An Efficacy Analysis of Olanzapine Treatment Data in Schizophrenia Patients With Catatonic Signs and Symptoms

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Thirty-five patients suffering from schizophrenia, as diagnosed by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, were preselected from 7 clinical trials according to a priori criteria of catatonic signs and symptoms based on 3 Positive and Negative Syndrome Scale (PANSS) items: scores for PANSS item 19 (mannerism and posturing) and either item 4 (excitement) or item 21 (motor retardation) had to exceed or equal 4 at baseline. This particular patient population represents a severely psychotic sample: mean ± SD PANSS total scores at baseline were 129.26 ± 19.76. After 1 week of olanzapine treatment, mean PANSS total score was decreased significantly (–13.14; $p < .001$), as was mean PANSS total score after 6 weeks of olanzapine treatment (–45.16; $p < .001$); additionally, the positive subscale, negative subscale, and mood scores improved significantly. A significant improvement in the catatonic signs and symptoms composite score was also observed at week 6 (–4.96; $p < .001$). The mean ± SD daily dose of olanzapine was 18.00 ± 2.89 mg after 6 weeks of treatment. The present data analysis suggests the efficacy of olanzapine in the treatment of severely ill schizophrenic patients with nonspecified catatonic signs and symptoms.
(J Clin Psychiatry 2001;62[suppl 2]:25–27)

The manifestation of motor symptoms in psychotic diseases is traditionally described under the term catatonia.[1] In the past 30 years, catatonia seems to have disappeared from Western clinical practice.[2] Transcultural studies suggest that the catatonic subtype of schizophrenia is more frequent among patients of Asian descent even if they live in Western countries.[3] Systematic investigations published in the past 10 years[4–7] have found that 7% to 10% of patients suffering from acute psychotic diseases have catatonic signs and symptoms. An even higher frequency of catatonic symptoms was reported in affective disorders (20% in depression and 31% in mania).[8,9]

A specific feature of the treatment of catatonic schizophrenia is the importance of the administration of benzodiazepines. Numerous case reports and 3 prospective trials have reported the effect of adjunct treatment with lorazepam and clonazepam on catatonic symptoms.[4,10–12] In a recent report of a randomized, placebo-controlled trial, lorazepam failed to show effects on the acute and chronic catatonic signs and symptoms.[13]

The purpose of the present analysis was to investigate the efficacy of the new atypical antipsychotic compound olanzapine in a specific patient population suffering from significant catatonic signs and symptoms.

METHOD

Data from patients meeting entry criteria were used in this 6-week efficacy analysis. The data from the 35 patients were collected from 7 different open-label and double-blind clinical trials from the Eli Lilly Regional Medical Center Database. Patients were recruited in Eastern European and some Middle Eastern countries. All patients in the original clinical trials had provided signed informed consent to the studies. Male and female patients with the following criteria were included in the statistical analysis: diagnosis of schizophrenia according to DSM-IV, age of 18 to 60 years, and meeting a priori defined criteria of catatonic signs and symptoms (scores for Positive and Negative Syndrome Scale [PANSS] items 19 [mannerism and posturing] and either item 4 [excitement] or item 21 [motor retardation] had to exceed or equal 4 at baseline). The common outcome measures of the trials were the PANSS total score and subscores.

For the PANSS total score and the subscores, the changes from baseline to 1, 2, 4, and 6 weeks were assessed using the paired t test. However, when it was concluded that the data did not follow a normal distribution (Shapiro-Wilk test), the Wilcoxon signed rank test was performed.

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Supported by an unrestricted grant from Eli Lilly and Company.
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Table 1. Change in PANSS Total Score and Subscores and BPRS Total Score From Baseline to Weeks 1, 2, 4, and 6[a]

	PANSS				BPRS
		Subscore			
Week	Total Score	Positive	Negative	Mood	Total Score
1	–13.14	–3.06	–3.54	–1.40	–8.06
2	–26.19	–6.42	–6.96	–2.19	–15.46
4	–42.86	–10.23	–11.54	–3.64	–24.73
6	–45.16	–10.80	–11.64	–3.68	–25.64

[a]Abbreviations: BPRS = Brief Psychiatric Rating Scale, PANSS = Positive and Negative Syndrome Scale.

