A Case Series: Evaluation of the Metabolic Safety of Aripiprazole

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Metabolic abnormalities occur frequently in patients treated with antipsychotics and are of growing concern to clinicians. This study sought to determine whether antipsychotic-associated metabolic abnormalities identified through intensive monitoring can be reversed by switching to aripiprazole. Recent evidence suggests that aripiprazole may exhibit a favorable metabolic safety profile. The study population is a subset of a large (n > 500) ongoing prospective cohort. Thirty-one consecutive patients with schizophrenia who were started on aripiprazole were included in the study. All patients underwent an extensive metabolic evaluation, including an oral glucose tolerance test, at baseline, at 6 weeks, and at 3 months post switch. Metabolic abnormalities were defined as any of the following: new onset diabetes, impaired fasting glucose, impaired glucose tolerance, metabolic syndrome (MetS) according to various definitions, and dyslipidemia. After 3 months of treatment with aripiprazole (mean daily dose 16.3 mg), there was a significant decrease in body weight, body mass index, and waist circumference. There was a significant reduction in fasting glucose, fasting insulin, insulin resistance index, and serum lipids levels (cholesterol, triglycerides, low-density lipoprotein (LDL), LDL/HDL, Chol/HDL, and non-HDL cholesterol). There was also a significant reduction in prolactin levels. All 7 cases of recent onset diabetes were reversed at 3 months follow-up. The MetS was reversed in 50% of patients at 3 months follow-up. Our results support the reversibility of recent onset diabetes on antipsychotic medication when detected early and followed by a switch to aripiprazole.

Key words: aripiprazole/diabetes/metabolic side effects/metabolic syndrome/schizophrenia

Introduction

Metabolic abnormalities have historically been associated with illnesses such as schizophrenia.1,2 The recent introduction of second-generation antipsychotics and their possible association with metabolic abnormalities has renewed interest in this issue.3–9

Many studies have since then provided convincing evidence for a high risk of diabetes and other glucose abnormalities, the metabolic syndrome (MetS),10–13 and mortality due to elevated cardiovascular risk in patients with schizophrenia.14–17 These metabolic abnormalities are of major clinical concern not only because of their direct somatic effects on morbidity and mortality but also because of their association with psychiatric outcome, such as a higher prevalence of psychotic and depressive symptoms, a lower functional outcome,18 a worse perceived physical health,19 and lower adherence to medication.20

Recent recommendations for physical health monitoring of patients with schizophrenia were established as a result of consensus meetings including psychiatrists and medical experts in different countries.21–26 These guidelines acknowledge differences between antipsychotic agents in their liability to induce metabolic side effects. Antipsychotics considered to have a safer metabolic profile are amisulpride, aripiprazole, and ziprasidone.27

Clinical trial data, based solely on fasting or random blood samples, support the claim of a safe metabolic profile for aripiprazole.28,29 Further, recent real-world database analyses corroborate the metabolic advantages of aripiprazole relative to other second-generation antipsychotics.30–32 However, one case of diabetic ketoacidosis was recently reported in a schizophrenic patient shortly after receiving a treatment with aripiprazole.33 This study explores the metabolic profile of aripiprazole in 31 patients who underwent an extensive metabolic follow-up including an oral glucose tolerance test (OGTT), the “golden standard” for the detection of abnormalities in glucose homeostasis.34–37 The study included 7 patients with recently detected diabetes and 6 patients...
with confirmed prediabetic abnormalities on their previous antipsychotic treatment.

