Effectiveness of Combining Atypical Antipsychotics and Psychosocial Rehabilitation in a Community Mental Health Center Setting

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This article presents a consecutive case series of 70 patients treated with olanzapine, case management, and psychosocial rehabilitation in a community mental health setting. This group demonstrated highly significant improvement on all analyzed measures of symptoms and psychosocial function at 6-month follow-up. These findings suggest that results of efficacy studies of olanzapine will generalize to the community mental health setting. Furthermore, prescribing olanzapine in combination with case management and rehabilitation yields positive functional outcomes.

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Efficacy studies of new medications focus on isolating drug effects in defined populations of patients in controlled settings. Such studies have demonstrated that the new atypical antipsychotics are as effective as or more effective than conventional antipsychotics, but have a lower incidence of associated adverse effects.[1–4] While such designs are critical to ensure that measured effects are the result of treatment with the medication under study, they inherently limit our ability to generalize study results to other settings. For example, most existing studies on atypical antipsychotics exclude patients with comorbid substance abuse or unstable medical illness, leaving the efficacy of these agents unclear in substantial subpopulations. Limiting prescription to a defined dose range without augmentation (e.g., an antidepressant for a schizoaffective patient) may also underestimate potential clinical benefits and exaggerate dropout rates compared with naturalistic practice.

Effectiveness studies provide a broader but less precise perspective. They augment our knowledge by following outcomes in patients prescribed medications in conventional clinical settings to evaluate overall treatment effects.[5–9] Effectiveness studies are pragmatic rather than explanatory trials.[10] In other words, they evaluate the outcomes of clinical decision making in natural clinical settings rather than focusing on cause-and-effect relationships. Effectiveness designs maximize external validity or generalizability of results as opposed to the internal validity that comes from the controlled clinical conditions in efficacy studies.

Effectiveness studies exert as little influence as possible on the clinical situation. As a result, they capture combined effects of multimodal treatment, including therapeutic alliance and patient expectancies. They can be either randomized or nonrandomized, and are open-label by definition, since this is part of conventional clinical practice. These designs typically lack rater blinding and always lack patient blinding, thereby increasing the potential for observer biases to influence outcome measures. Effectiveness studies are particularly well suited to clinical settings because they do not limit clinical practice by forcing it to adhere to experimental conditions.

Patients with psychotic disorders are primarily treated in public mental health settings such as community mental health centers (CMHCs) and state hospitals, yet these settings are rarely represented in atypical antipsychotic trials. In these settings, patients with comorbid substance abuse, poorly controlled medical illness, or psychotic symptoms associated with disorders other than schizophrenia and schizoaffective disorder are routine. In addition, CMHCs often provide services such as case management and rehabilitation treatments for patients with psychotic disorders. It is unclear what outcomes may be expected from treatment with atypical antipsychotics under these conditions.

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Negative symptoms of psychotic disorders are particularly associated with poor psychosocial functioning and difficulty in benefiting from rehabilitative treatments.[11] The evidence for efficacy of atypical antipsychotics in reducing the negative symptoms of psychotic disorders suggests the potential for synergistic effects between atypical antipsychotics and rehabilitative treatments that could lead to even greater functional gains when these interventions are combined.

Olanzapine's effects on negative symptoms of psychotic disorders are well characterized.[12] We are following a consecutive series of patients treated with olanzapine or remaining on typical antipsychotics in a CMHC with an international reputation for developing and implementing cutting-edge case management and psychosocial rehabilitation treatments.[13,14(p242)] The goals of this study are to evaluate olanzapine's effectiveness when prescribed in a CMHC setting and explore whether simultaneous access to rehabilitation treatment and olanzapine leads to enhanced functional outcomes. Pilot data from the overall study are presented in this article.

METHOD

A prospective design rating symptoms and psychosocial function in patients treated naturalistically with olanzapine or typical antipsychotic medication is being employed in an academic CMHC setting. All patients come from Community Support Services of the Mental Health Center of Greater Manchester (New Hampshire). This program serves patients meeting New Hampshire Division of Mental Health criteria for diagnosis and functional impairment who are living within the center's catchment area. It includes virtually all adults diagnosed with active psychotic disorders served within the mental health center and employs a clinical case management model of care following National Institute of Mental Health (NIMH) guidelines.[15] The Community Support Services program served 1271 patients during fiscal year 1996, approximately 71% of whom carried diagnoses of schizophrenia or schizoaffective disorder; 26%, affective disorders; and 1.5%, anxiety disorders.

