Metabolic Syndrome in Patients Enrolled in a Clinical Trial of Aripiprazole in the Maintenance Treatment of Bipolar I Disorder: A Post Hoc Analysis of a Randomized, Double-Blind, Placebo-Controlled Trial

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Objective: To compare the effects of maintenance treatment with aripiprazole or placebo on the incidence of metabolic syndrome in bipolar disorder.

Method: Patients with *DSM-IV* bipolar I disorder were stabilized on aripiprazole therapy for 6–18 weeks prior to double-blind random assignment to aripiprazole or placebo for 26 weeks. The rate of metabolic syndrome in each group was calculated at maintenance phase baseline (randomization) and endpoint for evaluable patients using a last-observation-carried-forward (LOCF) approach. Metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III criteria. The study was conducted from March 2000 to June 2003 at 76 centers in Argentina, Mexico, and the United States.

Results: At entry into the maintenance phase, 45/125 patients (36.0%) overall met criteria for metabolic syndrome. Mean changes in the 5 components of metabolic syndrome (waist circumference, triglyceride levels, high-density lipoprotein cholesterol level, blood pressure, and glucose level) from baseline to week 26 were small except for a meaningful reduction in triglycerides (placebo –18.9 mg/dL; aripiprazole –11.5 mg/dL). By the end of the maintenance phase (endpoint, LOCF), 5/18 placebo-treated patients (27.8%) and 4/14 aripiprazole-treated patients (28.6%) no longer met metabolic syndrome criteria. The proportion of patients with metabolic syndrome was similar in the placebo and aripiprazole groups at both baseline and week 26. There were no significant changes in any of the individual components of metabolic syndrome between aripiprazole- and placebo-treated patients during maintenance phase treatment.

Conclusions: The prevalence of metabolic syndrome in patients with bipolar disorder is higher than that commonly reported in the general population. The effect of 26 weeks of treatment with aripiprazole on the incidence of metabolic syndrome and its components was similar to placebo.

Trial Registration: clinicaltrials.gov Identifier: NCT00036348

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Individuals with major mental disorders are at high risk for morbidity and mortality, with cardiovascular (CV) disease as a primary contributor.[1] In fact, psychiatric inpatients and outpatients treated within the public sector die 25–30 years earlier than the general population.[2] Clustering of CV risk factors, such as abdominal obesity, hyperglycemia, dyslipidemia, and hypertension, is described as *metabolic syndrome* according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)[3] expert panel criteria, and it confers substantial CV risk above that of the simple arithmetic sum of the individual risk factors.[4]

Recent literature shows a higher prevalence of metabolic syndrome in patients with bipolar disorder than that expected for age- and gender-matched controls in the general population.[5,6] For example, the prevalence of metabolic syndrome in 194 Spanish patients was 60% higher than in controls, while a report from the Veterans Administration System showed that 49% of patients met the criteria for metabolic syndrome.[7] In both studies, low levels of high-density lipoprotein (HDL)-cholesterol (HDL-C), abdominal obesity, and hypertriglyceridemia were particularly common. Indeed, obesity is more prevalent in bipolar disorder than the general population[6,8] and is associated with a worse prognosis[9] and a history of attempted suicide.[6] Patients with bipolar disorder frequently present with considerable additional medical burden[9] yet are less likely to receive adequate care for CV-related conditions[10,11] and face substantial difficulties when accessing medical care.[12] As a result, implementation of programs to reduce the incidence of metabolic syndrome is likely to be more difficult in patients with bipolar disorder than in the general population.[6] Minimizing metabolic risks associated with psychotropic treatment in patients with bipolar disorder is, therefore, an important clinical priority.

Recently, there has been increasing interest in the use of atypical antipsychotics for bipolar disorder, but some atypical antipsychotics increase CV risk factors, while others may not.[13,14] In a recent study evaluating the prevalence of metabolic syndrome in 125 patients with bipolar disorder who had received at least 3 months' treatment with atypical antipsychotics (quetiapine, risperidone, or olanzapine), mood stabilizers, or a combination of atypical antipsychotics and mood stabilizers, 32% of patients met NCEP ATP III criteria for metabolic syndrome.[15] The rate of metabolic syndrome

was significantly higher in patients receiving atypical antipsychotics alone, or in combination with mood stabilizers, compared with patients receiving mood stabilizers alone.

