Chronic Neuroleptic Exposure in Bipolar Outpatients

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Background: Although the chronic use of neuroleptic medications is generally discouraged in patients with bipolar disorder, data on the actual extent of this practice are relatively scarce.

Method: All bipolar patients receiving treatment at the Connecticut Mental Health Center on September 1, 1994, were identified through a computerized administrative database; the medical record was then examined. Patients were included in the study if (1) the last two recorded diagnoses in the chart were concordant for bipolar disorder and (2) the patient had not been hospitalized in the past year.

Results: Of 49 patients meeting review criteria, 33 (67%) met criteria for chronic neuroleptic exposure. The mean ± SD continuous neuroleptic dosage for these 33 outpatients was 416 ± 527 mg/day chlorpromazine (CPZ) equivalents. The dosage distribution was skewed, with 17 (52%) receiving ≤ 200 mg/day CPZ equivalents.

Conclusion: Chronic neuroleptic administration occurred frequently in our sample of nonhospitalized bipolar outpatients.

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Although the chronic use of neuroleptic medications is generally discouraged in patients with bipolar disorder, data on the actual extent of this practice are relatively scarce.[1] We have previously reported that during the 6 months after discharge from inpatient treatment, subsequent continued neuroleptic exposure was substantial in bipolar patients who had been treated as inpatients with neuroleptics and lithium.[2] At 6-month follow-up, only 2 (5%) of the 40 patients were no longer receiving neuroleptics.

This observation is consistent with other observations. Keck et al.[3] described a 6-month, prospective, follow-up assessment of neuroleptic use in bipolar patients with an index hospitalization for mania. Of the 77 patients examined, 52 (68%) were receiving neuroleptics 6 months after discharge. Licht et al.[4] reported that of 111 patients admitted for treatment of acute mania and treated for at least 1 week with neuroleptics, 82 (74%) were discharged on neuroleptic therapy.[4] Finally, Sachs[5] reported that 37% of outpatients with bipolar and schizoaffective disorder in his clinic were prescribed neuroleptics.

We hypothesized that this high rate of neuroleptic use might be true only for recently hospitalized bipolar patients. The patients in our previous study all were hospitalized for mania, all were treated with neuroleptics while inpatients, and 68% of them were rehospitalized at least once during the 6-month follow-up. The current study was therefore designed to examine neuroleptic exposure in all bipolar outpatients currently followed at our clinic who had not been hospitalized in the past year.

METHOD

All bipolar patients receiving treatment at the Connecticut Mental Health Center (CMHC) on September 1, 1994, were first identified through a computerized administrative database; the medical record was then examined. Patients were included in the study if (1) the last two recorded diagnoses in the chart were concordant for bipolar disorder and (2) the patient had not been hospitalized in the past year. Patients were defined as having been maintained on neuroleptics when the medication record in their chart indicated that they had been prescribed the same

Table 1. Clinical Characteristics of the Sample Population (N = 33)

Gender	11 M, 22 F
Age (y)	50.5 ± 12 y, range 26–78
Race	26 white, 4 black, 3 Hispanic
Previous hospitalizations	3 ± 3, range 0–10
Years in treatment	13.6 ± 8 y, range 0–26

dosage of neuroleptic (± 10%) for at least the past 6 months. Chronic neuroleptic exposure was defined as receiving the same dosage of neuroleptics (< 10% decrease) for the previous 6 months. Other neuroleptic dosage not meeting criteria for maintenance was also noted. All dosages of neuroleptics were converted to chlorpromazine (CPZ) equivalents.[6] Only standing (e.g., no p.r.n.) dosages were used for calculations.

RESULTS

Charts were available for 82 of the 95 patients identified as bipolar from the administrative database. Twenty-two (27%) of the 82 charts were rejected. Twenty patients, when their charts were reviewed, were found not to carry a bipolar diagnosis on both of the two most recent determinations (18 were diagnosed as schizoaffective, bipolar type). There was insufficient information on 2 patients. Of the 60 evaluable cases, 49 patients (82%) had not been hospitalized in the previous year.

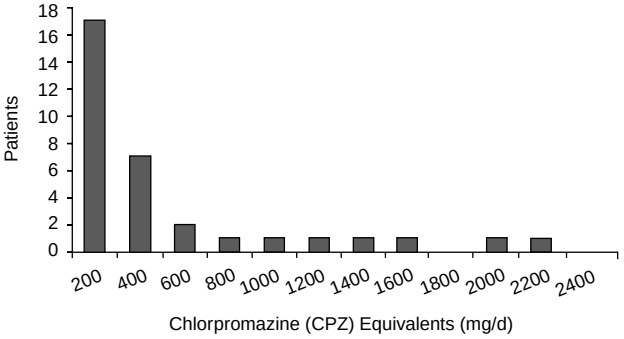
Of the nonhospitalized patients, 34 (69%) received neuroleptics at some time in the previous 6 months. During that period, 1 patient was tapered off neuroleptics entirely, while 33 of the patients met criteria for chronic neuroleptic exposure. Demographic characteristics of the 33 patients with chronic neuroleptic exposure are presented in Table 1.

The mean ± SD neuroleptic dosage for those outpatients with chronic neuroleptic exposure was 416 ± 527 mg/day CPZ equivalents. Chlorpromazine equivalent dosages ranged from 25 mg/day to 2083 mg/day, with a skew in the distribution toward lower dosages (Figure 1)—17 (52%) of the 33 patients were receiving 200 mg/day CPZ equivalents or less.

