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Reseacrh report

Which somatic symptoms are associated with an unfavorable course in Asian patients with major depressive disorder?

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ABSTRACT

Objective: To investigate the impact of somatic symptoms on the severity and course of depression in Asian patients treated for an acute episode of major depressive disorder (MDD).
Methods: Three-month prospective observational study of 917 patients with MDD in psychiatric care settings of which 909 had complete main baseline data. Depression severity was assessed using the physician-rated Clinical Global Impression of Severity (CGI-S) and 17-item Hamilton Depression Rating Scale (HAMD17), and somatic symptoms were assessed using the patient-rated 28-item Somatic Symptom Inventory (SSI). Cluster analysis using baseline SSI scores grouped patients into 3 clusters with no/few, moderate or severe somatic symptoms. Four factors of SSI (pain, autonomic symptoms, energy, and central nervous system) were defined and regression analyses identified which factors were associated with remission and response at 3 months follow-up.
Results: Baseline depression severity (HAMD17 and CGI-S scores) was associated with more severe somatic symptoms. Remission rates differed between clusters of patients: 68.4%, 54.7% and 29.3% for no/few, moderate and severe somatic symptoms, respectively ($p < 0.0001$). Corresponding response rates were 81.8%, 72.1% and 55.2% ($p < 0.0001$). Pain symptoms were the somatic symptoms most associated with these clinical outcomes at 3 months.
Limitations: Only patients diagnosed with MDD in psychiatric care were assessed.
Conclusions: Somatic symptoms are frequent among Asian patients in psychiatric care for MDD and are associated with greater clinical severity and lower response and remission rates. Among somatic symptoms, pain symptoms have the greatest prognostic value and should be taken into account when treating patients with depression.

1. Introduction

Major depressive disorder (MDD) is a psychiatric condition associated with stratified psychological, behavioral, and physical symptoms. Primary care patients with depression often present with somatic complaints (Kirmayer et al., 2004; Kroenke, 2003) and somatic presentation of depression is common in both inpatient and outpatient care settings across all cultures (Kapfhammer, 2006). Indeed, somatic symptoms are the main reason for the initial visit to the primary care physician (Kirmayer et al., 1993). A multicenter international study conducted by the WHO confirmed that two-thirds of patients present their depressive mood with somatic symptoms exclusively, and more than half complained of multiple medically-unexplained somatic symptoms (Simon et al., 1999). These findings indicate that somatic symptoms are important components of depressive episodes. Moreover, the presence of multiple somatic symptoms in patients with MDD has been associated with increased depression severity and greater health resource utilization (Garcia-Campayo et al., 2008).

A wide variety of somatic symptoms are reported by patients with depression, including changes in appetite and libido, lack of energy, sleep disturbance, non-painful somatic symptoms (e.g. dizziness, palpitations, dyspnea), and general aches and pains (e.g. headache, backache, musculoskeletal aches and gastro-intestinal disturbances) (Tylee and Gandhi, 2005; Kapfhammer, 2006). Previous attempts to categorize the different symptoms

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of depression have not incorporated analysis of differences in these various co-ocurring subtypes of somatic symptoms (Hung et al., 2006). Among the different somatic symptoms, pain is a frequent complaint in patients with depression, and painful physical symptoms (PPS) including headaches, stomach pain, back pain, and vague, poorly localized pain are reported by up to 76% of patients with depression (Kirmayer et al., 1993; Corruble and Guelfi, 2000; Bair et al., 2003, 2004; Munoz et al., 2005). The majority of patients with MDD report multiple pain complaints and a higher number of pain symptoms has been associated with more severe depression (Vaccarino et al., 2009). Moreover, the presence of pain predicts a longer time to remission of depression (Karp et al., 2005), and the resolution of physical symptoms is a strong predictor of full remission (Paykel et al., 1995).

Researchers have speculated that ethnicity may influence the somatic and psychiatric presentation of depression (Berganza et al., 2001; Parker et al., 2001a, 2010b). Some studies have indicated that Asian patients are more likely to report somatic symptoms rather than emotional/mood symptoms (Parker et al., 2001a, 2010b; Simon et al., 1999). A small study of 62 Chinese patients with depression reported that the majority presented with somatic complaints, including poor appetite (68%), insomnia (66%), chest discomfort (58%), palpitations (55%) and fatigue (45%) (Ji and Zhang, 2002). In an investigation of the association between depression and pain in a community population from Beijing, China, 64.2% of patients with MDD reported at least one chronic pain condition (Chen et al., 2012). In a recent study of Korean outpatients with MDD, 30.4% had PPS (Bahk et al., 2011).

