Recommendations for lab monitoring of atypical antipsychotics

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Mr. H, age 31, is admitted to an acute psychiatric unit with major depressive disorder, substance dependence, insomnia, and generalized anxiety. In the past, he was treated unsuccessfully with sertraline, fluoxetine, clonazepam, venlafaxine, and lithium. The treatment team starts Mr. H on quetiapine, titrated to 150 mg at bedtime, to address suspected bipolar II disorder.

At baseline, Mr. H is 68 inches tall and slightly overweight at 176 lbs (body mass index [BMI] 26.8 kg/m^2). The laboratory reports his glycated hemoglobin (HbA_{1c}) at 5.4%; low-density lipoprotein (LDL), 60 mg/dL; total cholesterol, 122 mg/dL; triglycerides, 141 mg/dL; and high-density lipoprotein (HDL), 34 mg/dL.

Within 1 month, Mr. H experiences a 16% increase in body weight. HbA_{1c} increases to 5.6%; LDL, to 93 mg/dL. These metabolic changes are not addressed, and he continues quetiapine for another 5 months. At the end of 6 months, Mr. H weighs 223.8 lbs (BMI 34 kg/m^2)—a 27% increase from baseline. HbA_{1c} is in the prediabetic range, at 5.9%, and LDL is 120 mg/dL.[1] The treatment team discusses the risks of further metabolic effects, cardiovascular disease, and diabetes with Mr. H. He agrees to a change in therapy.

The association between atypical antipsychotics and metabolic adverse effects is well established.[2] Over time, these effects can lead to metabolic syndrome, poor cardiovascular outcome, and type 2 diabetes mellitus. Each drug has its own risk profile, but all atypical antipsychotics have been shown to cause some metabolic adverse effects to a varying degree.[3-5] A dose-effect relationship, if present, is estimated to be small, and metabolic effects can occur at low dosages. Weight gain and other metabolic effects are seen most strikingly in patients who are antipsychotic-naïve, and in children and adolescents.[3,4,6] No antipsychotic should be considered body

Practice Points

- **All atypical antipsychotics carry a risk** of metabolic disturbance; clozapine and olanzapine have the highest risk, followed by quetiapine and risperidone.
- **Newer atypical antipsychotics may carry less of a risk** of metabolic side effects, but long-term data are lacking.
- **Obtain baseline and periodic monitoring** of BMI, waist circumference, HbA_{1c}, fasting plasma glucose, and fasting lipids.
- If you find **an abnormality of any of these parameters**, consider one or more of the following: switching to an agent that is less risky; decreasing the dose or discontinuing therapy; recommending diet and exercise; and referring the patient to a program or clinician with expertise in the management of weight, diabetes, or lipids.
- **Use monotherapy when appropriate** to decrease the risk of side effects.

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Table 1

Comparison of metabolic effects of atypical antipsychotics

Drug	Weight gain	Dyslipidemia	Hyperglycemia
Clozapine	+++	+++	+++
Olanzapine	+++	+++	+++
Risperidone	++	+	+
Quetiapine	++	++	++
Ziprasidone	+/0	+/0	+/0
Aripiprazole	+/0	+/0	+/0
Iloperidone[a]	++	+/0	+/0
Paliperidone	+	+	+
Asenapine[a]	+/0	+/0	+/0
Lurasidone[a]	+/0	+/0	+/0

+++: significant; ++: intermediate; +: low; +/0: low or neutral

[a]Limited data and/or long-term data are not available

Source: References 5,7

Clinical Point

Clozapine and olanzapine pose the highest risk of weight gain; aripiprazole and ziprasidone present the lowest risk

weight-neutral because all have the potential for significant weight gain (>7% in body weight).[3,4]

An increase in weight is thought to be associated with the actions of antipsychotics on H1 and 5-HT2c receptors.[7] Clozapine and olanzapine pose the highest risk of weight gain. Quetiapine and risperidone are considered of intermediate risk; aripiprazole and ziprasidone present the lowest risk (***Table 1***).[5,7]

Patients taking an atypical antipsychotic may experience an elevation of blood glucose, serum triglyceride, and LDL levels, and a decrease in the HDL level.[2] These effects may be seen without an increase in BMI, and should be considered a direct effect of the antipsychotic.[5] Although the mechanism by which dyslipidemia occurs is poorly understood, an increase in the blood glucose level is thought to be, in part, mediated by antagonism of M3 muscarinic receptors on pancreatic β-cells.[7] Clozapine and olanzapine pose the highest risk of dyslipidemia. Quetiapine and risperidone are considered of intermediate risk; the risk associated with quetiapine is closer to that of olanzpine.[8,9] Aripiprazole and ziprasidone present a lower risk of dyslipidemia and glucose elevations.[5]