The diagnostic categories were manic, N = 19 (psychotic, N = 6; in full remission, N = 5); mixed, N = 13 (psychotic, N = 5; in full remission, N = 0); and depressed, N = 1.

Various thymoleptics were concurrently prescribed for 28 (85%) of the 33 patients with chronic neuroleptic exposure. Of these, 21 (75%) received lithium as a sole thymoleptic; lithium and clonazepam, N = 3; lithium and carbamazepine, N = 2; lithium and valproic acid, N = 1; and carbamazepine, N = 1. Five patients were prescribed no thymoleptic (including 2 receiving depot preparations). The mean ± SD serum lithium level of the 27 patients receiving lithium was 0.78 ± 0.24 mEq/L.

Figure 1. Distribution of Neuroleptic Dosages[a] in Nonhospitalized Bipolar Outpatients



[a]Dosages are divided into 200-mg intervals. Column height represents number of patients prescribed dosage within that interval.

DISCUSSION

The chart review design of this study limits the interpretation of the results. Our goal was to determine the rate of chronic neuroleptic exposure in nonhospitalized bipolar outpatients, with schizoaffective patients excluded. Since a diagnostic interview was not performed, we relied on concurrence of the two most recent diagnoses entered by the primary clinician or attending physician in yearly chart summaries with the previous diagnosis in the administrative database. This method does not ensure that schizoaffective patients are eliminated from the sample, and it is possible that the diagnosis of some patients would have changed if a structured interview had been used.

It is not clear whether the high neuroleptic maintenance reported here is representative of the treatment of bipolar patients in other settings. As a public sector institution, the CMHC may treat more severely ill, including bipolar, patients. The majority of the CMHC outpatient population (N = 1154) tends to have diagnoses compatible with severe mental illness and is, by percentage, bipolar, 9%; schizoaffective, 17%; and schizophrenic, 26%. Nonetheless, our results agree with other observations. Several studies examining the prevalence of tardive dyskinesia among bipolar patients have reported current neuroleptic use rates ranging from 40% to 72%.[1] While these studies did not address the rate of chronic maintenance neuroleptic prescription in bipolar outpatients, almost all of the neuroleptic use in our patients was chronic maintenance use. In fact, for our population of patients, these results may be conservative since no prescribed p.r.n. usage was included in the calculations for chronic neuroleptic exposure. Future studies should examine chronic neuroleptic prescription rates at other sites.

The high rates of chronic neuroleptic prescription appear to place this population at risk. Chronic treatment with neuroleptics exposes patients to the well-known risk

of tardive dyskinesia—a risk that may be greater in patients with affective disorder.[7] Additionally, ongoing neuroleptic exposure may also make neuroleptic discontinuation more problematic. It has been proposed that chronic administration of neuroleptics may lead to "supersensitivity psychosis"—a sensitivity developed following neuroleptic exposure to dosage decreases that can result in psychotic decompensation.[8]

Why might bipolar outpatients be maintained on neuroleptics? The scope of this chart review does not permit us to address this question directly; however, several speculations deserve discussion. Lithium levels appear to have been adequate (0.80 ± 0.24 mEq/L), comparing favorably with those (0.83 ± 0.11 mEq/L) for the "standard group" in a prospective lithium maintenance study.[9] This would not support the hypothesis that neuroleptics were being employed to compensate for underdosing lithium. It is possible that many of the patients receiving thymoleptics were somewhat refractory to these medications and were experiencing residual bipolar symptoms. The majority of these patients were receiving lithium as their sole thymoleptic. We informally surveyed prescribing physicians for nine patients with chronic neuroleptic exposure from the current study. Six of these patients were viewed by the prescribing physician as exhibiting chronic psychotic or manic symptoms or both. Perhaps prescribers view these patients as lithium-refractory and employ neuroleptics to try to stabilize patients' symptomatology.

The relative benefit of neuroleptic medication versus anticonvulsant treatment for lithium-refractory bipolar patients should be investigated. Only 4 (12%) of the 33 bipolar outpatients chronically receiving neuroleptics in our sample were also receiving anticonvulsants.

Another possibility is that prescribers might believe that chronic neuroleptic treatment could also confer protection against relapse—independent of its ability to address residual symptoms. This belief could be based on the outcome of previous taper attempts occurring in the years prior to the chart review. The hypothesis that chronic neuroleptics can confer a maintenance benefit is supported by evidence that bipolar patients can relapse after neuroleptic withdrawal.[10]

Our data raise questions about what recommendations can be made about maintenance neuroleptic treatment in bipolar disorder. In general, it would seem a prudent treatment guideline that a trial of combinations of mood stabilizers be given at least as much weight as chronic neuroleptic exposure. At the same time, the potential for neuroleptic withdrawal leading to symptomatic exacerbation combined with the relatively low dosages used in the majority of the bipolar outpatients in our sample raises the possibility that there might be a role for neuroleptic maintenance in selected bipolar patients. Future research should address the risks and benefits of adjunctive neuroleptic maintenance versus use of multiple thymoleptics in patients who relapse on lithium alone.

Drug names: carbamazepine (Tegretol and others), clonazepam (Klonopin), valproic acid (Depakene and others).

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