Medication Compliance Among Patients With Bipolar Disorder and Substance Use Disorder

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Background: This study examined patterns of medication compliance and reasons for noncompliance among patients with bipolar disorder and substance use disorder.

Method: Forty-four patients with current bipolar disorder and substance use disorder were administered a structured interview regarding lifetime compliance with prescribed psychotropic medications.

Results: Patients who were prescribed both lithium and valproate were significantly ($p = .03$) more likely to report full compliance with valproate than with lithium. Side effects were the most common reason for lithium noncompliance, but were not cited as a reason for valproate noncompliance. Also, a common pattern of noncompliance among patients prescribed benzodiazepines, neuroleptics, and tricyclic antidepressants was the use of more medication than prescribed.

Conclusion: Valproate may have greater acceptability than lithium among patients with bipolar disorder and substance use disorder. Clinicians should also be aware that these patients may take higher doses of medication than prescribed.

(J Clin Psychiatry 1998;59:172–174)

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Supported by grants DA09400, DA08631, and DA00326 from the National Institute on Drug Abuse; grant AA09881 from the National Institute on Alcohol Abuse and Alcoholism; and a grant from the Dr. Ralph and Marian C. Falk Medical Research Trust.

Portions of this paper were presented at the 7th annual meeting and symposium of the American Academy of Addiction Psychiatry, Dec. 6–7, 1996, San Francisco, Calif.

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Noncompliance with medication is consistently associated with poor treatment outcome among patients with bipolar disorder.[1] In the first systematic study of medication compliance in this population, Jamison et al.[2] found that the most commonly reported reasons for lithium noncompliance included being bothered by the idea that one's moods are controlled by medication, feelings of depression, and being bothered by the idea of having a chronic illness. Keck et al.[3] studied compliance with anticonvulsants as well as lithium in patients hospitalized for mania. They reported that 64% of patients did not comply fully with their medication regimens, although compliance rates did not differ significantly according to the specific medication. Denial of illness and lack of control over one's life were the most commonly cited reasons for noncompliance.

Individuals with coexisting bipolar disorder and substance use disorder represent an important subgroup of patients with a particularly high rate of medication noncompliance.[4,5] However, patterns of medication compliance and reasons for noncompliance have never been studied in this population. In the present study of 44 patients with bipolar disorder and substance use disorder, we wanted to determine whether these patients complied differentially with the 2 approved mood stabilizers, lithium and valproate. We also investigated reasons for noncompliance with these and other psychotropic medications that these patients had been prescribed.

METHOD

We recruited McLean Hospital inpatients for this study by reviewing admission notes each day for a 6-month period in 1996 and approaching all patients with admitting diagnoses of bipolar disorder and substance use disorder. Patients who agreed to participate were administered the Structured Clinical Interview for DSM-IV (SCID)[6] after completing detoxification, to confirm the diagnoses of current bipolar disorder and substance use disorder.

In addition to the SCID, patients completed a 91-item questionnaire regarding sociodemographic characteristics and substance use patterns. Patients were then given a structured interview regarding medication compliance,

Table 1. Medication Compliance in Patients With Coexisting Bipolar Disorder and Substance Use Disorder (N = 44)*

Level of Compliance	Lithium N = 38		Valproate N = 26		Carbamazepine N = 18		SSRIs N = 33		TCAs N = 28		Benzodiazepines N = 34		Neuroleptics N = 31	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
100%	8	21.1	13	50.0	6	33.3	15	45.5	17	60.7	12	35.3	11	35.5
> 2/3, < 100%	18	47.4	6	23.1	6	33.3	13	39.4	6	21.4	9	26.5	9	29.0
1/3–2/3	7	18.4	5	19.2	5	27.8	2	6.1	3	10.7	7	20.6	7	22.6
< 1/3	5	13.2	2	7.7	1	5.6	3	9.1	2	7.1	6	17.6	4	12.9

*Abbreviations: SSRIs = serotonin selective reuptake inhibitors, TCAs = tricyclic antidepressants.

which we adapted from Jamison et al.[2] Lifetime information was gathered regarding all psychotropic medications that patients had been prescribed. For each medication, patients were asked: "Over your lifetime, have you taken this medication as prescribed (a) all the time, (b) more than two-thirds of the time, but not all the time, (c) between one-third and two-thirds of the time, or (d) less than one-third of the time?" If the answer was anything other than "all the time," patients were asked, "When you did not take this medication as prescribed, what was the most important reason for not taking it as prescribed?"

RESULTS

Sociodemographic and Diagnostic Characteristics

The study sample consisted of 44 patients, all of whom gave written informed consent. Patients were primarily female (54.5%, N = 24), white (90.9%, N = 40), single (45.5%, N = 20) or divorced (29.5%, N = 13), and unemployed (59.1%, N = 26). Their mean ± SD age was 37.3 ± 9.1 years. Twenty-three patients (52.3%) were diagnosed as both drug and alcohol dependent; 10 (22.7%) had drug dependence alone, and 11 (25.0%) had alcohol dependence alone. Cocaine (N = 9), cannabis (N = 9), and sedative-hypnotic drugs (N = 8) were the most common drugs of choice among patients with drug dependence. Thirty-six patients (81.8%) were diagnosed with bipolar I disorder, 7 (15.9%) had bipolar II disorder, and 1 patient (2.3%) had bipolar disorder not otherwise specified.