Methods

At our hospital and affiliated services, consistent with international guidelines, all patients treated with antipsychotic medication (AP) are being screened and monitored prospectively for metabolic abnormalities. The vast majority of patients are part of an extensive metabolic study including OGTTs, which was started in November 2003. The study population is a dynamic, naturalistic cohort. Decisions regarding AP are made by the treating psychiatrist and the patient, including dose reduction, dose augmentation, and switch strategies. These changes are recorded, and patients are monitored for metabolic abnormalities by means of laboratory tests, OGTTs, and clinical examinations. The baseline characteristics of the first 430 included patients of this dynamic cohort are described in detail elsewhere. The inclusions are still ongoing; currently, this cohort consists of 624 subjects (status at 30/07/2006, all diagnoses). The current study sample was derived from this large, dynamic cohort, with the condition of inclusion being that patients were either newly started on aripiprazole \( n = 2 \) or switched to aripiprazole \( n = 29 \). In 13 patients, the switch to aripiprazole was motivated by treatment-emergent glucose abnormalities. The other switches were done for clinical psychiatric reasons or patients' preference. Thus, all consecutive patients with a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition diagnosis of schizophrenia or schizoaffective disorder, both out- or inpatients, switched to or started on aripiprazole, were asked to participate in an extensive metabolic screening and prospective follow-up study of their metabolic parameters. At baseline, patients received a full fasting laboratory screening (including measurements of prolactin), clinical measurements, and an electrocardiogram.

The patients were evaluated 3 times with a full metabolic screening, which included a 75-g glucose load OGTT at 3 time points: at baseline on their prior AP, 6 weeks, and 3 months after initiation of aripiprazole. Patients were initiated on an overnight fast and were monitored during the OGTT. Fasting plasma glucose and insulin measurements allow calculating an index of insulin resistance (HOMA-IR). All laboratory analyses were performed in the same laboratory.

For the diagnosis of diabetes and prediabetic abnormalities, the American Diabetes Association criteria were used: diabetes (fasting glucose \( > 125 \, \text{mg/dl} \) and/or \( > 199 \, \text{mg/dl at 2 hours in the OGTT} \)), impaired fasting glucose (IFG 100–125 mg/dl), and impaired glucose tolerance (IGT, glucose 140–199 mg/dl at 2 hours in the OGTT). The presence of the MetS was assessed using the Adult Treatment Panel (ATP)-III criteria, the adapted ATP-III criteria (American Heart Association, fasting glucose \( \geq 100 \, \text{mg/dl} \), and the recent International Diabetes Federation (IDF) criteria.

Descriptive statistics were computed for the basic demographic and clinical variables as well as for the variables relevant for the evaluation of metabolic abnormalities. The influence of treatment with aripiprazole on continuous dependent variables was calculated by means of an analysis of variance (ANOVA) with repeated measures. The association between categorical variables was evaluated by a chi-square test.

To evaluate potential differential effects of aripiprazole in patients with and without metabolic abnormalities, 2 patient groups were distinguished: patients with diabetes or prediabetes (IFG/IGT) and patients without metabolic disturbances. A group \( \times \) assessment ANOVA was performed on glucose, insulin, and lipid parameters. Second, we evaluated the differential effects of 2 treatment regimens: aripiprazole monotherapy and aripiprazole with another antipsychotic. The group \( \times \) assessment interaction was evaluated with an ANOVA on glucose, insulin, and lipid parameters.

The study was approved by an ethical committee, and all patients gave written informed consent.

Results

Thirty-one consecutive patients participated in the study. Of these, 51.6% (16) were male. All were white and Belgian natives, and 61.3% (19) were hospitalized at the start of the study. The mean age of the patients was 36.7 years (SD 14.1), the mean duration of illness was 10.2 years (SD 8.3), and the mean lifetime number of admissions was 4.8 (SD 3.0). Mean Global Assessment of Functioning score at baseline was 61.9 (SD 9.1). The studied population comprised 77.4% (24) patients with schizophrenia and 22.6% (7) with schizoaffective disorder.

All but 2 patients were treated with AP at baseline. Duration of previous antipsychotic treatment exceeded 9 months in 77.4% (24) of patients and ranged between 3 and 6 months in 22.6% (7). Prior antipsychotic and comedication are shown in table 1. At endpoint, 74.2% (23) patients were on monotherapy with aripiprazole. The mean daily dose was 16.3 mg (SD 6.9). In all, 5 patients received the highest dose of 30 mg. All patients remained clinically stable.

