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Prescribing patterns of psychotropic medications and clinical features in patients with major depressive disorder with and without comorbid dysthymia in China

Running Title: dysthymia and major depression

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Prescribing patterns of psychotropic medications and clinical features in patients with major depressive disorder with and without comorbid dysthymia in China

Running Title: dysthymia and major depression

Abstract

Introduction: Little has been reported about the demographic and clinical features of **major depressive disorder (MDD) with comorbid dysthymia** in Chinese patients. This study examined the frequency of comorbid dysthymia in Chinese MDD patients together with the demographic and clinical correlates and prescribing patterns of psychotropic drugs.

Methods: Consecutively collected sample of 1,178 patients with MDD were examined in 13 major psychiatric hospitals in China. Patients' demographic and clinical characteristics and psychotropic drugs prescriptions were recorded using a standardized protocol and data collection procedure. The diagnosis of dysthymia was established using the Mini International Neuropsychiatric Interview (MINI). Medications ascertained included antidepressants, antipsychotics, benzodiazepines and mood stabilizers.

Results: One hundred and three (8.7%) patients fulfilled criteria for dysthymia. In multiple logistic regression analyses, compared to non-dysthymia counterparts, MDD patients with dysthymia had more depressive episodes with atypical features including increased appetite, sleep and weight gain; more frequent lifetime depressive episodes; and less likelihood of family history of psychiatric disorders. There was no significant difference in the pattern of psychotropic prescription between the two groups.

Conclusions: There are important differences in the demographic and clinical features of comorbid dysthymia in Chinese MDD patients compared with previous reports. The clinical profile found in this study has implications for treatment decisions.

Keywords Dysthymia, major depressive disorder, China

Introduction

Dysthymia is a common psychiatric disorder characterized by depressed mood with a fluctuating course lasting at least two years (Akiskal et al., 1980; Dunner, 2005; Keller et al., 1997). Dysthymia was subsumed under the broad and poorly-defined category of “neurotic depression” in DSM-II and then added to DSM-III to classify mild chronic depression in contrast to major depressive disorder (MDD) (Bruder et al., 2012). Dysthymia is often superimposed on an existing MDD episode, a phenomenon named double depression (Kellerand Shapiro, 1982). The relationship between MDD and dysthymia is controversial. Compared to MDD, patients with dysthymia including double depression are more likely to have a family history of mood disorder and present more frequent Axes I and II comorbidities with poorer long-term outcomes (Klein et al., 2000; Markowitz et al., 1992; Riso et al., 1996). This suggests that the two clinical syndromes may reflect different disease entities. Some authors regard them essentially different aspects of a single condition (Coryell et al., 1994; Keller et al., 1995).

This study conducted by the Mood Disorders Unit of the Chinese Society of Psychiatry, was part of the nationwide study entitled the “Diagnostic Assessment Service for People with Bipolar Disorders in China” that tested the usefulness of screening tools for bipolar disorder in patients initially diagnosed as MDD (Hu et al., 2012a; Hu et al., 2012b). The aim was to improve the validity of diagnosis of

bipolar disorder (BD) and rationalize its treatment. For this study, a secondary analysis of the data of that large project, set out (1) to determine the frequency of comorbid dysthymia in Chinese patients with MDD diagnosed with the Mini International Neuropsychiatric Interview (MINI); and (2) to explore its demographic and clinical correlates and prescribing patterns of antidepressants, antipsychotics, benzodiazepines and mood stabilizers.

Methods

Patients and settings

The survey was conducted in 13 major psychiatric hospitals/units located nationwide in China representing a range of clinical settings between September 1, 2010 and February 28, 2011. Patients were screened and recruited if they satisfied the following inclusion criteria: (1) age between 16 and 65 years, (2) inpatients or outpatients, (3) a diagnosis of DSM-IV MDD ascertained by the MINI, (4) ability to understand the aims of the study and a willingness to provide written informed consent. Exclusion criteria included (1) past diagnosis of BD; (2) history or current major medical condition(s); (3) depressive disorders associated with general medical conditions. The study protocol was approved the Clinical Research Ethics Committees of the respective study centers.