Furthermore, atypical antipsychotic use contributes to the increased prevalence of obesity among patients with bipolar disorder.[6] Aripiprazole is pharmacologically distinct from other atypical antipsychotics[16,17] and thus represents an agent with a low potential for weight gain, diabetes risk, or a worsening lipid profile.[18] Moreover, aripiprazole is not associated with significant changes in body weight or other metabolic parameters compared with placebo in patients with bipolar disorder.[19–21] The safety and efficacy of aripiprazole for the treatment of bipolar disorder have been demonstrated in short- and longer-term studies.[19,21,22] Recently, a double-blind, placebo-controlled, 26-week study showed that aripiprazole was superior to placebo in delaying the time to relapse of a mood episode and reducing the number of relapses in patients with bipolar I disorder with a recent manic or mixed episode.[20]

To our knowledge, previous registration trials of atypical antipsychotics have not evaluated the incidence of metabolic syndrome during maintenance phase treatment of bipolar disorder. The present analysis is believed to be the first to estimate the rate of metabolic syndrome and its individual components over long-term use with any atypical antipsychotic monotherapy versus placebo. The objectives of the current analyses were to investigate further the prevalence (ie, the number of cases in a population at a given time) and incidence (the number of new cases over time) of metabolic syndrome in patients with bipolar I disorder and to test whether aripiprazole differentially affects the risk for developing metabolic syndrome and its individual component items over 26 weeks of maintenance treatment.

METHOD

Study Design

The current analysis to assess the prevalence and incidence of metabolic syndrome and its components uses data collected during a previously reported 26-week, randomized, double-blind, parallel-group, placebo-controlled aripiprazole study in patients with bipolar I disorder conducted from March 2000 to June 2003 at 76 centers in Argentina, Mexico, and the United States.[20]

After stabilization (Young Mania Rating Scale[23] total score ≤ 10 and a Montgomery-Asberg Depression Rating Scale[24] total score ≤ 13 during 4 consecutive visits over a minimum of 6 weeks) with open-label aripiprazole (15 or 30 mg/d), patients were eligible for entry into the double-blind phase of the study. Patients were randomly assigned (1:1) to receive either the aripiprazole dose they had been taking at the end of stabilization or placebo for an initial 26-week treatment period, the results of which have been reported elsewhere.[20]

All study sites received prior institutional review board/institutional ethics committee approval before study initiation, and all patients provided written informed consent.

Patients

Participants met the criteria for bipolar I disorder according to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition,[25] with diagnoses being performed using the Structured Clinical Interview for *DSM*[26] or the Mini-International Neuropsychiatric Interview (MINI).[27] Details of the inclusion and exclusion criteria are available in the publication of the first 26-week double-blind phase.[20] Briefly, patients were eligible for entry into the stabilization phase of the study if they had either recently completed a 3-week, placebo-controlled acute mania study of aripiprazole, if they met eligibility criteria for an acute mania study but had declined participation, or if they had experienced a manic or mixed episode requiring hospitalization and treatment within the previous 3 months. All psychotropic medications, except lorazepam and anticholinergic agents, were discontinued prior to enrollment.

Efficacy Measures and Analyses

The primary efficacy endpoint of the original study was the time to relapse for a mood episode (manic, depressive, or mixed) during the initial 26-week, double-blind treatment period[20] and the 74-week, double-blind extension phase.[28] Time to relapse was defined as discontinuation due to lack of efficacy.

The current analysis assessed the prevalence of metabolic syndrome and each of its components at maintenance phase baseline (randomization) and at week 26 in evaluable patients who had metabolic measures for all 5 criteria for metabolic syndrome (last-observation-carried-forward [LOCF] analysis). Patients who were rolled over from a previous aripiprazole study did not have full results recorded across all metabolic syndrome criteria. Metabolic syndrome was defined according to the NCEP ATP III definition[29] as meeting at least 3 of the following 5 criteria: waist circumference > 102 cm (men) or > 88 cm (women); triglycerides ≥ 150 mg/dL; HDL-C < 40 mg/dL (men) or < 50 mg/dL (women); systolic blood pressure (BP) ≥ 130 mm Hg and diastolic BP ≥ 85 mm Hg; blood glucose ≥ 100 mg/dL. Blood samples for determination of serum triglycerides, HDL-C, and blood glucose were collected from combined fasting and nonfasting patients. Supine systolic and diastolic measurements were used for the analysis. Waist circumference was measured at minimal respiration at the smallest circumference of the waist (the "natural" waistline); data on waist circumference were not systematically collected after week 26. Mean change in weight and body mass index (BMI) was also measured.