At baseline, mean weight was 89.2 kg (SD 18.4, range from 54 to 132 kg), mean body mass index (BMI) was 30.8 kg/m\(^2\) (SD 6.1), and mean waist circumference was 105.8 cm (SD 14.6) (female patients mean waist 103.9 cm [SD 21.2], male patients mean waist 107.6 cm [SD 15.3]). After 3 months of treatment with aripiprazole, there was a highly significant decrease in weight (endpoint 83.7 kg [SD 17.8]), BMI (endpoint 28.9 [SD 5.8]), and waist circumference (endpoint 99.7 cm [SD 15.1]; \( P < .001, \) F, respectively 35.53, 33.25, and 24.99).
During treatment with aripiprazole, there was a decrease in all glucose and insulin values in the OGTT (figure 1). Improvements were already present at week 6. At 3 months, changes from baseline were significant for all glucose values as well as glycated hemoglobin (HbA1c) (table 2). For insulin, the change was only significant on fasting insulin values as well as on HOMA-IR, a measure of insulin resistance.

The study included 7 patients with confirmed treatment-emergent diabetes on their previous antipsychotic treatment (2 identified with fasting glucose measurements and 5 meeting criteria for diabetes at 120 minutes in the OGTT) (1 patient on first-generation antipsychotics, 1 on clozapine, 1 on olanzapine, 2 on quetiapine, and 2 on risperidone). At baseline, there were also 6 patients with repeated glucose abnormalities prior to the switch (2 patients with IFG, 1 on amisulpride, and 1 on clozapine; 3 with IGT [2 on amisulpride and 1 on risperidone]; 1 with IFG/IGT on a first-generation antipsychotic). The switch to aripiprazole was done shortly after the confirmation of the glucose abnormalities.

All newly detected cases of diabetes were reversed at 3 months follow-up. Six patients had a completely normal OGTT and 1 patient still had IGT. All fasting abnormalities at baseline were absent at 3 months follow-up (table 3). Prediabetic abnormalities dropped from 19.4% at baseline to 3.2% at endpoint ($P < 0.001$). All patients with confirmed prediabetic abnormalities (IFG and/or IGT) at baseline had normal glucose values in the OGTT at endpoint.

Lipid abnormalities were highly prevalent at baseline (table 4). Five patients already received treatment with a statin, which was maintained unchanged throughout the study. After 3 months of treatment with aripiprazole, there was a significant decrease in total cholesterol levels, triglyceride levels, low-density lipoprotein (LDL) cholesterol levels, and also non–high-density lipoprotein (HDL) cholesterol and CHOL/HDL and LDL/HDL ratios (table 4). There was no change in HDL cholesterol. There was only a significant reduction in the proportion of patients with abnormal lipid values for triglycerides.

There was a significant difference in the frequency of prevalence of MetS between baseline and 3 months follow-up (table 5). Regardless of the definition of MetS used, there was roughly a 50% reduction in prevalence (in 10 patients MetS was reversed). Treatment with aripiprazole has a significant effect on the components waist circumference, glucose, blood pressure, and triglycerides.

A total of 13 patients were diagnosed with diabetes or prediabetes (IFG/IGT) at study onset. The group × assessment ANOVA revealed a significant main effect of assessment ($P < .05$) for all glucose, insulin, and lipid

