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Hormone level may reflect mortality risk among dialysis patients

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A new study suggests that monitoring levels of a hormone called fibroblast growth factor 23 (FGF-23) may provide information crucial to the treatment of patients with kidney failure. In the Aug. 7 *New England Journal of Medicine*, researchers from Massachusetts General Hospital (MGH) report that patients with elevated levels of FGF-23 when beginning hemodialysis had a significantly increased risk of death within the first year of treatment, regardless of whether they had other risk factors. The study also found evidence that FGF-23 levels may differ between racial groups, which may relate to observed disparities in survival of dialysis patients.

"FGF-23 helps regulate serum phosphate levels; and we know that, among patients with kidney failure, elevated phosphate is associated with more rapid progression to renal failure and earlier death," says Myles Wolf, MD, MMSc, who led the study when he was with the MGH Renal Unit,. "The results of this study suggest that we need to be concerned about phosphate control even for patients whose serum phosphate levels are normal, and that may involve routine screening for FGF-23."

Along with removing waste material from the bloodstream, the kidneys also balance levels of electrolytes like sodium and potassium and minerals including phosphate. Previous studies have associated elevated phosphate levels in the serum – another name for plasma, the clear component of blood – with increased risk of death among dialysis patients. Although it has been known that levels of FGF-23, which regulates the metabolism of phosphate and vitamin D, are also elevated

in patients with kidney failure, whether FGF-23 levels had any impact on patient survival had not been investigated.

To determine whether an increase in serum FGF-23 was associated with the risk of death, the MGH researchers analyzed levels of both phosphate and FGF-23 in a large group of dialysis patients. Starting with data on more than 10,000 patients who began dialysis at more than 1,000 centers across North America, they examined the relationship between phosphate levels and the risk of death within the year after dialysis began and confirmed that mortality was modestly higher in those with the highest phosphate levels. They then compared serum FGF-23 levels of 200 patients who died during that first year with the levels of 200 patients who survived. To ensure that the effects of FGF-23 could be analyzed separately from those of phosphate, those 400 patients were selected to be equally balanced across the spectrum of serum phosphate levels.

Elevated FGF-23 levels proved to be a much more powerful predictor of death than serum phosphate measured at the same time. Among those with the highest FGF-23 levels, the mortality rate was 600 percent higher than in patients with the lowest levels, while patients with the highest phosphate levels had only a 20 percent elevation of risk. In addition, intermediate FGF-23 levels reflected an intermediate risk of death, an association not seen for phosphate levels. Even among patients with normal phosphate levels, elevated FGF-23 significantly increased the risk of death.

The data also showed that FGF-23 levels tended to be lower among black and Hispanic patients, something not reported in previous FGF-23 studies that primarily enrolled white and Asian patients. Black patients with the lowest FGF-23 levels had an even lower risk of death than did white patients with similar levels, which echoes previous observations of a reduced mortality rate among black dialysis patients.

"This is the first report of racial and ethnic differences in FGF-23 levels, and we are now investigating whether such differences are also seen in healthy patients and those with earlier stages of kidney disease," Wolf says. "We expect those differences may relate to previous observations of calcium, phosphorous and vitamin D metabolism differences among racial groups. We also need to investigate whether FGF-23 elevations are toxic in themselves or if they are simply a biomarker for abnormal phosphate balance.

"Incorporating FGF-23 levels into the management of kidney failure may have its greatest potential for treatment of the millions of patients with early-stage kidney disease who do not yet require dialysis, who usually have normal phosphate levels but quite high FGF-23," he adds. "Routinely monitoring FGF-23 may help determine which patients need to begin therapies that control phosphate levels, which may reduce mortality in this very high-risk group." As of August 1, Wolf has joined the University of Miami Miller School of Medicine as director of Clinical Research in the Nephrology Division.

Source: Massachusetts General Hospital