Dosing Schedule

Study medication was administered orally, once daily, at approximately the same time each day. During the stabilization phase, patients received open-label treatment with aripiprazole at a starting dose of 30 mg/d. The dose could be decreased to 15 mg/d at any time, depending on tolerability. After entry into the double-blind phase of the study, patients were assigned, in a double-blind manner, to continue the

dose of aripiprazole that they had been taking at the end of the stabilization phase or to receive placebo. Based on the investigator's assessment of therapeutic effect and tolerability, the dose of aripiprazole could be increased to 30 mg/d or decreased to 15 mg/d at any time during the study.

Statistical Analysis

The effects of aripiprazole and placebo on the incidence of metabolic syndrome and its components were compared using the Fisher exact test on 2×2 frequency tables of metabolic syndrome absent/present, or component value normal/abnormal, as applicable. Mean change from baseline in the components of metabolic syndrome was evaluated using analysis of covariance with treatment as main effect and baseline component value as covariate. A P value of $\leq .05$ was considered to be statistically significant. Analyses were performed on LOCF data. For the determination of metabolic syndrome status, the last available observation for each of the 5 components was selected. Therefore, the 5 components used for evaluation may not necessarily have been measured at the same time point.

RESULTS

Patient Disposition and Baseline Characteristics

A total of 567 patients entered the stabilization phase of this study, of whom 206 patients completed the stabilization phase and 161 entered the double-blind phase and were randomly assigned to placebo (n = 83) or aripiprazole (either 15 or 30 mg) (n = 78). In total, 67 patients completed the initial 26-week, double-blind period. Details of patient disposition during stabilization and the initial 26-week, double-blind phase of the study[20] have been described previously, as have the baseline characteristics of patients randomly assigned to double-blind treatment.[20] Demographic characteristics among the 125 patients who had metabolic syndrome criteria evaluable at maintenance phase baseline were similar between those patients in the placebo and those in the aripiprazole groups: mean ± SD age: 40.8 ± 10.7 vs 38.2 ± 12.8 years; female: (73% vs 66%). In the placebo group, 21% were experiencing a mixed state as the index episode, and 79% were experiencing an index episode of mania, while in the aripiprazole group these values were 40% and 60%, respectively. The proportion of patients with rapid-cycling in the placebo group was 13% and in the aripiprazole group was 21%. The majority of patients in either group were white (placebo = 63%; aripiprazole = 64%). This analysis presents, for the first time, the baseline rates of metabolic syndrome and the 5 individual components of the metabolic syndrome among patients stabilized on aripiprazole monotherapy for 6–18 weeks. At maintenance phase baseline (randomization), metabolic syndrome was present in 38.8% of patients randomly assigned to placebo and 32.8% of patients assigned to aripiprazole, giving an overall prevalence of 36.0%. Examination of the prevalence of metabolic syndrome among the subgroup of patients who did not have prior aripiprazole exposure, ie, *de novo* patients (n = 59), showed no difference from the population of rollover patients with prior aripiprazole use (n = 51) (metabolic syndrome rate: *de novo* [n = 22/59], 37.3%; rollover from prior aripiprazole use [n = 19/51], 37.3%). Also, at maintenance phase baseline, the mean (SD) values of glucose, triglycerides, HDL-C, blood pressure, and waist circumference were similar in the patients randomly assigned to placebo and those assigned to the aripiprazole group. The mean values were generally at or above the threshold for abnormal values. Patients in both groups had a mean duration of prior aripiprazole exposure of approximately 14 weeks (Table 1).

Table 1. Metabolic Parameters at Maintenance Phase Baseline

Parameter	Placebo (n = 67)	Aripiprazole (n = 58)
Metabolic syndrome present, n (%)	26 (38.8)	19 (32.8)
Metabolic syndrome absent, n (%)	41 (61.2)	39 (67.2)
Duration of prior aripiprazole, mean (SD), d	96.3 (31.3)	101.0 (43.4)
Combined fasting and nonfasting glucose, mean (SD), mg/dL	95.2 (29.6)	91.1 (18.6)
Combined fasting and nonfasting triglycerides, mean (SD), mg/dL	158.5 (133.4)	152.1 (98.8)
Combined fasting and nonfasting HDL-C, mean (SD), mg/dL	52.9 (20.4)	47.0 (14.0)
Supine systolic BP, mean (SD), mm Hg	117.3 (13.0)	118.6 (12.4)
Supine diastolic BP, mean (SD), mm Hg	74.3 (9.3)	73.4 (9.3)
Waist circumference, mean (SD), cm	98.2 (20.0)	101.4 (17.0)

Abbreviations: BP = blood pressure; HDL-C = high-density lipoprotein cholesterol.