### Table 1. Medication Regimes

| n = 31 | Baseline, % (n) | 3 months, % (n) |
|--------|----------------|----------------|
| Anticholinergic | 6.5 (2) | 3.2 (1) |
| Benzodiazepine | 32.3 (10) | 32.3 (10) |
| Antidepressant | 38.7 (12) | 35.5 (11) |
| Mood stabilizer | 19.3 (6) | 16.1 (5) |
| Somatic medication | 61.3 (19) | 51.6 (16) |
| Antidiabetic medication | 0 (0) | 0 (0) |
| Blood pressure lowering | 16.1 (5) | 16.1 (5) |
| Lipid-lowering medication | 16.1 (5) | 16.1 (5) |
| Antipsychotic treatment | | |
| No antipsychotic | 6.5 (2) | 0 (0) |
| First-generation antipsychotic | 6.5 (2) | 0 (0) |
| Amisulpride | 16.1 (5) | 0 (0) |
| Clozapine | 9.7 (3) | 3.2 (1) |
| Risperidone | 19.3 (6) | 3.2 (1) |
| Quetiapine | 22.6 (7) | 12.9 (4) |
| Olanzapine | 19.3 (6) | 6.5 (2) |
| Aripiprazole | 0 (0) | 100 (31) |
parameters under study except for insulin at 60 minutes and HDL. A significant main effect of group \((P < .05)\) was observed for all glucose and insulin parameters but for none of the lipid parameters. A significant group \(\times\) assessment interaction \((P < .05)\) was observed for most glucose and insulin parameters except glucose at 30 minutes, insulin at 30 and 60 minutes, and insulin area under the curve. Glucose and lipid parameters were practically stable in the patients group without metabolic abnormalities at baseline, whereas these parameters improved in patients with metabolic disturbances at study onset. For the lipid parameters, none of the group \(\times\) assessment interactions reached significance.

A total of 8 patients combined aripiprazole with another antipsychotic. The results of patients treated with aripiprazole monotherapy did not significantly differ from those of patients combining aripiprazole with another antipsychotic.

Prolactin levels dropped significantly during aripiprazole treatment from 54.9 ng/ml (SD 60.3, min 3–max 249) to 11.2 ng/ml (SD 9.9, min 0.6–max 50.9) \((F = 15.38, P < .001)\). Changes were most pronounced in patients with high baseline prolactin levels (treatment with either amisulpride or risperidone, \(F = 30.4, P < 0.001\)).

### Table 2. Glucose and Insulin Homeostasis in an OGTT

| Parameter   | Baseline, Mean \((\pm SD)\) | 3 months, Mean \((\pm SD)\) | % Change From Baseline | \(P\)  |
|-------------|-----------------------------|-----------------------------|------------------------|-------|
| FGLU (mg/dl)| 95.5 \((\pm 15.2)\)         | 87.7 \((\pm 7.6)\)          | \(-8.1\)               | 0.002 |
| GLU30 (mg/dl)| 170.0 \((\pm 38.3)\)       | 144.0 \((\pm 42.4)\)       | \(-15.0\)              | 0.001 |
| GLU60 (mg/dl)| 181.0 \((\pm 70.4)\)       | 143.7 \((\pm 46.6)\)       | \(-20.5\)              | 0.001 |
| GLU120 (mg/dl)| 125.9 \((\pm 61.5)\)      | 99.5 \((\pm 30.5)\)        | \(-21.0\)              | 0.010 |
| GAUC        | 18.4 \((\pm 5.7)\)          | 15.1 \((\pm 3.3)\)         | \(-18.1\)              | 0.001 |
| HbA1c (%)  | 5.7 \((\pm 0.5)\)           | 5.5 \((\pm 0.3)\)          | \(-3.4\)               | 0.002 |
| FINS (\(\mu\)IU/ml) | 16.9 \((\pm 18.4)\)  | 9.2 \((\pm 5.6)\)          | \(-45.4\)              | 0.007 |
| INS30 (\(\mu\)IU/ml) | 115.5 \((\pm 122.7)\)  | 76.9 \((\pm 45.9)\)        | \(-33.4\)              | 0.054 |
| INS60 (\(\mu\)IU/ml) | 159.4 \((\pm 200.8)\)  | 117.2 \((\pm 159.0)\)      | \(-26.5\)              | 0.070 |
| INS120 (\(\mu\)IU/ml) | 131.4 \((\pm 250.5)\) | 53.0 \((\pm 51.6)\)       | \(-59.6\)              | 0.062 |
| IAUC        | 14.8 \((\pm 19.6)\)         | 9.3 \((\pm 9.5)\)          | \(-31.3\)              | 0.044 |
| HOMA-IR    | 4.5 \((\pm 6.1)\)           | 2.0 \((\pm 1.3)\)          | \(-54.2\)              | 0.014 |