Newer atypical antipsychotics, such as asenapine, iloperidone, paliperidone, and lurasidone, seem to have a lower metabolic risk profile, similar to those seen with aripiprazole and ziprasidone.[5] Patients enrolled in initial clinical trials might not be antipsychotic naïve, however, and may have been taking a high metabolic risk antipsychotic. When these patients are switched to an antipsychotic that carries less of a metabolic risk, it might appear that they are experiencing a decrease in metabolic adverse events.

Metabolic data on newer atypical antipsychotics are limited; most have not been subject to long-term study. Routine monitoring of metabolic side effects is recommended for all atypical antipsychotics, regardless of risk profile.

Recommended monitoring

Because of the known metabolic side effects that occur in patients taking an atypical antipsychotic, baseline and periodic monitoring is recommended (***Table 2***).[2,10] BMI and waist circumference should be recorded at baseline and tracked throughout treatment. Ideally, obtain measurements monthly for the first 3 months of therapy, or after any

Table 2

Recommended monitoring for a patient taking an atypical antipsychotic

Parameter	Baseline	1 Mo	2 Mo	3 Mo	6 Mo	Annually
Body mass index[a]	X	X	X	X	X	X
Waist circumference	X	X	X	X	X	X
HbA_{1c}[b]	X			X		X
Fasting plasma glucose	X			X		X
Fasting lipid panel	X			X		X

[a]Encourage patients to monitor their weight in addition to being weighed at the clinic

[b]Unless patient develops diabetes mellitus, in which case American Diabetes Association guidelines for managing diabetes are recommended

Source: References 2,10

medication adjustments, then at 6 months, and annually thereafter. Encourage patients to track their own weight.

HbA_{1c} and fasting plasma glucose levels should be measured at baseline and throughout the course of treatment. Obtain another set of measurements at 3 months, then annually thereafter, unless the patient develops type 2 diabetes mellitus.[2]

Obtaining a fasting lipid panel at baseline and periodically throughout the course of treatment is recommended. After baseline measurement, another panel should be taken at 3 months and annually thereafter. Guidelines of the American Diabetes Association recommend a fasting lipid panel every 5 years—however, good clinical practice dictates obtaining a lipid panel annually.

Managing metabolic side effects

Assess whether the patient can benefit from a lower dosage of current medication, switching to an antipsychotic with less of a risk of metabolic disturbance, or from discontinuation of therapy. In most cases, aim to use monotherapy because polypharmacy contributes to an increased risk of side effects.[10]

Weight management. Recommend nutrition counseling and physical activity for all patients who are overweight. Referral to a health care professional or to a program with expertise in weight management also might be beneficial.[2] Include family members and significant others in the patient's education when possible.

Impaired fasting glucose. Encourage a low-carbohydrate, high-protein diet with high intake of vegetables. Patients should obtain at least 30 minutes of physical activity, five times a week. Referral to a diabetes self-management class also is appropriate. Consider referral to a primary care physician or a clinician with expertise in diabetes.[2]

Impaired fasting lipids. Encourage your patients to adhere to a heart-healthy diet that is low in saturated fats and to get adequate physical activity. Referral to a dietician and primary care provider for medical management of dyslipidemia might be appropriate.[2]

Clinical Point

Record BMI and waist circumference of patients taking atypicals at baseline and track them throughout treatment

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continued

Clinical Point

ADA guidelines recommend a fasting lipid panel every 5 years; however, good clinical practice dictates obtaining a lipid panel annually

Related Resources

- American Diabetes Association. Guide to living with diabetes. www.diabetes.org/living-with-diabetes.
- MOVE! Weight Management Program for Veterans. www.move.va.gov.

Drug Brand Names

Aripiprazole • Abilify	Olanzapine • Zyprexa
Asenapine • Saphris	Paliperidone • Invega
Clonazepam • Klonopin	Quetiapine • Seroquel
Clozapine • Clozaril	Risperidone • Risperdal
Fluoxetine • Prozac	Sertraline • Zoloft
Iloperidone • Fanapt	Venlafaxine • Effexor
Lithium • Eskalith, Lithobid	Ziprasidone • Geodon
Lurasidone • Latuda	

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