Bone, Vitamin D and CKD

FGF-23 & Kloth in CKD-MBD

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방 기 태

Purpose: The wealth of data regarding fibroblast growth factor-23 (FGF23) and Klotho in chronic kidney disease (CKD) has risen exponentially over the past decade. This lecture is an attempt to summarize pivotal aspects of previous research, provide an update of recent findings and define important areas for future investigation.

Recent findings: The phosphaturic hormone FGF23 increases dramatically as renal function declines. Identification of contributing stimuli to the rise in FGF23 is fundamental and recent evidence suggest a multifactorial cause which entails perturbed osteocyte function and renal mechanisms such as Klotho deficiency and, somewhat paradoxically, systemic Klotho excess. Circulating FGF23 predicts adverse outcomes, particularly cardiovascular disease, in CKD as well as in the general population. The concept of FGF23 merely as a biomarker and regulator of mineral metabolism is currently challenged by data linking FGF23 to pathological processes such as cardiac hypertrophy. Conversely, tissue level of the FGF23 coreceptor Klotho declines in early CKD and this deficiency is linked to accelerated ageing, cellular senescence, vascular calcification, oxidative stress and renal fibrosis. At present, methodological difficulties limit the utility of soluble Klotho measurements. Animal proof-of-concept studies have demonstrated beneficial effects of Klotho delivery in CKD, whereas anti-FGF23 therapy using neutralizing antibodies improved biochemical and bone parameters at the expense of increased vascular calcification and mortality.

Summary: Pathological alterations of FGF23-Klotho in CKD are implicated as clinical biomarkers and may provide novel therapeutic strategies to alleviate the cardiovascular risk and slow CKD progression.