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Original Article

Medication prescribing patterns for patients with bipolar I disorder in hospital settings: adherence to published practice guidelines

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Objective: The purposes of this paper were to examine the medication prescribing patterns for bipolar I disorder in hospital settings and to compare them to recently published expert consensus guidelines for medication treatment of bipolar disorder.

Methods: Data were obtained from the 1996–2000 CQI + SM Outcomes Measurement System, on patients age 18 or older admitted to psychiatric inpatient units from over 100 medical–surgical hospitals. A total of 1864 patients with a primary discharge diagnosis of bipolar I or II disorder were identified from a large cohort of hospitalized patients. Patient characteristics were assessed at hospital admission and medication usage, at discharge. The medication analysis focused on the 1471 individuals with bipolar I *mania* or bipolar I *depression* (with or without psychotic features), representing 54% and 25% of admitted bipolar patients, respectively.

Results: At admission, the typical bipolar patient (mean age 57) had experienced a relatively severe and chronic course of illness. The array of psychotropic agents used was broad, with no single prescribing pattern predominant. Only one in three bipolar I (*manic* or *depressed*) patients with psychotic features was discharged on medications recommended by expert guidelines as preferred or alternate recommended treatment. Absent psychotic features, this dropped to one in six patients. Surprising was the relatively high use of antidepressants for patients with mania, particularly those without psychotic symptoms.

Conclusions: Results suggest that a substantial proportion of patients with bipolar I disorder are discharged from hospitals on medications not generally recommended by current practice guidelines.

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Disease impact

Bipolar I disorder is a chronic and often devastating disease that affects about 1.0% of the general population (1–6). Severe physical and psychosocial impairments are common (2, 7), which have been associated with high rates of medical and psychiatric care, family dysfunction, divorce, substance abuse and suicide (8–10). To illustrate this, bipolar disorder was ranked sixth among the top ten leading worldwide causes of disability-adjusted life years in 1990 for persons aged 15–44 years (11).

The direct and indirect economic costs of bipolar disorder are staggering (12). One decade ago, it was estimated that the total costs of the disorder exceeded $45 billion in the USA alone (13). More recent work suggests that the health care costs for bipolar disorder exceed those for depression or diabetes (14). The mortality rates for untreated bipolar disorder are comparable to many types of heart disease and cancer, with rates of death by suicide (around 19%) perhaps the highest for any psychiatric or medical disorder (9).

Treatment guidelines

The successful management of bipolar I disorder depends on early detection, appropriate pharmacologic and psychosocial treatments, and an understanding of the long-term cyclic, recurrent, and relapsing nature of the disorder. Recurrent episodes of mania and depression, often secondary to medication noncompliance (15–18), have a deteriorative effect on patient functioning, response to treatment and prognosis (7, 9, 19–22). To provide guidance to psychiatrists and other mental health professionals about the most appropriate treatments for patients with bipolar disorder, various practice guidelines and treatment algorithms have been developed. The hope is that such guidelines will reduce unnecessary variation in clinical practice, facilitate rational clinical decision-making, improve quality of care, increase efficiency of treatment and allow for systematic examination of specific treatments on outcomes (23).

Some guidelines have been developed by panels of recognized experts [International Psychopharmacology Algorithm Project (24); European Algorithm Project (25, 26)]. Others have used panels of experts combined with additional detailed commentary from clinicians in the field [American Psychiatric Association (APA) (8); Canadian Network for Mood and Anxiety Treatments (CANMAT) (27, 28); Department of Veterans Affairs (29)]. The Texas Medication Algorithm Project (TMAP) (23, 30) was generally based on the 1996 Expert Consensus Guidelines (31) and the 1994 APA Guidelines. The 2000 Expert Consensus Guidelines (32) were developed most rigorously, using survey methodology (33) with 65 leading American experts on bipolar disorder, and the RAND modified Delphi approach for ascertaining expert consensus (34).

For the purpose of this descriptive analysis, actual practice patterns for bipolar I *mania* and bipolar I *depression* were compared with the 2000 Expert Consensus Guidelines (32, 35). Table 1 summarizes the preferred strategies and alternate strategies for pharmacotherapies recommended by the 2000 Expert Consensus Guidelines for bipolar I *mania* (with, or without psychotic features) and for bipolar I *depression* (with, or without psychotic features).