All patients in this program have access to psychosocial rehabilitation interventions that are an integral part of the community support program. Rehabilitation interventions are research based and state-of-the-art and include individual placement and support vocational rehabilitation,[16] social skills training modules,[17] and integrated substance abuse treatment.[18,19] Every client in the program is assigned a case manager, who is responsible for identifying functional impairments using functional assessment and Mental Health Statistics Improvement Project[20] scales and designing a treatment plan to address those impairments.

The study group for the project comprises the first 120 patients prescribed olanzapine within this program who consented to participate. The comparison group comprises the first 50 patients who expressed an intention to continue treatment with typical neuroleptics and who consented to participate. Data have been gathered since October 1996, when olanzapine became available for clinical use in the United States.

The clinical ratings include the 24-item Brief Psychiatric Rating Scale (BPRS) and an expanded version of the Case Manager Rating Scale (CMRS+),[21–23] administered at baseline and every 6 months for 1 year. Clinical diagnoses are confirmed or modified during the baseline interview using DSM-IV[24] criteria and are recorded on the baseline log. Additional measures are being used in the larger study, but data from these measures are not yet available.

Baseline data collection occurs prior to switching a patient to olanzapine for the study group. We collect the same baseline data on the comparison group patients at the point of consent and follow them with the same protocol for 1 year.

Raters are not blinded to study condition. Therefore, several steps have been taken to reduce the risk of rater bias influencing the measurement of outcomes. A minimum of 10% of all subjective ratings will be separately rated by a second rater who also knows the client (CMRS+) or observes the same interview (BPRS), but who is blind to the primary rater's scoring. Interrater reliability analyses will be performed to ensure that systematic rater bias is not significant. Also, measuring major constructs on more than one rating scale (i.e., psychiatric symptoms on both BPRS and CMRS+) will allow us to examine the consistency of results gathered from different perspectives.

Pilot data were examined for the subset of the olanzapine-treated study group who had baseline and 6-month measures available. Two patients in this early group stopped taking olanzapine within a week and returned to conventional antipsychotic treatment. All other patients took olanzapine throughout the 6-month study period. We did not separate their outcomes for this pilot analysis.

Only the BPRS and CMRS+ scores were entered in the database at the time of this pilot analysis. Larger numbers of completed 6-month CMRS+ scales were available, since they are completed by the case manager and do not require scheduling an interview with the subject. We conducted a prestudy/poststudy comparison, evaluating change from baseline to 6 months in BPRS and CMRS+ overall scores and in selected individual item scores. Statistical significance was evaluated using a paired t test.

RESULTS

Seventy patients had data entered on either the BPRS or CMRS+ at baseline and 6 months at the time of this analysis. All patients in this sample were from the olanza-

Table 1. Characteristics of Pilot Sample (Olanzapine and Psychosocial Treatment Group, N = 70)

Characteristic	N	%
Gender		
Male	43	61
Female	27	39
Age, y		
≤ 30	10	14
31–40	29	41
41–50	14	20
51–60	13	19
≥ 61	4	6
Primary Diagnosis		
Schizophrenia	43	61
Schizoaffective disorder	15	21
Bipolar I disorder	8	11
Psychotic disorder NOS	1	1
Delusional disorder	1	1
Major depression	1	1
Obsessive-compulsive disorder	1	1

Table 2. Pilot Outcomes on the 24-Item BPRS (N = 33)[a]

Scale	Baseline Mean Score	6-Month Mean Score	p Value
BPRS total	70.1	45.8	.0001
Hallucinations	4.1	3.4	.008
Delusions	4.6	3.7	.015
Disorganization	3.2	1.9	.0001
Self-neglect	2.8	1.8	.001
Blunted affect	3.4	1.6	.0001

[a]Abbreviation: BPRS = Brief Psychiatric Rating Scale. Ratings on BPRS subscales are as follows: 1 = not present, 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe.

pine treatment group. Table 1 summarizes available demographic and diagnostic characteristics of this group.

