Blood pressure drug combination reduces heart attack deaths

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Thousands of patients with high blood pressure could benefit from changing their drug treatment regimen to reduce their risk of cardiac death.

The current U.S. hypertension treatment guidelines recommend using a thiazide diuretic – a drug that increases the volume of urine – alone as the initial drug therapy for high blood pressure. But a failure of diuretic drugs to decrease deaths from heart attacks, an important consequence of hypertension, prompted Vanderbilt University Medical Center researchers to analyze data from existing clinical trials of diuretic drugs.

They found that combining a thiazide diuretic with a "potassium-sparing" drug to treat hypertension reduced both sudden cardiac death and total coronary mortality by 40 percent. The findings call into question the current treatment guidelines.

"The recommendations can now be re-examined in light of these new findings," said John Oates, M.D., senior author of the study published in the September/October issue of the *Journal of the American Society of Hypertension*. The Joint National Committee, under the direction of the National Heart, Lung, and Blood Institute, publishes clinical practice guidelines for hypertension – new guidelines are expected in 2009.

Thiazide diuretics successfully reduce blood pressure for many patients, but they are also known to deplete potassium, said Oates, a professor of Medicine and hypertension specialist. This potassium "wasting" has

sparked concern over the years with studies suggesting a link between potassium loss and sudden cardiac death.

Oates and colleagues examined data from controlled clinical trials that compared a thiazide diuretic/potassium-sparing (ENaC inhibitor) drug combination to placebo. They generated new, previously unpublished data on sudden death in these trials, and then analyzed the results of the trials in a meta-analysis – a statistical evaluation of data combined from multiple trials. They found a 40 percent reduction in total cardiac mortality and in sudden cardiac death in elderly patients with hypertension taking the drug combination, compared with those receiving placebo.

"It was very striking," Oates said.

The investigators also performed a new meta-analysis of the clinical trials of thiazides given without a potassium-sparing drug, adding new trials to the mix. They found no benefit in coronary mortality and a 26 percent increase in sudden death. Even though the increase was not statistically significant, it was "going in the direction in which you didn't want to go," Oates said.

Observational studies previously had found an increase in sudden cardiac death in patients taking a thiazide diuretic alone, and one showed that sudden death was greater at higher doses of thiazides, he said. Studies in animal models of heart attacks also have demonstrated that low potassium levels (caused by thiazide diuretics) can spark the abnormal heart rhythms that lead to sudden death.

Do thiazide diuretics given alone have an adverse effect of increasing the risk of sudden cardiac death in patients with high blood pressure? It's possible.

"There's biologic plausibility for an adverse effect of the thiazides," Oates said. "If it's true, it's probably the largest adverse effect in the history of modern pharmacology. The number of individuals affected over the last 50 years would be staggering."

And since the current U.S. clinical practice guidelines for hypertension recommend a thiazide diuretic without a potassium-sparing drug, millions of patients may be at increased risk of coronary death, Oates pointed out.

Oates acknowledges that potassium-sparing drugs may reduce coronary mortality through a mechanism unrelated to their prevention of potassium loss. As studies proceed to determine how these drugs reduce death risk, he said, it's time to add them to thiazides as recommended first-line treatment for high blood pressure in the elderly.

Source: Vanderbilt University Medical Center