The specific mood stabilizers recommended for all clinical presentations of bipolar *mania* or bipolar *depression* include lithium, valproate and carbamazepine. In addition, a new anticonvulsant lamotrigine is recommended for bipolar *depression*. Atypical antipsychotics are preferred by the Expert Consensus Guidelines over conventional antipsychotics as first-line adjunctive treatment for bipolar *mania* and for psychotic bipolar *depression*, particularly when long-term use (2–5 months following resolution of acute episode) is required. Specific antidepressant agents recommended for bipolar *depression* include buproprion, the selective serotonin reuptake inhibitors (SSRIs) and venlaxafine. No guidance regarding specific benzodiazepines to use with bipolar patients is provided.

Study purpose

While the treatment recommendations specified in published guidelines may not address the specific and unique needs of every bipolar patient, and are not intended to represent standards of medical care per se (36), they do provide a helpful clinical framework. Describing the psychotropic agents prescribed for bipolar patients admitted to a psychiatric unit in acute-care hospitals throughout the USA can be informative regarding current treatment practices in this important setting. The specific objective of this study was to profile clinician-prescribing practices for bipolar patients within hospital settings, and to delineate the extent to which they are consistent with recently published treatment guidelines.

Methods

Data source

Retrospective analyses were conducted on data collected between January 1, 1996 and March 31, 2000. Data came from the CQI + SM Outcomes

Table 1. Pharmacologic therapies recommended by Expert Consensus Guidelines (32)

Bipolar I mania with psychotic features
Mood stabilizer and antipsychotic
Mood stabilizer, antipsychotic and benzodiazepine
Bipolar I mania without psychotic features
Mood stabilizer alone
Mood stabilizer and benzodiazepine
Mood stabilizer and antipsychotic
Bipolar I depression with psychotic features
Mood stabilizer, antipsychotic and antidepressant
Electroconvulsive therapy
Mood stabilizer and antipsychotic
Mood stabilizer and antidepressant
Bipolar I depression without psychotic features
Mood stabilizer and antidepressant
Mood stabilizer alone
Electroconvulsive therapy

Preferred treatments specified within the Expert Consensus Guidelines (32) are italicized. Alternate treatments specified within the Expert Consensus Guidelines (32) are not italicized.

Measurement System database developed by Mental Health Outcomes in Lewisville, TX. The system tracks information on patients, age 18 and older, admitted to psychiatric inpatient units from over 100 acute care medical–surgical hospitals in 31 states.

Patients with a diagnosis of bipolar I or II disorder represented a subset (n = 1864 or 7.0%) of a large national cohort of patients (n = 26559), hospitalized in psychiatric treatment programs across the USA. Included in the subset were bipolar patients aged 18–64 years admitted to adult psychiatric units (n = 869), and patients aged 55 years or older admitted to geropsychiatric units (n = 995).

Assessment procedures

Programs participating in the CQI^{SM} + System invite the first 17 patients admitted per month (regardless of diagnosis) to complete a series of assessments within 72 h of admission, within 48 h of discharge and at 3 months (*geriatric programs*) or 6 months (*adult programs*) following hospital discharge. Overall, the assessments include several self report, informant report, and clinician/staff-rating scales. For this study, demographic characteristics and clinical status variables of all patients with a primary discharge diagnosis of bipolar I or bipolar II disorder were selected from an *admission questionnaire*, completed by patients and informants. Discharge medications were identified by a *medication usage questionnaire*, which was completed by the hospital staff based on the patients' medical records. Clinician-prescribing patterns were analyzed only for the two largest subsets of bipolar patients [i.e. patients with bipolar I *mania* (ICD-9 Codes: 296.00–296.06) or with bipolar I *depression* (ICD-9 Codes: 296.50–296.56)].

Results

Patient demographics and diagnosis

Patient demographics at admission are shown in Table 2. Overall, the bipolar group was 63% female, predominantly Caucasian (90%), educated at a High School level or beyond (73%) and averaged 57 years old (SD = 20; range 18–102). About half (49%) were separated, divorced or widowed, with only one-third (33%) currently married. Most were unemployed or 'retired' (85%), and were living in their private residence (75%) prior to hospital admission.