Thirty-three patients completed baseline and 6-month BPRS ratings (Table 2). The mean total BPRS score was 70.1 at baseline prior to prescription of olanzapine and fell to a mean of 45.8 after 6 months of taking the medication, a statistically significant improvement (p = .0001). As the minimum score on the BPRS is 24, this change represents a 53% reduction in the mean BPRS total score. Individual items selected to represent the positive, negative, and disorganization symptom clusters all demonstrated statistically significant improvements as well. The disorganization and blunted affect items demonstrated the most highly significant change compared with previous treatment.

Sixty-seven patients had baseline and 6-month ratings on the CMRS+ in the database (Table 3). The illness factors scale showed statistically significant improvement, dropping from a mean of 38.4 at baseline to 31.0 at 6-month follow-up (p = .0001). As the minimum score on the CMRS+ illness scale is 17, this change represents a 35% reduction in mean psychiatric symptoms as rated by case managers. The selected individual item scores demonstrated statistically significant improvements as well. Case manager ratings replicate the improvement in negative symptoms rated by psychiatrists on the BPRS. They also indicate improvements in cognitive impairment and substance abuse.

Table 3. Pilot Outcomes on CMRS+ (N = 67)[a]

Scale	Baseline Mean Score	6-Month Mean Score	p Value
CMRS+ illness scale[b]	38.4	31.0	.0001
Negative symptoms	3.2	2.8	.002
Cognitive impairment	2.2	1.8	.008
Alcohol use	2.1	1.7	.001
Drug use	1.7	1.4	.008
CMRS+ psychosocial scale[c]	36.1	30.2	.0001
Social relationships	4.0	3.2	.0001
Vocational function	4.0	3.3	.002

[a]Abbreviation: CMRS+ = Case Manager Rating Scale, expanded version.
[b]Ratings on CMRS+ illness scale are as follows: 1 = not present, 2 = mild, 3 = moderate, 4 = severe, 5 = extremely severe.
[c]Ratings on CMRS+ psychosocial scale are as follows: 1 = highly functional, 2 = substantially functional, 3 = moderately functional/moderately impaired, 4 = substantially impaired, 5 = highly impaired.

Case managers also rated study participants' functional outcomes as improved on the psychosocial function scale of the CMRS+ (see Table 3). Overall psychosocial function improved from a mean overall score of 36.1 prior to olanzapine treatment to a mean of 30.2 at 6 months (p = .0001). As the minimum score on the CMRS+ psychosocial function scale is 12, this change represents a 24% improvement in mean functional ability as rated by case managers. Social relationships and vocational function item scores were examined as well and were also statistically significantly improved.

DISCUSSION

These pilot data indicate substantial improvement in psychiatric symptoms and functional outcomes in patients naturalistically treated with olanzapine, case management, and psychosocial rehabilitation in a CMHC setting. While representing only a subset of the population to be analyzed in the larger project, these results alone qualify as a substantial case series of treatment of patients with psychotic disorders with olanzapine in this setting.

This case series includes 8 patients diagnosed with bipolar disorder. Seventeen percent of the sample had a diagnosis other than schizophrenia and schizoaffective disorder. This diagnostic heterogeneity reflects the population of patients receiving antipsychotic therapy. The prognosis of those disorders is generally better than for schizophrenia and may have contributed to the outcomes found for the overall sample.

A large reduction in psychiatric symptoms over 6 months of treatment was found for patients in this analysis. The BPRS as rated by treating psychiatrists and the CMRS+ illness factors scale as rated by case managers have highly consistent results, suggesting a valid finding. Improvement of this magnitude indicates a clinically rel-

evant change in psychopathology. The improvement in positive and negative symptoms is consistent with that found in previous studies.[3,12] The improvements in cognitive impairment are consistent with a double-blind trial of olanzapine, risperidone, and haloperidol.[25] Previous studies have also demonstrated improvements associated with olanzapine treatment in vocational functioning and quality-of-life measures.[3,26] The consistency of our findings with those of previous studies and the magnitude of the effects suggest that patients treated with olanzapine in a CMHC setting will achieve at least similar benefit to that found in more controlled settings, despite being diagnostically heterogeneous and including substantial comorbidities.[21,22]

We also found evidence for substantial improvements in psychosocial functioning in this case series. It is interesting to speculate how the strong improvements in disorganization, blunted affect, cognitive impairment, and substance abuse may have contributed to the functional improvements documented here. A wide range of clinical changes appears to be associated with the initiation of olanzapine with psychosocial rehabilitation, many of which could lead to synergistic interactions contributing to functional outcomes.