Note: OGTT, oral glucose tolerance test; glucose values in OGTT: FGLU, fasting; GLU30, at 30 min; GLU60, at 60 min; GLU120, at 120 min; GAUC, area under the curve. Insulin values in OGTT: FINS, fasting; INS30, at 30 min; INS60, at 60 min; INS120, at 120 min; IAUC, area under the curve; HbA1c, glycated hemoglobin; HOMA-IR, insulin resistance index.

### Table 3. Glucose Abnormalities Among Patients Receiving Aripiprazole Treatment

| Abnormality               | Baseline, \% \((n)\) | 3 months, \% \((n)\) | \(P\)  |
|---------------------------|-----------------------|----------------------|-------|
| All abnormalities         | 41.9 (13)             | 3.2 (1)              | 0.001 |
| IFG, IGT                  | 19.4 (6)              | 3.2 (1)              |       |
| Diabetes                  | 22.6 (7)              | 0 (0)                |       |
| Fasting abnormalities     | 32.3 (10)             | 0 (0)                | 0.003 |
| IFG (100–125 mg/dl)       | 25.8 (8)              | 0 (0)                |       |
| Diabetes (≥126 mg/dl)     | 6.5 (2)               | 0 (0)                |       |
| Abnormalities at 120 min in OGTT | 35.5 (11)  | 3.2 (1)              | 0.004 |
| IGT (140–199 mg/dl)       | 12.9 (4)              | 3.2 (1)              |       |
| Diabetes (≥200 mg/dl)     | 22.6 (7)              | 0 (0)                |       |

Note: IFG, impaired fasting glucose, IGT, impaired glucose tolerance, OGTT, oral glucose tolerance test.
not only be explained by the interruption of the previous antipsychotic treatment. In 7 patients with recently detected diabetes that emerged during the course of treatment with antipsychotics, diabetes was reversible after a switch to aripiprazole. In another 6 patients with confirmed prediabetic abnormalities, these abnormalities were also reversed after a switch to aripiprazole. Remarkably, this improvement occurred rather quickly, within 3 months.43

Switching to aripiprazole also resulted in an important weight loss in most patients (on average more than 5 kg and 6 cm reduction in waist circumference in 3 months time).

The prevalence of MetS, a risk factor for both diabetes and cardiovascular disease, is high in patients with schizophrenia and is at least double compared with an age-adjusted community sample.10,13 The combined effect of aripiprazole on weight/waist circumference, blood pressure, serum lipids, and glucose results in a reduction of 50% in the prevalence of MetS and could result in substantial physical health gains in the long run.44 The beneficial effect of aripiprazole was recently confirmed in an analysis of data of 4 long-term clinical trials.31

There was a significant reduction in prolactin levels, mainly due to normalizing elevated prolactin induced by the previous antipsychotic agents.45