Mean Change From Baseline in Components of Metabolic Syndrome

At baseline (entry into 26-week double-blind treatment), 125 patients had data available for all 5 metabolic syndrome criteria, and 94 patients also had evaluable data on the 5 components of metabolic syndrome at endpoint (placebo n = 49; aripiprazole n = 45). The least squares mean change from baseline to week 26 in each of the 5 components of metabolic syndrome is shown in Figure 1. Most of the changes that occurred over this time period were minimal. The largest change was seen in triglyceride levels, with a decrease of –18.9 mg/dL in the placebo group and –11.5 mg/dL in the aripiprazole group. Glucose levels showed the second largest change, with a decrease of –0.4 mg/dL in the placebo group and an increase of 4.1 mg/dL in the aripiprazole group (Figure 1).

In addition to the mean change in components of metabolic syndrome, the mean change in weight and BMI was also calculated. Small changes in weight from baseline to endpoint were seen in both the placebo (mean [SD] baseline = 88.1 [25.3] kg; least squares mean change ± SE at endpoint = –1.9 ± 1.1 kg) and aripiprazole groups (baseline = 84.1 [20.4] kg; endpoint = +0.3 ± 1.1 kg, $P = .147$). Similarly, minimal changes in BMI from baseline to endpoint were seen with placebo (baseline = 30.8 [8.3] kg/m^2; endpoint = –0.9 ± 0.4 kg/m^2) or aripiprazole (baseline = 30.9 [7.4] kg/m^2; endpoint = +0.1 ± 0.4 kg/m^2, $P = .110$).

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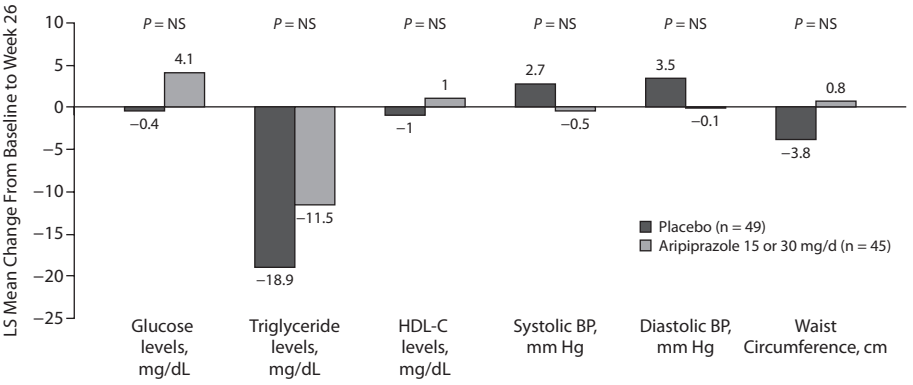
Metabolic Syndrome Status During Double-Blind Treatment

The percentages of patients who met the criteria for metabolic syndrome at week 26 stratified by the presence/absence of metabolic syndrome at maintenance phase baseline are shown in Figure 2.