The improvements in substance abuse found here are the first to our knowledge associated with olanzapine treatment. However, the simultaneous delivery of specific substance abuse rehabilitation leaves the significance of this finding unclear until we can compare it with outcomes for the group of patients who remained on conventional antipsychotics. It seems likely that the improvements in negative symptoms, cognitive abilities, and social function should assist the effective delivery of substance abuse services.

The baseline point for patients who were treated with olanzapine varied and will be analyzed as part of the interpretation of the larger study's outcomes. This is of importance to the interpretation of study results since patients who start the study at a point of symptom exacerbation may be expected to demonstrate some improvement with time, regardless of treatment. This phenomenon, known as regression to the mean,[27] can lead to artificially elevated estimation of treatment effects. Improvements resulting from the natural course of illness are difficult to separate from effects of treatment that is initiated at a point of greatest symptoms. Studies that recruit patients during episodes of active illness are susceptible to this confound.

Active psychosis was not a requirement for entry into this study. In fact, there were no minimum symptom requirements, and some patients were quite stable at baseline. However, the decision to switch antipsychotic medication defined the baseline point and usually occurred when the patient was not doing well with previous treatment. These pilot data came from the first patients who tried taking olanzapine in this CMHC and could be overrepresented with patients who were doing particularly poorly on previous treatment. However, side effects such as tardive dyskinesia or extrapyramidal symptoms were the primary reasons many patients chose to switch to olanzapine, reasons that would be less likely to elevate baseline symptom measures. Baseline disease status measures will allow us to control for regression to the mean in the larger study analysis.

The vast majority of the patients who entered this study had already been in treatment at this CMHC with access to psychosocial rehabilitation for some time. Most were also taking antipsychotic medication at the baseline point. Therefore, the outcomes reported here are not merely due to new onset of treatment for most patients. Ongoing psychosocial rehabilitation may be exerting a positive influence on outcomes over time. Some patients may have become more able to access psychosocial rehabilitation after switching to olanzapine and may have started using services for the first time during the study period. The decision to participate in rehabilitation was based entirely in clinical care and was not controlled in this study.

Patients were entered into this study when an olanzapine prescription was initiated, regardless of whether the previous antipsychotic was discontinued. Many patients had an overlap between their previous antipsychotic and olanzapine treatment, and some had olanzapine prescribed as augmentation of previous antipsychotic medication. There was no restriction on prescription of additional medications such as mood stabilizers, antidepressants, or benzodiazepines. Therefore, some patients in this analysis were taking medications besides olanzapine that could have contributed to their outcomes at 6 months.

All these variables are being tracked in the larger study, and we will be able to control for their effects when doing the final analyses. As those analyses are beyond the scope of this preliminary evaluation, we must keep in mind that there are many variables associated with being in this study group besides olanzapine treatment that could have contributed to the robustly positive outcomes. In total, however, this case series indicates that the combination of olanzapine with case management and psychosocial rehabilitation results in improved outcomes over time.

The larger study will also include parallel data from a group of patients who continued on conventional antipsychotics, but who had access to the same case management and rehabilitation treatments. Inclusion of this comparison group will allow for estimation of the amount of improvement that may be due to differences in medication effects rather than the rehabilitative treatments. We hypothesize that overall outcomes will be better with olanzapine treatment plus rehabilitation than with either conventional antipsychotics plus rehabilitation or olanzapine without rehabilitation as studied elsewhere.[3] Should the final study data be consistent with this hypothesis, an experimental trial of combined olanzapine and rehabilitation treatment would be in order.

CONCLUSION

Patients treated with olanzapine are showing promising symptom reductions and improved functional abilities in the context of well-organized case management and psychosocial rehabilitation. These findings suggest that data from the efficacy studies of olanzapine will generalize to the CMHC setting. Data on the group of patients treated with conventional antipsychotics are needed to gauge the significance of these pilot findings relative to other antipsychotics and to evaluate the relationship between olanzapine's effects and rehabilitation treatments.

Drug names: haloperidol (Haldol and others), olanzapine (Zyprexa), risperidone (Risperdal).

Disclosure of off-label usage: The authors of this article have determined that, to the best of their clinical estimation, the following agent mentioned in this article is not approved for treatment of bipolar disorder, depression, and obsessive-compulsive disorder: olanzapine.

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