SOUTHWESTERN NEWS

Media Contact: Amy Shields
214-648-3404
amy.shields@utsouthwestern.edu

EMBARGOED UNTIL 5 A.M. CDT TUESDAY, SEPT. 9, 2003

TWO COMMONLY PRESCRIBED DIABETES DRUGS MAY CAUSE HEART FAILURE AND FLUID BUILDUP, RESEARCHERS REPORT

DALLAS – Sept. 9, 2003 – Two diabetes medications taken by more than 6 million Americans may lead to serious side effects, including the onset of congestive heart failure and pulmonary edema, according to researchers at UT Southwestern Medical Center at Dallas.

In today's issue of the *Mayo Clinic Proceedings*, the researchers report that the oral drugs pioglitazone and rosiglitazone can cause or exacerbate heart failure and pulmonary edema and should be avoided in patients with left ventricular dysfunction (impaired pumping ability of the heart) or chronic renal insufficiency.

Both medications – among a class of drugs known as thiazolidinediones – are used for the treatment of non-insulin dependent (type 2) diabetes mellitus, said Dr. Abhimanyu Garg, professor of internal medicine and the study's senior author.

"Many physicians are prescribing these drugs in patients with chronic renal insufficiency because a first-line diabetes drug, metformin, is not recommended for them. These new data suggest that such patients may be at particularly high risk of developing heart failure," said Dr. Garg. "These are newer agents, and we need to become more familiar with their side effects so that we can use them judiciously."

Congestive heart failure, which affects 3 million Americans, is an imbalance in pump function in which the heart fails to maintain adequate circulation of blood. The most severe manifestation of congestive heart failure is pulmonary edema, or fluid in the lungs. Patients with coexisting type 2 diabetes have an increased mortality rate.

The researchers reviewed the records of six patients with type 2 diabetes who were treated at the Dallas Veterans Affairs Medical Center emergency room after experiencing shortness of breath, weight gain and swelling of the feet – all signs and symptoms of congestive heart failure and pulmonary edema.

These symptoms developed after one to 16 months of therapy with pioglitazone or

(MORE)

rosiglitazone. In three patients, doses of these medications were increased three weeks to three months prior to the onset of congestive heart failure.

The researchers provided follow-up care to the patients during clinic visits.

After discontinuing the medications and administering diuretics, the patients no longer exhibited the signs and symptoms of congestive heart failure and pulmonary edema.

The Food and Drug Administration approved rosiglitazone and pioglitazone in 1999. The prescribing information indicates that the drugs should not be used by individuals with New York Heart Association (NYHA) Class III and IV status, particularly in combination with insulin.

"Our data indicates that patients with NYHA Class I or II cardiac status may also be at risk of thiazolidinedione-associated cardiac failure," said Dr. Asra Kermani, the study's lead author and an assistant professor of internal medicine at UT Southwestern who sees patients at the VA.

The New York Heart Association functional classification for patients with heart failure is used to characterize patients' limitation from left ventricular failure. Class I represents no limitation of physical activity; Class II, slight limitation of physical activity; Class III, marked limitation of physical activity; and Class IV, unable to carry on any physical activity without symptoms.

Because the mean age of the patients in the study was 69, additional studies need to be undertaken to identify the patient groups at risk for these complications, the researchers noted.

"We need further studies to understand the mechanism by which thiazolidinediones cause fluid overload and deterioration in cardiac status," Dr. Kermani said.

###