CKD-MBD

The Role of FGF 23 and Klotho in Vascular Disorder

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Fibroblast growth factor 23 (FGF23) is a phosphorus regulating protein secreted by bone cells, mainly osteoblast. It regulates phosphorus homeostasis and the serum level of FGF23 increases progressively as kidney function declines, even before the rise of plasma phosphorus level. FGF23 levels increase in chronic kidney disease as an appropriate adaptation to maintain phosphate homeostasis. However, previous studies showed that elevated FGF23 level may exert its negative effects. Several studies demonstrated that elevated FGF23 is independently associated with mortality in early stage CKD, advanced CKD, incident hemodialysis patients, and even in patients with normal kidney function. Furthermore, elevated FGF23 is associated with adverse cardiovascular outcomes in patients with normal kidney function and advanced CKD patients. Several studies showed elevated FGF23 is related with left ventricular hypertrophy (LVH) in CKD and HD patients.

Klotho is a single-pass transmembrane protein expressed in the distal tubule of the kidney, parathyroid gland and choroid plexus. Membrane Klotho acts as a co-receptor for FGF23. The extracellular domain is shed from the cell surface and performs multiple renal and extrarenal functions. Emerging evidence from clinical and basic studies reveal that CKD is a state of renal Klotho deficiency, which may serve as an early biomarker and a pathogenic contributor to chronic progression and complications in CKD including vascular calcification, LVH, and secondary hyperparathyroidism. Klotho is a promising candidate as an early biomarker, and as a novel therapeutic agent for CKD.