Meta-analysis examines cardiovascular effects of diabetes medications

October 27 2008

The diabetes medication metformin may be associated with a lower risk of death from cardiovascular disease, according to a meta-analysis of previously published studies in the October 27 issue of *Archives of Internal Medicine,* one of the JAMA/Archives journals. No associations were found between other diabetes medications and beneficial or harmful cardiovascular effects, in part because of insufficient data, the authors note.

"A wide variety of oral diabetes medications are currently available for the treatment of type 2 diabetes mellitus," they write as background information in the article. "With the addition of newer oral therapies to the market in the late 1990s (e.g., thiazolidinediones and meglitinides), it is critical to evaluate how these agents compare with older medications. This is particularly important in light of the expense of many of the newer therapies." The specific effects of these medications on cardiovascular health remains unclear, and recent controversy has surrounded possible cardiac risks associated with one newer drug, rosiglitazone.

Elizabeth Selvin, Ph.D., M.P.H., of the Johns Hopkins Bloomberg School of Public Health, Baltimore, and colleagues performed a meta-analysis of data from 40 clinical trials published on or before Jan. 19, 2006. All the trials assessed the benefits or harms of oral diabetes medications approved for use in the United States, including combinations of therapies commonly prescribed by physicians, and included information about heart attack, stroke or other cardiovascular

events. The average age of participants ranged from 52 to 69 and 27 of the studies (68 percent) were less than one year in duration.

"Treatment with metformin hydrochloride was associated with a decreased risk of cardiovascular morality [death] compared with any other oral diabetes agent or placebo; the results for cardiovascular morbidity [illness] and all-cause mortality were similar but not statistically significant," the authors write. "No other significant associations of oral diabetes agents with fatal or non-fatal cardiovascular disease or all-cause mortality were observed. When compared with any other agent or placebo, rosiglitazone was the only diabetes agent associated with an increased risk of cardiovascular morbidity and mortality, but this result was not statistically significant."

Poor quality and inconsistent reporting of cardiovascular data, along with the lack of long-term studies, make it difficult to draw firm conclusions, the authors note. "Our study demonstrates that there have been few trials of oral diabetes therapies that have lasted longer than six months and that reporting of adverse events for cardiovascular disease is poor," they continue.

"There is a critical need for studies of oral diabetes medications with long-term outcomes. The relatively modest differences in blood pressure, cholesterol levels and weight observed after treatment with oral diabetes medications in short-term trials may not translate to changes in long-term cardiovascular risk. Only long-term trials can provide definitive conclusions regarding the comparative efficacy of oral diabetes medications and long-term risks."

Citation: *Arch Intern Med.* 2008;168[19]:2070-2080.
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Source: JAMA and Archives Journals