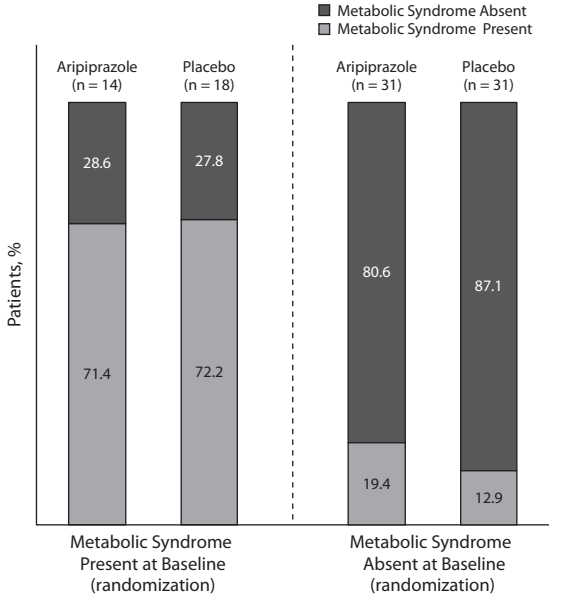
Of the patients who had metabolic syndrome at baseline (aripiprazole, 14/45; placebo, 18/49), the majority still met criteria for the syndrome at week 26 (aripiprazole, 10/14; 71.4%; placebo, 13/18, 72.2%, $P > .99$). Metabolic syndrome had resolved in 5/18 patients (27.8%) in the placebo group and 4/14 patients (28.6%) in the aripiprazole group (Figure 2). Among the patients who did not have metabolic syndrome at baseline (aripiprazole, 31/45; placebo, 31/49), the majority still did not have metabolic syndrome at week 26. A small proportion of patients had developed metabolic syndrome (aripiprazole, 6/31 [19.4%]; placebo, 4/31 [12.9%], $P = .73$; Figure 2).

Figure 1. Mean Change From Maintenance Phase Baseline to Week 26 in the Components of the Metabolic Syndrome[a,b]



[a]Mean ± SD baseline values for aripiprazole vs placebo were as follows: glucose levels = 90.4 ± 19.7 vs 95.4 ± 32.4 mg/dL; triglyceride levels = 139.3 ± 74.2 vs 164.1 ± 148.3 mg/dL; high-density lipoprotein cholesterol (HDL-C) levels = 49.7 ± 14.4 vs 52.7 ± 21.7 mg/dL; systolic blood pressure = 118.5 ± 13.1 vs 117.6 ± 13.4 mm Hg; diastolic blood pressure = 72.6 ± 9.8 vs 73.6 ± 9.9 mm Hg; waist circumference = 99.3 ± 14.8 vs 100.4 ± 22.0 cm. [b]Last-observation-carried-forward data set.
Abbreviations: LS = least squares, NS = not significant.

Figure 2. Incidence of Metabolic Syndrome at Maintenance Phase Endpoint (week 26), Stratified by the Presence/Absence of Metabolic Syndrome at Maintenance Phase Baseline (randomization)[a]



[a]Last-observation-carried-forward data set.

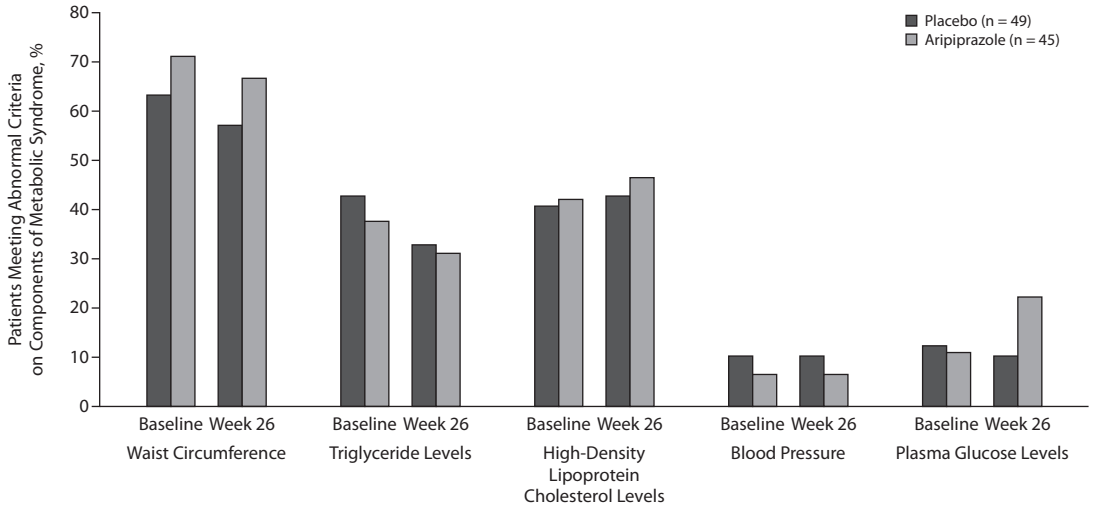
Proportion of Patients Who Met Abnormal Criteria on Each of the 5 Components

The proportion of patients meeting criteria for each of the different components of metabolic syndrome (waist circumference > 102 cm [men] or > 88 cm [women]; triglycerides ≥ 150 mg/dL; HDL-C < 40 mg/dL [men] or < 50 mg/dL [women]; systolic BP ≥ 130 mm Hg and diastolic BP ≥ 85 mm Hg; blood glucose ≥ 100 mg/dL) was similar for both aripiprazole and placebo at randomization and at week 26 (Figure 3). At all time points and regardless of treatment assignment, a greater proportion of patients met the criteria for high waist circumference, high triglyceride levels, or low HDL-C levels than for high glucose levels or high BP (Figure 3).