Bipolar I *mania* (n = 1007 or 54%) and bipolar I *depression* (n = 464 or 25%) (with or without psychotic features) represented the majority of bipolar patients discharged from the hospital. Smaller groups of patients had a primary discharge diagnosis of bipolar I *mixed* (n = 306 or 16%) or bipolar II disorder (n = 87 or 5%).

Table 2. Admission assessment of demographic variables for bipolar I and II inpatients

Variable	Bipolar cohort (n = 1864)
1. Mean age ± SD	57 ± 20
2. Race	
% Caucasian	90
% African American	6
3. Gender	
% Female	63
4. Work status	
% Unemployed or 'retired'	85
5. Marital status	
% Never married	18
% Married	33
% Separated, divorced or widowed	49
6. Living arrangement	
% Living at home (alone or with others)	75
% Nursing home	9
% Board and care	6
% Other (e.g. retirement facility, hospital)	10
7. Type of payor[a]	
% Medicaid	19
% Medicare	57
% Private insurance	28
8. Educational status	
% High School graduates or above	73

[a] Response choices within this category were not mutually exclusive.

Clinical status at hospital admission

The typical patient in our overall bipolar sample had experienced a severe and chronic clinical history. The most common secondary DSM-IV Axis I/II discharge diagnoses documented in the medical record were personality disorder (14%) and substance-related disorder (11%). The majority (81%) had previously been hospitalized at least once for psychiatric reasons, with about 40% having been hospitalized four or more times for psychiatric reasons during their lifetime. In addition, approximately one-third reported attempting suicide at least once within their lifetime.

Discharge medication prescribing patterns

The frequencies (by percentage) of different pharmacologic therapies prescribed for bipolar I *mania*

and bipolar I *depression* patients, presented separately for those with or without psychotic features, are listed in Tables 3 and 4. The vast majority of patients (89–98%) were discharged on at least one psychotropic agent. However, the array of agents used alone or in combination was broad. No single pharmacologic therapy was overwhelmingly preferred by clinicians in the treatment of either bipolar I *mania* or bipolar I *depression*.

Bipolar I mania

The most common treatments for bipolar I *mania* with psychotic features (n = 181) were a mood stabilizer/antipsychotic combination (29%), mood stabilizer alone (9%), mood stabilizer/antipsychotic/benzodiazepine combination (9%), antipsychotic alone (8%) or mood stabilizer/antipsychotic/antidepressant combination (8%).

In contrast, bipolar I *mania* without psychotic features (n = 796) was most commonly treated with an antidepressant alone (20%), a benzodiazepine/antidepressant combination (10%) or a mood stabilizer/antipsychotic combination (9%). While only 2% of patients with bipolar I *mania* with psychotic features were prescribed no psychotropic agents at discharge, a higher percentage of patients with bipolar I *mania* without psychotic features received no psychotropic agents at discharge (11%).

Bipolar I depression

The most common treatments for bipolar I *depression* with psychotic features (n = 46) were an antipsychotic/antidepressant combination (20%), a mood stabilizer/antipsychotic/antidepressant combination (20%), an antidepressant alone (13%), or mood stabilizer/antipsychotic/antidepressant/benzodiazepine combination (11%). Bipolar I *depression* without psychotic features (n = 398) was most commonly treated with a mood stabilizer/antipsychotic/antidepressant combination (14%), a mood stabilizer/antidepressant/benzodiazepine combination (11%), a mood stabilizer/antidepressant combination (10%) or an antidepressant alone (10%). The percentage of patients with bipolar I *depression* with, or without psychotic features who were

Table 3. Medication treatments for patients diagnosed with bipolar I mania

	Percentage	
	Bipolar I *mania* with psychotic features (n = 181)	Bipolar I *mania* without psychotic features (n = 796)
Mono-therapy		
Mood stabilizer[a] alone	9	**5**
Antipsychotic alone	8	5
Benzodiazepine alone	1	2
Antidepressant alone	1	20
Dual-therapy		
Mood stabilizer and antipsychotic	**29**	**9**
Mood stabilizer and benzodiazepine	4	**2**
Mood stabilizer and antidepressant	1	3
Antipsychotic and benzodiazepine	6	1
Antipsychotic and antidepressant	4	7
Benzodiazepine and antidepressant	1	10
Poly-therapy		
Mood stabilizer, antipsychotic and benzodiazepine	**9**	5
Mood stabilizer, antipsychotic and antidepressant	8	4
Mood stabilizer, benzodiazepine and antidepressant	2	3
Antipsychotic, benzodiazepine and antidepressant	3	0
Mood stabilizer, antipsychotic, benzodiazepine and antidepressant	7	2
Other psychotropic combinations (not including those listed above)	5	10
No psychotropic therapy	2	11
ECT with or without pharmacologic therapies	1	2