Medication Compliance

Lithium was the medication most commonly prescribed (N = 38), followed by benzodiazepines (N = 34), serotonin selective reuptake inhibitors (N = 33), antipsychotic agents (N = 31), tricyclic antidepressants (N = 28), other antidepressants (N = 27), valproate (N = 26), carbamazepine (N = 18), and stimulants (N = 8). Among the 23 patients who received both lithium and valproate, 21 had been prescribed lithium first.

Levels of medication compliance for the most commonly prescribed medications are summarized in Table 1. Over 60% of patients reported complying with each medication "more than two-thirds of the time," although likelihood of full compliance varied by medication. Specifically, when we compared lifetime compliance with lithium versus valproate, 26 (68.4%) of 38 patients prescribed lithium and 19 (73.1%) of 26 patients prescribed valproate reported taking that medication as prescribed "at least two-thirds of the time" or "all the time." However, more than twice the percentage of patients reported complying "all the time" with valproate (13 of 26, 50.0%) as did with lithium (8 of 38, 21.1%). Among patients who had been prescribed lithium and/or valproate, 15 had been prescribed only lithium, 3 had been prescribed only valproate, and 23 had been prescribed both. Patients who were prescribed both medications were significantly more likely to comply fully with valproate than with lithium; 4 of these 23 patients complied fully with both medications, 11 complied with neither, 7 complied only with valproate, and 1 patient complied only with lithium (McNemar test, p = .03). There were no differences in the level of compliance according to subtype of bipolar disorder.

Table 2. Most Common Reasons* for Noncompliance With Lithium vs. Valproate

Medication	Primary Reason for Noncompliance
Lithium (N = 38)	Physical side effects (N = 8)
	Saw no need for the medication (N = 6)
	Wanted to use drugs or alcohol (N = 3)
	Hassle to take medication/see physician/fill prescription (N = 3)
	Confusion/forgot to take (N = 2)
Valproate (N = 26)	Hassle to take medication/see physician/fill prescription (N = 4)
	Wanted to use drugs or alcohol (N = 3)
	Confusion/forgot to take (N = 2)

*Only includes reasons endorsed by more than 1 patient. Ns represent number of patients.

As shown in Table 2, side effects were the most commonly cited primary reasons for overall medication noncompliance, accounting for 20 (14.0%) of the 143 instances of noncompliance. Side effects (lethargy, weight gain, and tremors) were the most commonly cited reasons for lithium noncompliance, accounting for 8 (26.7%) of 30 cases of noncompliance. Six patients (20.0%) failed to comply because they saw no need for lithium. However, no one reported failing to take valproate as prescribed for either of these reasons. Rather, patients cited a "hassle" to take medication (4 of 13 cases, 30.8%) as the most common reason for not complying with valproate.

Another commonly reported pattern of noncompliance occurred among some patients prescribed benzodiaz-

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epines, neuroleptics, tricyclic antidepressants, and stimulants. These patients reported taking *more* medication than prescribed, either (1) because they were impatient with waiting for the medication to work (N = 16) or (2) to become intoxicated (N = 9).

DISCUSSION

There are several explanations for our finding of greater compliance with valproate than with lithium. First, patients may have taken lithium for a longer time, thus having more opportunities to be noncompliant. Second, some patients who stopped lithium because they felt it to be unnecessary may have subsequently accepted the need for medication at a later stage of illness, perhaps after being switched to valproate. Although these explanations may reflect artifactual rather than substantive differences between valproate and lithium, it is noteworthy that no patients reported noncompliance with valproate because of side effects, although this was the most common reason for not taking lithium as prescribed. This finding suggests that valproate may have greater patient acceptability among this group of patients.

The tendency in our population to take more medication than prescribed is noteworthy. The escalation of benzodiazepine dosage by patients with substance use disorders is well-known[7]; the use of higher-than-prescribed doses of antidepressants and neuroleptics, although less common, has been reported elsewhere.[8,9] The finding that these patients sometimes took extra doses because of impatience with the drugs' slow onset of action should alert clinicians to this phenomenon.

Unlike the findings by Jamison et al.,[2] no patients reported noncompliance because of being bothered by having their moods controlled by medication. Perhaps patients with substance use disorders, who habitually self-administer mood-altering agents, are less upset by this aspect of taking prescribed medication than are other individuals with bipolar disorder.

Our study is limited by reliance on a single interview, potentially introducing poor recall or recall bias. We also did not obtain serum levels because of the retrospective nature of the interviews; serum levels can be helpful (particularly if they are very low or zero) in monitoring current compliance with lithium and valproate. In a prospective study of medication compliance that we are conducting with this cohort, we are obtaining corroborating data from current prescribing physicians and collateral informants. However, since a number of the patients in this study had had many prescribing physicians over the years, gathering information from all of them was not feasible for this study of lifetime compliance patterns.

CONCLUSION

Patients with bipolar and substance use disorders represent a challenging and understudied population. Although our data are based on a relatively small sample, they suggest that medication compliance might be increased by considering valproate as a mood stabilizer for these patients. Indeed, preliminary results from a small (N = 9) open-label study by Brady et al.[10] support the efficacy of valproate for these patients. Moreover, attention to issues of medication compliance, including the use of excessive doses of medication, is critical in optimizing treatment in this population.

Drug name: carbamazepine (Tegretol and others).

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