Cincinnati Criteria for Mixed Mania and Suicidality in Patients With Acute Mania

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The association between suicidality and diagnoses of mixed mania, as defined using both DSM-IV and Cincinnati criteria, was studied in 576 consecutive manic inpatients. Of the whole sample, 51 (8.9%) had suicidal ideation and 13 (2.3%) attempted suicide during the index episode. Suicidality was significantly more frequent in patients with a diagnosis of mixed mania, whether the diagnosis was made by DSM-IV or Cincinnati criteria. A multiple logistic regression analysis revealed that an additive combination of a diagnosis of mixed mania, the depression severity, and the Global Assessment of Functioning (GAF) score was significant in predicting suicidal ideation, when using the DSM-IV criteria. A diagnosis of mixed mania alone was significant in a similar analysis, when using the Cincinnati criteria. The adjusted odds ratio for a diagnosis of mixed mania to having suicidality was much higher when using the latter criteria (4.0 *v* 14.0). A subsequent logistic regression analysis indicated that the Cincinnati mixed mania alone, rather than an additive combination of the DSM-IV mixed mania and the depression severity, achieved the most appropriate prediction of suicidal ideation in the sample. These findings did not differ, even when suicidality was defined as having a suicide attempt during the index episode. Our finding that suicidality was more strongly associated with Cincinnati mixed mania than with DSM-IV mixed mania is probably due to that suicidal patients who do not meet DSM-IV criteria for mixed mania are classified into mixed mania, or/and that the depressive syndrome, related to suicidality, is more appropriately assessed among manic patients, when using the Cincinnati criteria. There was no evidence that marital status, employment, a lifetime history of alcohol or substance abuse, or a history of suicide attempts before the index episode was significantly associated with suicidality in the sample. Manic patients with suicidality may have a greater severity of residual depressive symptoms at discharge.

SUICIDE RISK in bipolar patients is generally high. An exhaustive review by Goodwin and Jamison[1] showed that 18.9% of deaths in bipolar patients were due to suicide. Although previous studies on suicidality in bipolar patients tended to be restricted to depressive episodes, several recent studies have emphasized that mixed states (or mixed mania), as defined as a simultaneous admixture of both depressive and manic syndromes, may also mediate the high suicide risk in bipolar patients.[2-6] Using a narrow definition of mixed mania that requires patients to simultaneously meet both full manic and depressive syndromes, Dilsaver et al.[2] reported that 54.5% of patients with mixed mania had suicidal ideation, in contrast to 2.0% of patients with pure mania. Strakowski et al.[3] also found a significantly higher frequency of suicidal ideation in patients simultaneously meeting DSM-III-R criteria for both manic and major depressive episodes than in pure manic patients.

Interestingly, Strakowski et al.[3] provided evidence that the severity of current depressive symptoms, rather than the presence of a full depressive syndrome per se, is associated with suicidal ideation among manic patients, suggesting that narrow definitions of mixed mania may not play a definite role in predicting suicidality in these patients. DSM-III-R and DSM-IV adopt a narrow definition of mixed mania. However, there are several studies indicating that broader definitions of mixed states result in a more meaningful subtyping of mixed mania in terms of demographic variables,[7-11] natural course,[7-9,11,12] and specific treatment responses.[13,14] The association between a broader definition of mixed mania and suicidality has not been well studied. One study reported that suicidal ideation is not infrequent in manic patients, even when full major depression does not accompany mania.[5,6] However, it is unclear whether or not a broader definition of mixed mania plays a more definite role in predicting suicidality in manic patients, as compared with a narrow definition of mixed mania.

McElroy et al.[4,11] proposed one of well-known broad definitions of mixed mania, the Cincinnati

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criteria, which require the presence of three or more symptoms of major depression during a full manic episode. The present study examined the association between mixed mania and suicidality in 576 hospitalized patients with acute mania. For diagnosing mixed mania, both Cincinnati and DSM-IV criteria were used.

