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3 Schizophrenia Drugs May Raise Diabetes Risk, Study Says

By ERICA GOODE

Three drugs commonly prescribed for schizophrenia and other psychotic illnesses increased patients' risk of developing diabetes when compared with older antipsychotic medications, researchers said yesterday, presenting the results from a long-awaited study of patients treated at veterans hospitals and clinics across the country.

The drugs -- Zyprexa, made by Eli Lilly, Risperdal, made by Janssen Pharmaceutica, and Seroquel, made by AstraZeneca -- were associated with higher rates of diabetes than older generation drugs for schizophrenia like Haldol, the study found. But the increased risk was statistically significant only for Zyprexa and Risperdal, the researchers said, possibly because of the smaller number of subjects who took Seroquel.

Younger patients, under age 54, who took Zyprexa or Risperdal showed the highest risk of developing diabetes, the study, led by Francesca Cunningham of the Department of Veterans Affairs at the University of Illinois at Chicago, found.

The results add to a growing number of reports linking Type 2 diabetes to some drugs in the class of antipsychotics known as atypicals.

"These findings are absolutely consistent with everything we've looked at and seen," said Robert Rosenheck, a professor of psychiatry and public health at Yale and an author of an earlier study that found an increased risk of diabetes with Zyprexa, Risperdal, Seroquel and Clozaril, made by Novartis.

Experts said the new findings underscored the need for patients who take the drugs and doctors who prescribe them to be alert for the symptoms of diabetes, including increased thirst, frequent urination, increased appetite and rapid weight gain.

Atypical antipsychotics, studies indicate, are less likely than older drugs to produce side effects like tardive dyskinesia, a devastating movement disorder. The newer drugs also appear more effective in preventing relapse in patients with schizophrenia and may be more effective in treating certain aspects of the illness.

More than 15 million prescriptions were written last year for Zyprexa and Risperdal, the two leading atypical antipsychotics, according to industry figures.

Researchers in the last two years have found higher rates of diabetes and hyperglycemia, medical conditions that are usually reversible, among patients taking the newer drugs. But many of the studies have been based on case reports in medical journals or filed voluntarily by doctors with the Food and Drug Administration, making it difficult to determine the size of the problem or whether it is associated with particular drugs or with the class of drugs as a whole.

The new study, scientists said, is important because of its careful methodology and substantial size: the researchers based their analyses on medical records from 19,878 veterans treated with an older or newer drug between October 1998 and October 2001.

Of 5,981 veterans who took Zyprexa, 200, or 3.34 percent, developed diabetes, compared with 170, or 2.43

percent, of 7,009 veterans taking Haldol or another older medication. Of 5901 patients taking Risperdal, 193, or 3.27 percent, developed diabetes; 21, or 2.39 percent, of 877 veterans taking Seroquel developed the illness. All three drugs raised a patient's chances of developing the illness by about 50 percent, but the meaning of the increased risk among patients taking Seroquel was unclear because of the smaller number of subjects who took the drug, the researchers said.

"We need a larger number of observations to be certain what its risk is and whether it differs from other drugs," said Bruce Lambert, an associate professor of pharmacy administration at the University of Illinois at Chicago and an author of the study.

The study was financed in part by Bristol Myers Squibb, the maker of Abilify, an atypical that had not entered the market when the study began and has not been systematically studied for a link to diabetes.

The study's findings have not been submitted for publication and have not undergone systematic peer review by other researchers. Its findings are also limited by the fact that the patients were not randomly assigned to different drugs and that the researchers did not know the patients' family history of diabetes or what other risk factors, including excess weight, they might have had.

Laura Bradbard, a spokeswoman for the F.D.A., which has been tracking the diabetes issue, said the agency was reviewing the findings, which were presented yesterday in Philadelphia at a meeting of the International Society for Pharmacoepidemiology, along with other studies.

The agency is considering whether to add or strengthen warnings in the labeling of certain drugs or on the class of drugs as a whole.

How atypical antipsychotics might produce or uncover diabetes is unknown. Weight gain, a side effect of some drugs, may play a significant role, researchers believe. But P. Murali Doraiswamy, chief of the division of biological psychiatry at Duke University, said that in some cases the illness has come on rapidly, before patients have time to gain weight.

Dr. Doraiswamy and other researchers said the only way scientists would be able to tell for certain how large the problem is and whether the risk is higher with some drugs would be to do a large study that randomly assigned patients to different drugs in advance and then followed them over time, a project that would require that the drug companies pool their resources or that the government finance the project.