Instrument and assessment

MDD patients receiving treatment in the participating hospitals were consecutively referred by their treating psychiatrists to the research team for eligibility screening. Eligible patients were invited to participate in the study. Their basic demographic and clinical characteristics were recorded in a form designed for the study during a clinical interview supplemented by a review of the medical records. The diagnosis of dysthymia was established using the Chinese version of the MINI, Version 5.0 (Sheehan et al., 1998; Si et al., 2009).

All the thirteen interviewers were trained in the use of MINI in 20 MDD patients using standard reliability procedures prior to the main study. The kappa values of their assessment of dysthymia were above 0.80. After a full explanation about the study, participating patients met an interviewer for a confirmatory diagnostic interview.

Statistical analysis

Data were analyzed with the SPSS 20.0. Comparisons of the basic demographic and clinical characteristics between dysthymia and non-dysthymia patients were performed by chi-square tests, *t*-tests and Mann-Whitney U test, as appropriate. Multiple logistic regression analysis with the “Enter” method was used to determine the demographic and clinical variables that were independently

associated with dysthymia. Comorbid dysthymia was the dependent variable, while variables that significantly differed between the two groups at the significance level of 0.10 in the above univariate analyses were entered as independent variables. Statistical significance was set at P<0.05 (two-tailed).

Results

A total of 1,757 patients were invited to participate in the study; 270 (15.4%) refused, 309 (17.6%) fulfilled DSM-IV criteria for **BD** and 1,178 (67.0%) for MDD. Of the 1,178 MMD patients, 103 (8.7%) had MINI-verified dysthymia which amounted to 9.0% of females and 8.3% of males.

Table 1 presents the basic demographic and clinical characteristics for the whole sample and separately by diagnoses. In multiple logistic regression analysis four variables including frequent depressive episodes, depressive episodes with atypical features, family history of psychiatric disorders and use of antidepressants were entered as independent variables. Dysthymia patients had more depressive episodes with atypical features including increased appetite, sleep and increased weight gain (p=0.01, odds ratio=1.8, 95% CI=1.1-3.0); more frequent lifetime depressive episodes (p=0.01, odds ratio=1.1, 95% CI=1.01-1.2); and less likelihood of family history of psychiatric disorders (p=0.03, odds ratio=0.5, 95% CI=0.2-0.9).

Discussion

Dysthymia is a common psychiatry disorder and frequently associated with MDD, supervening in approximately 77% of MDD patients in the US (Klein et al, 2000). The proportion of dysthymia in MDD patients (8.7%) found in this study was lower than two recent findings in China. In a convenience sample of 1,970 female patients with MDD, 18.0% were diagnosed having dysthymia using the CIDI (Sang et al., 2011). In the extended survey of this project with the same methodology, the corresponding figure is decreased to 9.9% (587/5,950) (Wu et al., 2013). The discrepancy in rates might be due to diagnostic instruments and selection criteria (convenience vs. consecutive sampling; female sex vs. both sexes). To the best of our knowledge no previous studies in China on MDD patients with dysthymia had used the MINI.

Dysthymia often co-exists with medical conditions (Sansone et al., 2004). In this study, compared to MDD without dysthymia, MDD patients with dysthymia was had more frequent atypical depressive features (increased appetite, sleep and weight gain) that could contribute to increased risk of metabolic syndrome (Murray et al., 2009). Dysthymia has a high rate of comorbidity, such as anxiety (Wu et al, 2013) and suicide (Nock et al., 2009). In this study anxiety and suicide

attempts were more frequent in the dysthymia group, but the difference did not reach statistically significant level.

