID; Phillips et al., 2007). The schizophrenia clinical subtypes identified were: paranoid, 64 (53.3%), undifferentiated, 44 (36.7%); disorganized 10 (8.3%); others 2 (1.7%). The patients had a mean age of 28.9 ± 9.7 years, and a mean duration of illness of 23.6 ± 19.8 months.

A complete medical history and physical examination were obtained from all patients with schizophrenia. Patients with severe physical diseases were excluded. Neither the depressed or non-depressed patients suffered from alcohol or illegal drug abuse/dependence. Psychiatric disorders were ruled out among healthy controls by a psychiatric evaluation.

The Institutional Review Board (IRB) at Beijing HuiLongGuan hospital approved this study and each subject gave written informed consent for participating after the study had been fully explained.

2.2. Demographic characteristics

Research staff administered a detailed questionnaire that asked for general information, socio-demographic characteristics, smoking behavior, and medical and psychological conditions. Additional information was collected from available medical records and collateral data sources (from family and/or treating clinician).

2.3. Clinical measures

Four psychiatrists who were blind to the clinical status assessed the patient's psychopathology with the PANSS (Kay et al., 1987; He and Zhang, 2000) and depressive symptoms with the Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960; Zhang, 1993). To ensure consistency and reliability of ratings across the study, these four psychiatrists, who had worked at least 5 years in clinical practice, simultaneously attended a training session in using the PANSS and the HAMD before the start of the study. After training, they maintained an inter-rater correlation coefficient of 0.82 for the PANSS total score and 0.85 for HAMD total score.

We employed HAMD for a comprehensive measure of depressive symptoms. The scoring is based on the first 17 items. Eight items are scored on a 5-point scale, ranging from 0 (not present) to 4 (severe). Nine items are scored from 0 (none) to 2 (symptom-specific severity descriptor). Patients were classified into two groups using HAMD rating cut-offs: ≤7 = not depressed (NDP) and ≥8 = depressed (DP) (Park et al., 2016). Then moderate to severe depressive symptoms were defined as a total score of 14 or above on the HAMD-17 (Liu et al., 2014).