DISCUSSION

Analysis of data from this long-term, multicenter, randomized study investigating the safety and efficacy of aripiprazole as monotherapy in patients with bipolar I disorder suggests that the prevalence of metabolic syndrome in patients with bipolar I disorder is higher than observed in the general population; 36% of patients with bipolar I disorder entered the maintenance phase of this study with metabolic syndrome compared to 20% of adults in a similar age group in the US population.[30] The rate of metabolic syndrome at baseline did not differ for patients without prior aripiprazole exposure enrolled *de novo* (37.2%) or those patients who were rolled over from a previous aripiprazole study (37.3%). Thus, prior involvement in a clinical trial and potential treatment with aripiprazole was not expected to affect the outcomes of the analyses presented herein. Given that metabolic syndrome is associated with a 2- to 3-fold increased risk of mortality due to coronary heart disease[4,31] and a 7-fold risk of developing type 2 diabetes,[32] the increased prevalence of metabolic syndrome is a particular cause for concern in those with bipolar disorder who are already at increased risk of medical morbidity and mortality versus the general population.[33] Furthermore, in addition to significantly increasing the risk for CV disease, metabolic syndrome (or at least some of its components) has been associated with worsened psychiatric

Figure 3. Prevalence of Each of the 5 Components of Metabolic Syndrome in Patients With Bipolar I Disorder at Randomization and Week 26[a]



[a]Last-observation-carried-forward data set.

outcomes, including a greater likelihood of attempted suicide.[6]

Results of this analysis also showed that treatment with aripiprazole can be used both short- and longer-term without compromising the metabolic status of patients with bipolar disorder. After 26 weeks of treatment with aripiprazole, resolution of the metabolic syndrome occurred in almost 30% of patients who initially met criteria for this disorder at baseline. Furthermore, the likelihood of developing new-onset metabolic syndrome during maintenance phase treatment was low and not significantly different from that of placebo. If any signal for improvement or worsening of metabolic syndrome is to be identified, it will likely come from a population that is sufficiently enriched for the risk factors under study, while in this trial 36% of patients met criteria for metabolic syndrome on entry into the maintenance phase. Reversal of metabolic syndrome has previously been observed in a small case series evaluation of patients with schizophrenia following 3 months of treatment with aripiprazole.[34] A larger, randomized trial of 173 overweight subjects with schizophrenia treated with olanzapine found that switching to treatment with aripiprazole for 16 weeks resulted in significant reductions in body weight, triglyceride levels, total cholesterol levels, and HDL-C levels.[35] Taken together, these observations suggest that there is a low risk of metabolic compromise associated with aripiprazole treatment in patients with bipolar disorder, consistent with long-term studies of aripiprazole in patients with schizophrenia.[36,37]

Of the 5 components of metabolic syndrome, waist circumference, HDL-C levels, and triglyceride levels had the highest proportion of abnormalities in both the aripiprazole and placebo groups at randomization as well as at week 26. The effect of 26 weeks of treatment with aripiprazole on the components of metabolic syndrome was also similar to placebo. Criteria for abdominal obesity, as measured by waist circumference, were met by over 60% of patients and consistently demonstrated the highest prevalence of the 5 components of metabolic syndrome, suggesting that measurement of waist circumference is a practical means for assessing metabolic risk in patients with bipolar disorder. This finding is in agreement with a study investigating the most clinically useful and cost-effective screening methods for metabolic syndrome, which showed that the presence of abdominal obesity was the most sensitive measure for detecting metabolic syndrome.[38] Thus, measuring body weight and/or waist circumference may provide the best and easiest method for evaluating metabolic health. The incidence of clinically significant weight gain in the population studied herein has previously been reported: 7 of 56 patients in the aripiprazole group and no patients in the placebo groups showed ≥ 7% weight gain.[20] The 7 patients showing clinically significant weight gain were distributed across BMI categories. The pragmatic utility of screening for abdominal obesity is underscored by recent evidence suggesting that, even among normal-weight individuals, an enlarged waist circumference indicates a worrisome level of underlying cardiometabolic abnormalities.[39]