The current data generate several possible hypotheses. First, the onset of clinically significant complications such as the MetS and diabetes may be prevented and even reversed by using an antipsychotic with a good metabolic safety profile such as aripiprazole. This, in turn, underscores the need for a more thorough metabolic screening, as suggested in the literature.37 Although such monitoring may be costly, the rate of abnormalities in the analysis suggests that early intervention may prove cost effective.34–37 Indeed, antidiabetic, antihypertensive, and lipid-lowering medication would add considerably to health care budgets, as do the complications caused by diabetes, hypercholesterolemia, and hypertension. Secondly, it can be hypothesized that aripiprazole, with its superior metabolic profile, can be used in first line as the most cost-effective option to improve and even normalize the metabolic status of patients who develop metabolic abnormalities. Third, based on the current data, one can hypothesize that adding aripiprazole to the antipsychotic treatment would also result in an amelioration of metabolic parameters and thus could be used in those patients where a switch to another antipsychotic is unwanted for psychiatric reasons such as treatment-resistant psychosis. This could be an interesting treatment option for treatment-resistant patients on clozapine, which has been shown to have a deleterious metabolic safety profile. This treatment option clearly merits further investigation.

There are several limitations to the current study. Patient recruitment was restricted to one site, which may limit the generalizability of the findings. However, the study population was drawn from a large cohort of more than 500 patients followed over more than 1 year, all from the same institution and all were subjected to the same intensive metabolic monitoring. Information on the first 430 patients of this cohort has already been published elsewhere.10

Because of the assumed metabolic advantage of aripiprazole, there was a selection bias; patients with metabolic abnormalities were more likely to be switched to or started on aripiprazole. In the larger cohort of patients in the metabolic study at our hospital, information is

### Table 4. Lipid Levels Among Patients Receiving Aripiprazole Treatment

| n = 31 | Baseline, Mean (±SD) | 3 months, Mean (±SD) | P   |
|--------|----------------------|----------------------|-----|
| **Absolute values** | | | |
| CHOL (mg/dl) | 196.0 (±33.5) | 171.5 (±34.4) | **0.001** |
| TG (mg/dl) | 192.0 (±99.3) | 132.6 (±58.2) | **0.001** |
| HDL (mg/dl) | 49.5 (±16.7) | 48.9 (±14.8) | 0.793 |
| LDL (mg/dl) | 109.2 (±32.3) | 95.3 (±29.0) | **0.002** |
| Non-HDL (mg/dl) | 146.6 (±31.0) | 122.6 (±31.1) | **0.001** |
| LDL/HDL | 2.4 (±0.8) | 2.1 (±0.9) | **0.039** |
| CHOL/HDL | 4.1 (±1.3) | 3.8 (±1.3) | **0.004** |

| % Abnormal values | Baseline, % (n) | 3 months, % (n) | P   |
|-------------------|-----------------|-----------------|-----|
| CHOL (≥190 mg/dl) | 48.4 (15) | 29.0 (9) | 0.118 |
| TG (≥150 mg/dl) | 71.0 (22) | 42.0 (13) | **0.020** |
| HDL (M < 40 mg/dl, F < 50 mg/dl) | 54.8 (17) | 51.6 (16) | 0.799 |
| LDL (≥115 mg/dl) | 32.3 (10) | 19.4 (6) | 0.246 |
| CHOL/HDL (≥4) | 54.8 (17) | 29.0 (9) | **0.039** |
| LDL/HDL (≥3) | 22.6 (7) | 16.1 (5) | 0.520 |

**Note:** CHOL, total cholesterol levels; TG, triglyceride levels; HDL, high-density lipoprotein cholesterol levels; LDL, low-density lipoprotein cholesterol levels; non-HDL, non-HDL cholesterol levels.
A further important limitation is the lack of a control group. However, except the changes in drug therapy, no significant changes in lifestyle habits were noticed throughout the study. It is likely that the observed metabolic improvements might have resulted simply from discontinuation of the previous AP. Even if this were so, it is apparent that aripiprazole does not interrupt the metabolic improvement associated with discontinuation. Also no new cases of glucose abnormalities were observed. Finally, in some cases, a metabolic improvement was observed when aripiprazole was added to another antipsychotic.

Another limitation is that the duration of the study was only 3 months, and the observed favorable evolution on metabolic parameters should be confirmed over time. However, recent database studies and a large naturalistic trial suggest that the favorable metabolic profile of aripiprazole may persist for up to 1 year.30–32 Future research should address these issues more specifically in large, multisite samples.