A large, prospective, observational study of East Asian patients treated for an acute episode of MDD in psychiatric care settings found that 52% had PPS at baseline (Lee et al., 2009), and the presence of pain was associated with greater depression severity, a worse quality of life, and poorer clinical outcome at 3 months follow-up (Ang et al., 2009).

The aim of the present analysis of a 3-month prospective observational study in East Asian patients with depression is to better understand the impact of somatic symptoms on both the severity and course of depression. Since somatic symptoms are a heterogeneous group, we also want to analyze whether certain specific somatic symptoms have a greater impact than others on the course of depression

2. Methods

2.1. Study design and population

Data for this post-hoc analysis were based on a prospective, observational study designed to assess the frequency of somatic symptoms in East Asian patients treated for an acute episode of a MDD in the psychiatric care setting. The study enrolled patients from 40 study sites across six East Asian countries and regions: China (Mainland), Hong Kong, South Korea, Malaysia, Singapore and Taiwan. Patients were recruited from 14 June 2006 to 15 February 2007, with individual patients being followed for a period of 3 months.

Inpatients and outpatients, at least 18 years of age, who presented with a new or first episode of MDD, as defined by the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV-TR) (American Psychiatric Association (APA), 2000) or International Classification of Diseases, 10th Revision (ICD-10) (World Health Organisation (WHO), 2007), were considered eligible for study entry. Additional inclusion criteria were: a Clinical Global Impressions of Severity scale (CGI-S) (Guy, 1976) score ≥ 4 (moderately ill or worse) at study entry; at least 2 months free of depression symptoms before the onset of the current episode; and consent to participate in the study.

Patients were excluded if their current depressive episode had persisted for more than 6 continuous months; if they had a previous or current diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, bipolar disorder or dementia; were experiencing chronic treatment-resistant pain or pain of an inflammatory origin related to an identified medical condition; or if they were simultaneously participating in another study that included a treatment intervention or an investigational drug.

All patients who satisfied the entry criteria and agreed to participate in the study were enrolled up to the sample size allocated. No further selection or stratification was involved.

All treatment decisions were based solely on the healthcare provider's usual practice in the provision of care to patients with MDD, independently of participation in the study. Adverse events were reported to the correspondent health authorities according to each country's local rules, regulations and legislation. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonization good clinical practice guidelines. The study was approved and reviewed by the institutional or ethical review board of at least one site in each participating country or region. Written informed consent was obtained from all patients or their legal representative prior to enrollment.

2.2. Measures

Demographic and clinical data, including prior course of MDD and current medical conditions (comorbidities), were collected at the baseline visit. Severity of depression was assessed at baseline and 3 months using the physician-rated CGI-S and the 17-item Hamilton Depression Rating Scale (HAMD17) (Hamilton, 1960). Response was defined as more than a 50% reduction in HAMD17 total score from baseline to end-point. Remission was defined as a HAMD17 total score of ≤ 7 at study end-point. Somatic symptoms were assessed using the 28-item modified Somatic Symptom Inventory (SSI) (Kroenke et al., 1994), which is a patient self-report scale that assesses the extent to which each of 28 somatic symptoms has bothered the patient over the previous week, using a scale ranging from 1 (“not at all”) to 5 (“a great deal”). Total score was calculated by adding all items. For patients who were employed in the 3 months before study entry and/or during the study, the impact of depression-related illness on work productivity (e.g. hours worked and days absent from work) was evaluated through a questionnaire. Patient perception of quality of life and health status was assessed using the EuroQOL Questionnaire-5 Dimensions (EQ-5D). For patients who were hospitalized during the study, the number of admissions and length of hospital stay were collected. Data involving treatment patterns, including antidepressants and other prescribed medications and treatments for MDD and pain were collected at baseline and during the study. The baseline characteristics of patients with and without PPS (PPS+ defined as a mean score ≥ 2 on the 7 pain-related items of the SSI) have been reported previously (Lee et al., 2009), as have the changes in disease severity, treatment patterns and quality of life over the 3-month observation period (Ang et al., 2009).

Training and assessment (rating of a videotaped patient interview) were performed to ensure consistency between investigators with respect to HAM-D17 ratings. A maximum variation of $+3$ or -3 from the prespecified HAM-D17 total score was considered acceptable, and, in addition, 60% agreement with the