

Abstract

“CHARACTERIZATION OF FGF-23 AS A CARDIAC RISK MARKER AND AS A REFLECTOR OF PHOSPHATE HOMEOSTASIS”

High phosphate levels are linked to cardiovascular morbidity and mortality. Fibroblast growth factor 23 (FGF-23) is a central phosphate-regulating hormone, potentially better reflecting phosphate load than a single phosphate measurement.

In chronic kidney disease (CKD), FGF-23 plasma levels rise while renal function declines. High FGF-23 levels predict progression of chronic kidney disease and end-stage renal disease (ESRD). Furthermore, present reports suggest that high FGF-23 levels associate with cardiovascular diseases, such as vascular calcification and left ventricular hypertrophy, particularly in the presence of CKD. However little is known about FGF-23 and cardiovascular disease in non-CKD patients.

In our HOM SWEET HOME study (Heterogeneity of Monocytes in Subjects Who Undergo Elective Coronary Angiography – The Homburg Evaluation study), a cohort of 1309 patients admitted for elective coronary angiography at the Department for Internal Medicine III - Cardiology, Angiology and Intensive Care Medicine at the Saarland University Medical Center, we analyzed FGF-23 plasma levels, diuretic intake and prevalent cardiovascular disease (i.e. left ventricular hypertrophy and prevalent atrial fibrillation).

We found that high FGF-23 plasma levels are independently associated with loop diuretic intake. Moreover, FGF-23 was linked to the presence of left ventricular hypertrophy and to atrial fibrillation.

In our DIAL HOME study (DIALysis in HOMburg study) we investigated a cohort of 40 ESRD patients in our outpatient dialysis center at the Department for Internal Medicine IV - Nephrology and Hypertension at the Saarland University Medical Center. We performed serial measurements of chronic kidney disease - mineral and bone disorder (CKD-MBD) parameters over a study period of four weeks, assessing plasma phosphate and calcium before each dialysis session and plasma FGF-23, parathyroid hormone and alkaline phosphatase at the end of each study week. We tested the hypotheses that FGF-23 has a lower intraindividual variability than conventional CKD-MBD parameters and that FGF-23 is a reflector of the time-averaged plasma phosphate levels of the preceding four weeks.

Against our expectations, variability of FGF-23 was higher than variability of conventional CKD-MBD parameters. Moreover, the correlation between FGF-23 and time-averaged plasma phosphate did not surpass the correlation between FGF-23 and a single plasma phosphate value.

In conclusion, we firstly confirm a strong association between elevated FGF-23 plasma levels and prevalent cardiac disease even in the absence of CKD. Secondly, we describe an association between FGF-23 plasma levels and loop diuretic intake. Further investigations should aim to identify the pathophysiological pathways behind these associations.

Finally, we reject the hypothesis that, in CKD patients, FGF-23 may serve as a stable CKD-MBD parameter reflecting time-averaged phosphate plasma levels. Thus, FGF-23 should not be used in clinical practice as an indicator of persistent hyperphosphatemia.