Poorer outcomes linked with certain hormone for patients with early-stage chronic kidney disease

14 June 2011

Patients in the early stages of chronic kidney disease who had elevated levels of the endocrine hormone fibroblast growth factor 23 (that regulates phosphorus metabolism) had an associated increased risk of end-stage renal disease and death, according to a study in the June 15 issue of *JAMA*.

Circulating levels of fibroblast growth factor 23 (FGF-23) increase progressively as kidney function declines. A high level of FGF-23 is associated with mortality in patients with end-stage renal disease, but little is known about its relationship with adverse outcomes in the larger population of patients with earlier stages of chronic kidney disease, according to background information in the article.

Tamara Isakova, M.D., M.M.Sc., of the University of Miami Miller School of Medicine, and colleagues examined the relationship between elevated FGF-23 levels and risk of death and end-stage renal disease in 3,879 individuals with chronic kidney disease stages 2 through 4. The participants were enrolled in the Chronic Renal Insufficiency Cohort between June 2003 and September 2008.

At study enrollment, the average estimated glomerular filtration rate (GFR; measure of the kidneys' ability to filter and remove waste products) was 42.8 mL/min/1.73 m2. During a median (midpoint) follow-up of 3.5 years, 266 participants died and 410 reached end-stage renal disease. The researchers found that median FGF-23 levels were significantly higher in those who died or reached end-stage renal disease than in those who remained event-free. "Adjusting for demographic characteristics, estimated GFR and other chronic kidney disease-specific risk factors did not alter the relationship between elevated FGF-23 levels and risk of death observed in unadjusted analyses. Participants in the highest vs. the lowest quartile demonstrated a 4.3-fold greater risk of death, and the intermediate quartiles demonstrated intermediate risks," the researchers write. In the fully adjusted models, the graded increase in risk of death persisted across the spectrum of FGF-23 levels.

Reduced estimated GFR was the strongest predictor of end-stage renal disease in fully adjusted analysis, and estimated GFR modified the relationship between FGF-23 and risk of end-stage renal disease. "Although the median FGF-23 was higher in more advanced chronic kidney disease, elevated levels of FGF-23 were independently associated with greater risk of end-stage renal disease in participants with baseline estimated GFR between 30 and 45 mL/min/1.73 m2 and 45 mL/min/1.73 m2 or higher but not in those with estimated GFR lower than 30 mL/min/1.73 m2. In contrast, the risk of death according to FGF-23 was homogenously significant across categories of estimated GFR," the authors write.

The researchers note that FGF-23 unexpectedly was more strongly associated with mortality than traditional cardiovascular disease- and chronic kidney disease-specific risk factors, most notably, reduced estimated GFR and proteinuria (the presence of excessive protein). "These data emphasize the potential of FGF-23 as a novel risk factor for mortality in chronic kidney disease."

They add that the mechanisms that underlie the association between elevated levels of FGF-23 and mortality are unclear.

"If the results of the current study are confirmed and experimental studies support the hypothesis of direct toxicity of FGF-23, future research should

evaluate whether therapeutic or preventative strategies that lower FGF-23 can improve outcomes."

More information: *JAMA*. 2011;305[23]2432-2439.

Provided by JAMA and Archives Journals