METHOD

Patients

All patients who were hospitalized at the Psychiatric Hospital of the Ludwig-Maximilian University in Munich, Germany for any affective disorder during the period of 1980 to 1997 were considered as subjects in this study. Routine clinical diagnoses were made according to the International Classification of Diseases system (ICD-9 or ICD-10),[15,16] but a broad range of 196 psychiatric and related somatic symptoms were, as part of the routine documentation at the hospital, systematically evaluated for all patients at both admission and discharge by using a standardized instrument (the AMDP system; see below), which allowed for precise diagnoses of DSM-IV manic episode, nonmixed and mixed, and mixed mania according to the Cincinnati criteria.[4,9] The following inclusion criteria were used: (1) patients be diagnosed using the ICD system as currently having a manic or mixed episode (ICD-9 diagnosis of 296.0, 296.2, or 296.4; or ICD-10 diagnosis of F30 F31.0, F31.1, F31.2, F31.6, or F38.00); (2) patients be younger than 70 years; and (3) patients who met DSM-IV criteria for manic episode, nonmixed or mixed. Finally, 576 consecutive inpatients with DSM-IV manic episode, nonmixed or mixed, were included for the following analyses. All patients gave informed consent to be assessed using several instruments described below. Of the subjects, 292 (51%) were women, and 284 (49%) were men. Their mean age was 38.6 (SD 12.6) years. Their mean age at onset of first affective episode was 28.9 (SD 10.7) years. Fifty-eight patients (10.1%: 38 women and 20 men) met criteria for DSM-IV manic episode, mixed, while 88 patients (15.3%: 55 women and 33 men) met criteria for mixed mania according to Cincinnati criteria. The frequency of mixed mania as defined using DSM-IV or Cincinnati criteria was constant during the whole study period when the frequency was compared between three entry periods, 1980 to 1985, 1986 to 1990, and 1991 to 1997. Both diagnoses were significantly correlated in the whole sample ($\kappa = 0.67$, $P < .0001$). The patients were treated with medications as clinically appropriate during the hospital stay. Before admission, the majority of the patients had received various medications including mood stabilizers (58%) and/or antipsychotics (36%). There was no significant association between presence of these medications and diagnoses of mixed mania.

Clinical Assessments

The Association for Methodology and Documentation in Psychiatry (AMDP) system[17] was used to assess psychiatric symptoms. The AMDP system is a comprehensive rating instrument, developed on the basis of German traditional descriptive psychopathology on functional psychoses; it is commonly used in most psychiatric institutes in German-speaking countries. Each psychiatric symptom of the AMDP system is scored from 0 (absent) to 3 (severe) with defined anchor statements by using a semistructured interview method. Several studies indicated moderate to high inter-rater agreements for most included symptoms.[18,19] Rater-training sessions are performed regularly in our hospital to establish and maintain high inter-rater reliability of the instrument. Inter-rater reliability of all AMDP items in our hospital, calculated based on joint interviews by multiple raters of over 50 diagnostically diverse patients, ranged from 0.65 to 0.92 (analysis of variance intraclass correlation). Based on the AMDP ratings, several summary scales for depressive, manic, and paranoid-hallucinatory syndromes (the AMDP scores for depressive, manic, and paranoid-hallucinatory syndromes), which have been validated in large psychiatric samples,[20-22] can be calculated by summing up the scores on 13 items (rumination, loss of feeling, loss of vitality, depressed mood, hopelessness, feeling of inadequacy, feeling of guilt, inhibition of drive, worse in the morning, interrupted sleep, shortened sleep, early waking, decreased appetite) for depressive syndrome, seven items (flight of idea, euphoria, exaggerated self-esteem, increased drive, motor restlessness, logorrhea, excessive social contact) for manic syndrome, and 13 items (delusional mood, delusional perceptions, sudden delusional ideas, delusional ideas, systematized delusions, delusional dynamics, delusions of reference, delusions of persecution, verbal hallucinations, bodily hallucinations, depersonalization, thought withdrawal, other feelings of alien influence) for paranoid-hallucinatory syndrome. The Global Assessment of Functioning (GAF) score was also assessed for all subjects at both admission and discharge. All subjects gave written informed consent to be assessed by using the instruments. Well-trained psychiatrists administered these two instruments.

The presence of suicidality was defined in this study by using the highest score on the AMDP suicide item at admission. The item scores the severity of suicidality as follows: 0 (absent); 1 (mild): frequent thoughts that she/he would be better off dead; 2 (moderate): frequent thoughts about committing suicide or mental rehearsal of suicide; 3 (severe): suicide attempt during the index episode. The present study defines suicidality as a score equal to or higher than 1, since this definition appears to be equivalent to that used in previous similar studies.[2,3]

Statistical Analyses

Clinical and demographic variables were compared between patients with and without suicidality by using chi-square test for categorical variables and Mann-Whitney tests for continuous variables. The frequencies of mixed mania as defined by the DSM-IV and Cincinnati criteria were also compared between the two groups. The nonparametric tests were used for all examined continuous variables, since the distributions of these variables were not normally distributed. In each of these univariate analyses, the significance level was adjusted at a $P < .0025$ (.05 divided by 20 tests) level by using Bonferroni's method.

An adjusted odds ratio for patients with mixed mania to having suicidal ideation was computed by using multiple logistic regression analysis. This analysis was performed for mixed mania as defined by the DSM-IV and Cincinnati criteria separately. Several other variables, which were, in the above univariate analyses, associated with suicidal ideation at a $P < .10$ level, were entered into the logistic analyses. A second logistic