



Office of the Ombudsman for Mental Health and Mental Retardation



Hyperglycemia and Diabetes Alert



This Medical Alert is based on the work of the Medical Review Subcommittee and should be posted prominently. The Office of the Ombudsman for Mental Health and Mental Retardation works to improve the services provided to people with disabilities by communicating important information found in the Medical Review Subcommittee's reviews of deaths and serious injuries. Thank you for promptly reporting deaths and serious injuries. You are helping us to meet our mission.

In 2004, the Food and Drug Administration (FDA) asked all manufacturers of atypical antipsychotic medications to add a warning statement describing the increased risk of hyperglycemia and diabetes in patients taking these medications. The atypical antipsychotic class includes Zyprexa[®] (olanzapine, Eli Lilly), Clozaril[®] (clozapine, Novartis), Risperdal[®] (risperidone, Janssen), Seroquel[®] (quetiapine, AstraZeneca), Geodon[®] (ziprasidone, Pfizer), and Abilify[®] (aripiprazole, Bristol Myers Squibb and Otsuka American Pharmaceutical).

WARNINGS

Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia [too much thirst], polyuria [release of large amounts of urine], polyphagia [excessive eating], and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

<http://www.fda.gov/medwatch/SAFETY/2004/safety04.htm#drugs>

By the end of August, 2004, all manufacturers of atypical antipsychotics had complied with the FDA's request.

In February 2004, the American Diabetes Association released the following statements: "People who take antipsychotic drugs for the treatment of a variety of mental illnesses may be at increased risk for obesity, diabetes and high cholesterol – all of which can lead to heart disease. Because of this, a joint panel of the American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity has issued a consensus statement asking doctors to carefully screen and monitor patients on these medications for signs of rapid weight gain or other problems that could lead to diabetes, obesity and heart disease and refer them to specialists if necessary.... Therefore, the panel recommended that doctors prescribing antipsychotic drugs first perform baseline screenings of:

- Personal and family history of obesity, diabetes, dyslipidemia (cholesterol and triglyceride levels), blood pressure or cardiovascular disease;
- Weight and height;
- Waist circumference;
- Blood pressure;
- Fasting plasma glucose; and
- Fasting lipid profile.

In addition to recommending the referral to specialists for clients with significant weight gain, new onset diabetes, and other cardiovascular risk factors, the panel recommended “frequent follow-up monitoring of any patient receiving second generation antipsychotics (SGAs).”

The entire press release can be reviewed at the website of the American Diabetes Association:

<http://www.diabetes.org/for-media/2004-press-releases/jan-27-04.jsp>

The FDA’s MedWatch Warnings and the joint panel recommendations were too late for the following clients of the Office of the Ombudsman for Mental Health and Mental Retardation.

Could This Happen to Your Client? Case Studies

#1. A 25-year-old woman with psychosis, mild mental retardation, gastroesophageal reflux disease, and other medical conditions, died on 8/17/2003, the day she was admitted to the hospital. With no known diagnosis of diabetes, the client was found to have severe ketoacidosis, which despite interventions, led to her cardiac arrest and death. The client had been prescribed Zyprexa (since 2002) and Seroquel. Prior to her death, she had lived in an adult foster care home. She had been on pass at her parent’s home on 8/17/2003 and had been admitted to the hospital from there. She was under private guardianship. Although she was under the care of both a psychiatrist and a primary care physician, neither physician monitored the client for the development of diabetes despite the expression of concerns about the client’s weight gain. The only record of a blood glucose measurement was on 6/12/2002 when the client was in for a physical exam.

#2. A 41-year-old man, with chronic paranoid schizophrenia, was found dead in his apartment on 12/08/2003. An autopsy was performed. His manner of death was natural, and the immediate cause of death was attributed to ketoacidosis. The client had been prescribed Clozaril and had no reported diagnosis of diabetes. He last saw his psychiatrist in January and August 2003. Records from those visits indicate that no laboratory tests were ordered, although the client did have his white blood cell counts checked every two weeks per the Clozaril protocol. Prior to his death, the client had lived in his own apartment and received ARMHS services. He last saw his case manager on 12/04/2003. Although he was under the care of a psychiatrist, the client’s last annual physical had been performed in 1998.

The Medical Review Subcommittee reviewed and closed both of these cases with the following recommendations:

1. The MRS recommends that clients receiving antipsychotic medications be monitored for the development of diabetes and receive at least an annual physical exam.
2. The MRS recommends that the client’s case manager and residential facility (when applicable) audit the client’s records to ensure that annual physical exams are obtained.
3. The MRS requested the development of a Medical Alert to share with case managers, providers, the Minnesota Medical Association, and the Minnesota Psychiatric Society.

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May, 2005