RESULTS

Data from 35 patients were analyzed. The mean ± SD age of patients was 36.47 ± 11.24 years. Men were predominantly represented in the sample: data from 23 men and 12 women were analyzed. The mean ± SD ages of men and women were 32.9 ± 9.5 years and 43.3 ± 11.5 years, respectively. All 35 patients were analyzed 1 week after baseline. Twenty-six patients were analyzed 2 weeks after baseline, 22 were analyzed 4 weeks after baseline, and 25 were analyzed 6 weeks after baseline. The mean ± SD PANSS total score at baseline was 129.26 ± 19.76. The mean ± SD PANSS subscores were as follows: positive subscale, 29.97 ± 7.66; negative subscale, 34.57 ± 8.23; and mood, 10.54 ± 3.83. Mean ± SD Brief Psychiatric Rating Scale (BPRS) total score, extracted from the PANSS, was 52.11 ± 11.41 at baseline.

After 6 weeks of treatment, the mean ± SD PANSS and BPRS total scores decreased to 85.56 ± 30.14 and 26.6 ± 16.5, respectively. The weekly changes in PANSS total score from baseline were –13.14 ($p < .001$), –26.19 ($p < .001$), –42.86 ($p < .001$), and –45.16 ($p < .001$) after 1, 2, 4, and 6 weeks, respectively (Wilcoxon signed rank test). A similar trend of changes was detected in the PANSS positive subscale, negative subscale, and mood scores and in the BPRS total score (Table 1).

The mean ± SD composite score of catatonic signs and symptoms (consisting of posturing and mannerism [item 19] plus excitement [item 4] and motor retardation [item 21]) was 12.80 ± 1.97 at baseline and decreased significantly to 7.96 ± 3.28 for week 6 ($p < .001$).

Across the different dose-scheduling trials, after 6 weeks of treatment, the mean ± SD dose of olanzapine was 18.00 ± 2.89 mg/day.

DISCUSSION

Data from 35 hospitalized schizophrenic patients from 7 different clinical trials were analyzed. Patients were selected according to our a priori defined criteria of potential catatonic signs and symptoms. The mean PANSS total score (129.26) reflects the fact that this particular patient population was severely ill.

Our data show the effect of olanzapine on a severely ill schizophrenic patient population, characterized by at least moderately severe posturing and mannerism and at least moderate excitement or motor retardation. There is no specific consensus on which and how many motor signs and symptoms constitute a catatonic syndrome or how many clinically distinguishable distinct catatonic syndromes exist.[4,14–16] In sampling populations that were culturally quite different, we used a global approach for the assessment of catatonic signs and symptoms based on the 3 motor symptom items of the PANSS.

This particular patient population was free from any significant benzodiazepine treatment during the study (since all benzodiazepine use was excluded from the trial), with the exception of limited use of short-acting sleep inducers. Our data suggest that this specific, severely ill patient population received significant benefit from olanzapine treatment: PANSS total scores decreased clinically significantly after 2 weeks of treatment until the endpoint of the acute data analysis (after 6 weeks, mean PANSS total score had decreased by 45.16). In all psychopathologic clusters (positive, negative, and mood subscores), 6 weeks of olanzapine treatment had a clinically and statistically significant benefit (–10.80, –11.64, and –3.68, respectively; $p < .001$). Significant improvement was also observed in the a priori defined catatonic signs and symptoms subscore: the mean ± SD change from baseline to week 6 was –4.96 ± 3.53 ($p < .001$).

The present analysis showed the efficacy of olanzapine in the treatment of schizophrenic patients with nonspecified catatonic signs and symptoms. Several classic authors emphasize that catatonic patients must be observed in different situations over a long period of time to get a clear picture of the range and severity of catatonia.[1,17–19]

Controlled clinical trials are needed to compare olanzapine with other antipsychotics in the treatment of patients with catatonic signs and symptoms. Further clinical trials are also needed with atypical antipsychotic compounds to specify the pharmacologic effect on a wide range of catatonic signs and symptoms as measured by specifically designed scales (e.g., the Bush-Francis Catatonia Rating Scale[15] or the more comprehensive Modified Rogers Scale[20]).

Drug names: clonazepam (Klonopin and others), lorazepam (Ativan and others), olanzapine (Zyprexa).

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