Given the high prevalence of metabolic syndrome and the high levels of each of the individual component items at baseline, the findings of the present study suggest an urgent need for appropriate monitoring of metabolic health in patients with bipolar disorder to enable early intervention and, expectantly, a reduction in medical morbidity. Ideally, intervention should involve the provision of diet and exercise counseling to all patients with bipolar disorder, before the components of metabolic syndrome become evident and certainly once they are evident.[6] Despite uniform agreement that monitoring for metabolic syndrome is a necessary facet of clinical care, less than 20% of public mental health patients receive baseline glucose testing when atypical antipsychotics are initiated, and less than 10% receive baseline

lipid testing.[40] Even after the publication of highly cited guidelines for improving the standard of care for managing metabolic risk, routine cardiometabolic monitoring has only marginally improved.[41]

Until recently there has been a paucity of data on the effects of atypical antipsychotics on metabolic syndrome in patients with bipolar disorder. In 2004, when guidelines for metabolic risk monitoring were jointly published by the American Psychiatric Association and the American Diabetes Association, relatively limited epidemiologic data were available on aripiprazole and ziprasidone, the 2 atypical antipsychotics regarded as having the least risk of weight gain or other metabolic problems.[18] Nearly 5 years later, there remain no long-term clinical trial data available on metabolic syndrome with ziprasidone in the treatment of bipolar disorder.

The long-term metabolic effects of antipsychotic use among patients with bipolar disorder have not been well documented; thus, the present data provide a valuable evidence base to help guide clinical decision-making. However, the findings of this analysis should be considered in light of several limitations. First, while this study enrolled a significant number of patients into the stabilization phase of this study (n = 567), data on metabolic status were missing for some of the patients who were rolled over from previous aripiprazole studies. Thus, while the mean exposure to aripiprazole (14 weeks) was similar for both the placebo and aripiprazole groups, we cannot with certainty account for any potential effect of being rolled over into this study from another aripiprazole clinical trial. Nevertheless, the rate of metabolic syndrome on entry into the maintenance phase was similar both for patients who had previously received aripiprazole in another study and for patients entering de novo. The metabolic effects of aripiprazole in patients with bipolar II disorder cannot be assessed, as these patients were excluded from participation. Likewise, we cannot determine whether index episode influences the incidence of metabolic syndrome, as all patients were required to have experienced a recent manic or mixed episode. As this is not a true epidemiologic study, the rates of metabolic syndrome may be overestimated or underestimated. Overestimation of metabolic syndrome in both treatment arms may also have occurred from the inclusion of select samples of triglyceride and glucose levels that were nonfasting. Such laboratory values still remain clinically informative, as nonfasting triglyceride levels highly correlate with cardiovascular risk. In fact, triglyceride levels measured 2–4 hours postprandially show a strong association with incident cardiovascular events.[42,43] It should be understood that this study was originally designed as a maintenance trial with time to relapse into a mood episode as the primary outcome measure. Rates of metabolic syndrome and the individual component items of metabolic syndrome were assessed as post hoc analyses. Thus, the study was neither designed nor powered to detect differences in the prevalence of metabolic syndrome between treatments. An additional limitation includes the potential for variation in the manner by which waist circumference was measured by study personnel. Thus, these analyses should still be considered exploratory. Additional data characterizing metabolic health outcomes beyond 26 weeks of observation would be useful. It should also be considered that the study population reported here for the 26-week double-blind phase of the study represents an enriched population of patients who responded to and were stabilized on aripiprazole treatment following a manic or mixed episode. Additional data in patients following a depressive episode may be of interest.

CONCLUSIONS

This study indicates that treatment of bipolar disorder with aripiprazole over 26 weeks does not compromise the metabolic status of this already at-risk patient group. The high prevalence of metabolic syndrome in this study population at baseline further underscores the need for appropriate monitoring of metabolic health in patients with bipolar disorder.

Drug names: aripiprazole (Abilify), lorazepam (Ativan and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal and others), ziprasidone (Geodon).

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