In conclusion, the choice of a specific antipsychotic should take into account the metabolic risk profile of a patient as well as the metabolic risk of the antipsychotic agent.23,26 When severe metabolic abnormalities emerge during treatment with an antipsychotic, a switch to an agent with a good metabolic safety profile should be considered as first treatment option if acceptable for the patient.

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Table 5. Metabolic Syndrome According to ATP-III, ATP-III A, and IDF Definitions Among Patients Receiving Aripiprazole Treatment

|               | Baseline, % (n) | 3 months, % (n) | P   |
|---------------|----------------|----------------|-----|
| **ATP-III**   |                |                |     |
| Waist (M > 102 cm, F > 88 cm) | 58.1 (18) | 29.0 (9) | **0.021** |
| BP (≥130/85 mmHg) | 71.0 (22) | 29.0 (9) | **0.001** |
| HDL (M < 40 mg/dl, F < 50 mg/dl) | 54.8 (17) | 51.6 (16) | NS   |
| TG (≥150 mg/dl) | 71.0 (22) | 42.0 (13) | **0.020** |
| Glucose (≥110 mg/dl) | 19.3 (6) | 0 (0) | **0.010** |
| **ATP-III A** |                |                |     |
| Waist (M > 102 cm, F > 88 cm) | 61.3 (19) | 29.0 (9) | **0.011** |
| BP (≥130/85 mmHg) | 71.0 (22) | 29.0 (9) | **0.001** |
| HDL (M < 40 mg/dl, F < 50 mg/dl) | 54.8 (17) | 51.6 (16) | NS   |
| TG (≥150 mg/dl) | 71.0 (22) | 42.0 (13) | **0.020** |
| Glucose (≥110 mg/dl) | 32.3 (10) | 0 (0) | **0.001** |
| **IDF MS**    |                |                |     |
| Waist (M ≥ 94 cm, F ≥ 80 cm) | 67.7 (21) | 35.5 (11) | **0.011** |
| BP (≥130/85 mmHg) | 71.0 (22) | 29.0 (9) | **0.001** |
| HDL (M < 40 mg/dl, F < 50 mg/dl) | 54.8 (17) | 51.6 (16) | NS   |
| TG (≥150 mg/dl) | 71.0 (22) | 42.0 (13) | **0.020** |
| Glucose (≥110 mg/dl) | 32.3 (10) | 0 (0) | **0.001** |

Note: ATP-III, Adult Treatment Panel; BP, blood pressure; TG, triglyceride levels; HDL, high-density lipoprotein cholesterol levels; NS, not significant.

available on another 162 patients that were recently started on a specific antipsychotic with a similar metabolic follow-up of 3 months. A preliminary analysis showed a 4.9% incidence rate of new onset diabetes within 3 months of the start of an antipsychotic (8 cases, 3 on olanzapine [n = 50, 6.0%], 2 on quetiapine [n = 24, 8.3%], 2 on clozapine [n = 18, 11.1%], 1 on risperidone [n = 47, 2.1%], and no new cases on amisulpride [also 4 cases of reversible diabetes] [n = 23, 0%]). Baseline rates before the start of the antipsychotic treatment of ATP-III MetS were lower on all other antipsychotics (amisulpride 36.4%, clozapine 29.4%, olanzapine 12%, quetiapine 16.7%, and risperidone 23.4%) compared to the baseline MetS rates of patients started on aripiprazole. Prevalence of MetS at 3 months of treatment increased substantially with clozapine (41.2%), olanzapine (30%), and quetiapine (29.2%). Prevalences of MetS remained stable on amisulpride (40.9%) and dropped slightly with risperidone (21.3%). Even with higher baseline rates of metabolic abnormalities treatment with aripiprazole did not induce new glucose abnormalities. Compared with other antipsychotics, it is the only agent which significantly reduces rates of MetS.46
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