Hypertension drug dramatically reduces proteinuria in kidney disease patients

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Taking a much higher than recommended dose of the hypertension drug candesartan cilexetil effectively lowered the amount of protein excreted in the urine of patients with kidney disease, according to a study appearing in the April 2009 issue of the *Journal of the American Society Nephrology* (*JASN*). By reducing such proteinuria, the drug could potentially prevent the development of serious complications such as end-stage kidney disease and therefore save many patients' lives.

Many research efforts are focused on finding ways to lower urinary protein excretion in patients with kidney disease because doing so may postpone kidney failure and prevent the development of cardiovascular disease. Investigators in Canada recently reported the results of a multicenter trial that evaluated whether high doses of the hypertension drug candesartan cilexetil could reduce proteinuria better than the maximum approved dose. This drug is an angiotensin receptor blocker, an agent that reduces blood pressure by blocking several of the effects of the hormone angiotensin II, including tightening and thickening of the arteries, secretion of the hormone aldosterone, and reabsorption of sodium by the kidney. Because angiotensin receptor blockers also have effects on fibrosis and inflammation in the kidney, these drugs are also used to prevent or slow the progression of kidney failure.

The trial, led by Ellen Burgess, MD, of the University of Calgary in Alberta, Canada, enrolled 269 patients who had persistent proteinuria despite treatment with the highest approved dose of candesartan (16 mg daily at the time the study was initiated). Patients were randomized to

receive 16, 64, or 128 mg daily of candesartan for 30 weeks.

The investigators found that patients taking 128 mg of candesartan experienced more than a 33% reduction in proteinuria compared with those receiving 16 mg candesartan by the end of the study. This reduction was in addition to the reduction in proteinuria that the patients would have had when they first started taking candesartan at 16 mg daily.

"We were surprised to see such a dramatic effect since, in the end, several other studies using higher-than-approved doses of angiotensin receptor blockers were not able to show benefit," said Dr. Burgess.

Additional research is needed to determine the optimal dose of candesartan for lowering proteinuria. However this study proves that "proteinuria that persists despite treatment with the maximum recommended dose of candesartan can be reduced by increasing the dose of candesartan further," the authors wrote. While high dose therapy with candesartan was well-tolerated, 11 patients dropped out of the study due to high blood potassium levels. Therefore, the researchers recommend that potassium levels be monitored during treatment with this drug.

More information: The article, entitled "Supramaximal Dose of Candesartan in Proteinuric Renal Disease," will appear online at jasn.asnjournals.org/ on Wednesday, February 11, 2009, doi 10.1681/ASN.2008040416.

Source: American Society of Nephrology