Introduction

Cardiovascular and Metabolic Risks Associated With Schizophrenia and Antipsychotic Drug Treatment

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With the development of the atypical antipsychotic drugs—clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and more to follow—has come an increasing understanding of the metabolic and cardiovascular side effects of these drugs, which have an impact on morbidity and mortality. These drugs represent major advances in the treatment of schizophrenia, bipolar disorder, psychotic depression, and senile psychoses, but differ in side effects. As with all drugs, this class has both its benefits and its risks, and many of those risks have only come to light recently. The challenge for the clinician is to weigh the benefits and risks of each drug for each patient that he or she treats.

Cardiac side effects of noncardiac drugs have been recognized as potentially dangerous only in the last 10 to 15 years. One of the earliest instances of a noncardiac drug receiving a "black box" warning in its product information, the strongest warning issued by the U.S. Food and Drug Administration (FDA), was in 1992, when the FDA added the warning to the antihistamines terfenadine and astemizole. The cardiovascular side effects of the atypical antipsychotics were first noticed with sertindole, an atypical drug that received an "approvable" letter from the FDA and was available in Europe in the 1990s. A number of sudden deaths occurred during the postmarketing period, possibly precipitated by QT interval prolongation. The drug was never marketed in the United States and was withdrawn in Europe in 1998. It has recently been reintroduced in Europe with a restrictive, cautionary labeling. Since the experience with sertindole, both metabolic and cardiovascular effects have been noted in several of the atypical drugs. People with schizophrenia and other psychiatric illnesses are known to be at increased risk for death from a variety of causes, including cardiovascular and metabolic causes. In other words, there is an underlying vulnerability for cardiovascular events upon which psychotropic drugs can cause more damage than they would in other populations.

This supplement will discuss the metabolic and cardiovascular side effects of antipsychotics and weigh those against the clear benefits of antipsychotic treatment. Michael Davidson, M.D., reviews concerns about atherosclerosis and sudden cardiac death in patients with schizophrenia independent of antipsychotic treatment. Many of the risk factors for atherosclerosis in the schizophrenic population are modifiable, and ways in which psychiatrists can identify and understand these risks are discussed. There is a need for preventive services,

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argues Dr. Davidson, that is unfulfilled in this population, and it may be up to the psychiatrist to coordinate with other health care professionals to provide optimal care for his or her patients.

Alexander H. Glassman, M.D., discusses cardiovascular changes and risks associated with psychotropic agents, especially the atypical antipsychotics, and the risk factors that make some patients more sensitive to this type of side effect. According to Dr. Glassman, it is important to screen patients for cardiac vulnerabilities at baseline and during psychotropic drug treatment to attempt to discern any cardiovascular changes before they are manifested as dangerous cardiovascular events.

In his article, W. Victor R. Vieweg, M.D., reviews cardiac electrophysiology, focusing on the measurement of the QT interval and its role as a marker for potentially fatal arrhythmias. Agencies such as the FDA have increased their interest in the QT interval as a useful though limited predictor for arrhythmia, and clinicians should be aware of the QT-prolonging effects of psychotropic drugs and drug-drug interactions when prescribing such drugs.

This supplement concludes with a treatment algorithm that is intended to help the clinician manage patients with cardiovascular risk factors, such as long QT syndrome, and metabolic risk factors, such as overweight and high cholesterol, that can lead to cardiac disease. It is important to remember that the atypical antipsychotics are a remarkable group of drugs. Their lower risk for tardive dyskinesia and extrapyramidal symptoms and their beneficial effects on the negative symptoms of schizophrenia and overall quality of life for schizophrenic patients deservedly make them the first line of treatment for psychosis, but clinicians must weigh individual risk factors for cardiac and metabolic side effects before selecting a particular first-line treatment for a patient.