Similar to findings in Chinese women (Wu et al, 2013), patients with double depression have more depressive episodes. The mechanism of comorbid dysthymia with MD is still unclear. The greater severity of illness and higher familial loading (Kaschand Klein, 1996; Weissman et al., 1984) seems to support a biological causation, but other studies (Sang et al, 2011) including this study, found a lack of positive association with family history and co-morbid melancholia. Due to the greater severity of illness, MDD patients with dysthymia are more likely to be prescribed psychotropic medications. In this study, patients with double depression were more likely to receive antidepressants, antipsychotics and benzodiazepines compared to MDD patients without dysthymia, but the trend did not reach significant level.

The strengths of this study include its large, multi-centre sample and the standardized diagnostic assessment of dysthymia. However, the results should be interpreted with caution because of several limitations. First, owing to the cross-sectional nature of the study, the causal relationships between demographic and clinical characteristics and comorbid dysthymia could not be examined. Second, the symptomatology and clinical severity was not measured. Third, some potentially important variables related to dysthymia, such as negative life events,

history of childhood abuse, neuroticism and use of psychotherapy, were not evaluated. Fourth, the sampling was consecutive and not randomised, therefore it could not be generalized to the whole population of MDD Chinese patients. However, the participating institutions are major psychiatric hospitals located in different areas of China, thus the current sample is broadly representative.

In conclusion, the results found in this Chinese sample indicate that there are significant differences in clinical features between MDD with and without comorbid dysthymia. The lack of positive association with family history and comorbid melancholia in Chinese MDD patients are not consistent with previous reports that suggested dysthymia could be a biologically distinct syndrome.

Conflict of interest

None.

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Table 1. Basic demographic and clinical characteristics of MDD with or without dysthymia

	The whole sample (n=1,178)		Non-dysthymia (n=1075)		Dysthymia (n=103)		Statistics [a]		
							x^2	df	p
	N	%	N	%	N	%			
Male	385	32.7	353	32.8	32	31.1	0.1	1	0.71
Married/cohabitating	824	69.9	754	70.1	70	68.0	0.2	1	0.64
Employed	812	68.9	742	69.0	70	68.0	0.05	1	0.82
Education							1.1	3	0.77
Primary and junior secondary school	356	30.2	324	30.1	32	31.1			
Senior secondary school	312	26.5	285	26.5	27	26.2			
College and university	465	39.5	423	39.3	42	40.8			
Postgraduate	45	3.8	43	4.0	2	1.9			
Frequent depressive episodes (>4 in the past year)	90	7.6	74	6.9	16	15.5	9.9	1	**0.002**
Depressive episodes with increased appetite, sleep and weight gain	179	15.2	152	14.1	27	26.2	10.6	1	**0.001**
Depressive episodes with anxiety	915	77.7	830	77.2	85	82.5	1.5	1	0.21
Depressive episodes with suicidal ideation and/or attempts	665	56.5	604	56.2	61	59.2	0.3	1	0.55
Depressive episodes with psychotic symptoms	158	13.4	142	13.2	16	15.5	0.4	1	0.50
Seasonal depressive episodes	134	11.4	120	11.2	14	13.6	0.5	1	0.45
Melancholic features	629	53.4	568	52.8	61	59.2	1.5	1	0.21
Family history of psychiatric disorders	203	17.2	192	17.9	11	10.7	3.3	1	0.06
Use of antidepressants	820	69.9	740	68.8	80	77.7	3.4	1	0.06
Use of antipsychotics	226	19.2	200	18.6	26	25.2	2.6	1	0.10
Use of benzodiazepines	192	16.3	170	15.8	22	21.4	2.1	1	0.14
Use of mood stabilizers	44	3.7	42	3.9	2	1.9	1.0	1	0.31
	Mean	SD	Mean	SD	Mean	SD	t/z	df	p

Age (years)	40.5	12.8	40.5	12.7	40.3	13.4	0.1	1176	0.87
Age at onset (years)	34.6	12.5	34.8	12.4	32.7	12.8	1.5	1176	0.11
Lifetime depressive episodes	1.9	2.6	1.7	2.3	2.7	3.9	-3.1	---[b]	**0.001**

Bolded values are $p<0.05$;[a] multiple logistic regression analyses with the non-dysthymia cohort as the reference group; [b] Mann-Whitney U test.