Treatments recommended by Expert Consensus Guidelines (32) are highlighted in bold for each diagnostic subset.
[a] Mood stabilizer includes lithium, valproate, carbamazepine, gabapentin.

Table 4. Medication treatments for patients diagnosed with bipolar I depression

	Percentage	
	Bipolar I *depression* with psychotic features (n = 46)	Bipolar I *depression* without psychotic features (n = 398)
Mono-therapy		
Mood stabilizer[a] alone	0	**4**
Antipsychotic alone	7	2
Benzodiazepine alone	0	2
Antidepressant alone	13	10
Dual-therapy		
Mood stabilizer and antipsychotic	**7**	5
Mood stabilizer and benzodiazepine	0	2
Mood stabilizer and antidepressant	**2**	**10**
Antipsychotic and benzodiazepine	4	1
Antipsychotic and antidepressant	20	5
Benzodiazepine and antidepressant	4	6
Poly-therapy		
Mood stabilizer, antipsychotic and benzodiazepine	7	3
Mood stabilizer, antipsychotic and antidepressant	**20**	14
Mood stabilizer, benzodiazepine and antidepressant	2	11
Antipsychotic, benzodiazepine and antidepressant	2	3
Mood stabilizer, antipsychotic, benzodiazepine and antidepressant	11	8
Other psychotropic combinations (not including those listed above)	0	10
No psychotropic therapy	2	6
ECT with or without pharmacologic therapies	**2**	**3**

Treatments recommended by Expert Consensus Guidelines (32) are highlighted in bold for each diagnostic subset.
[a] Mood stabilizer includes lithium, valproate, carbamazepine, gabapentin.

prescribed no psychotropic agents at discharge was 2% and 6%, respectively.

Most frequently prescribed agents within medication category

Table 5 lists the percentages of bipolar I *mania* or bipolar I *depression* patients prescribed specific medications within each of four medication categories (mood stabilizers, antipsychotics, antidepressants, benzodiazepines). For example, of those with mania who were prescribed a mood stabilizer (n = 405), 59% were prescribed valproate and 38% were prescribed lithium. For those with either mania or depression, valproate and lithium were the most frequently prescribed agents. When benzodiazepines were prescribed, lorazepam and clonazepam were used most commonly. For patients with bipolar I *mania*, trazodone and sertraline were used in approximately equal proportions. For those with bipolar I *depression*, sertraline was used most often of the antidepressants. Of the antipsychotic agents prescribed for bipolar I *mania*, risperidone or conventional agents were used most frequently, while for bipolar I *depression* olanzapine or conventional agents were prescribed most often.

Electroconvulsive therapy (ECT)

Of note, a very small percentage of patients with bipolar I *mania* (3%) or bipolar I *depression* (5%) (with or without psychotic features) received electroconvulsive therapy (ECT), despite its well-documented efficacy in the treatment of both phases of the disorder (37–39).

Adherence to Expert Consensus Guidelines

Of the patients with bipolar I *mania* and having psychotic features, 38% were prescribed a recommended pharmacological therapy. More specifically, 29% were prescribed a mood stabilizer and an antipsychotic, while 9% were prescribed a combination of a mood stabilizer, an antipsychotic and a benzodiazepine (refer again to Table 3). Seventeen percent were discharged on a single mood stabilizer or an antipsychotic agent. Of note, about a quarter of the patients (26%) in this diagnostic subgroup were discharged without a mood stabilizer.

Even more strikingly, only 16% of the bipolar I *mania* diagnostic subgroup (without psychotic features) were prescribed a recommended pharmacologic therapy at discharge (see Table 3) consisting

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