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Class of diabetes drugs carries significant cardiovascular risks

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A class of oral drugs used to treat type 2 diabetes may make heart failure worse, according to an editorial published online in *Heart* Wednesday by two Wake Forest University School of Medicine faculty members.

"We strongly recommend restrictions in the use of thiazolidinediones (the class of drugs) and question the rationale for leaving rosiglitazone on the market," write Sonal Singh, M.D., M.P.H., assistant professor of internal medicine, and Curt D. Furberg, M.D., Ph.D., professor of public health sciences. Rosiglitazone and pioglitazone are the two major thiazolidinediones.

In the editorial Singh and Furberg say, "At this time, justification for use of thiazolidinediones is very weak to non-existent."

Oral drugs are given to control diabetes by lowering blood sugar.

But diabetics also experience elevated rates of high blood pressure and high levels of cholesterol and triglyceride, which "further compound their already increased risk of developing ischemic heart disease," Singh and Furberg say. Heart disease and high blood pressure "represent conditions that are major precursors of congestive heart failure."

About 22 percent of diabetics have heart disease. Among elderly patients with diabetes, more than half will develop congestive heart failure over a 10-year period, the editorial says.

The thiazolidinediones were approved for use based on the ability to reduce blood sugar.

In contrast, "we reported [in the journal *Diabetes Care*] in June 2007 that thiazolidinediones doubled the risk of congestive heart failure in patients with type 2 diabetes," is says. "The increased heart failure appears to be a class effect."

Singh and Furberg reported in *The Journal of the American Medical Association* in 2007 after an analysis of four long-term trials that use of rosiglitazone was associated both with increased heart attacks and a doubling of heart failure.

They said that results from three large randomized clinical trials published this past June all failed to demonstrate that intensive control of blood sugar reduces mortality or events from cardiovascular disease in patients with type 2 diabetes.

The three trials were ACCORD, ADVANCE, and the Veterans Affairs Diabetes study. In ACCORD, the patients who received intensive treatment to control blood sugar actually had more cardiovascular disease mortality than patients receiving standard treatment.

In ADVANCE, intensive control of blood sugar produced no benefit; there was no effect on cardiovascular events or deaths from cardiovascular causes compared to standard oral diabetes agents.

In the VA Diabetes trial, when intensive blood sugar control produced levels of blood sugar that were too low and led to loss of consciousness, that was a strong predictor of future cardiovascular events.

"The unfavorable findings from the three trials have not been fully realized by the medical community," Singh and Furberg say.

They say that at a recent U.S. Food and Drug Administration advisory committee meeting, there was "overwhelming support for requiring reductions" of heart disease and heart failure "before approval of new oral hypoglycemic agents."

Singh said in an interview, "Safer, cheaper and more effective treatment alternatives are available that do not carry these negative cardiovascular risks in patients with diabetes. The rationale for the use of the thiazolidinediones is unclear."

Source: Wake Forest University