The ERA-EDTA acknowledges the high clinical and scientific relevance of the CKD-MBD syndrome, reflected by several key publications in the journals of our society. We hereby summarize the content of several recent important papers, providing a link to their abstracts.

From January to June 2017, 17 CKD-MBD related articles, including editorial comments and experimental studies, have been published; 12 in Nephrology Dialysis and Transplantation and 5 in Clinical Kidney Journal. Links to CKD-MBD contents from the 2017 Madrid ERA-EDTA Congress can also be found at the end of this newsletter.

1) Another systematic review and meta-analysis comparing the efficacy and safety of sevelamer and lanthanum versus calcium-based and iron-based phosphate (P) binders in patients with CKD has been published by S. Habbous et al (Nephrol Dial Transplant 32 (1): 111) Sevelamer was associated with a nonsignificant 38% reduction in mortality [relative risk (RR) 0.35, 1.08] and significantly lower hospitalization rates and hypercalcemia compared with calcium-based P-binders (CBPBs). Lanthanum and iron-based P-binders did not show superiority for any clinically relevant outcomes. Low-density lipoprotein-cholesterol values and coronary artery calcification (CAC) scores were lower for patients treated with sevelamer than CBPBs, and patients treated with CBPBs had greater increases in CAC scores, but these endpoints were not associated with reduced mortality. A related editorial by G.J. Elder (Nephrol Dial Transplant 32 (1): 5) summarizes that there seems little to recommend CBPBs apart from cost, but a reasonable conclusion is that calcium is down, but not out. A different approach is reported by A. Lenglet et al (Nephrol Dial Transplant 32 (5): 870) on the NICOREN randomized study, designed to compare nicotinamide with sevelamer in hemodialysis patients. Both drugs were equally effective in lowering serum P, but tolerance of nicotinamide was largely inferior. Extremely high N-methyl-2-pyridone-5-carboxamide (2PY) levels probably contributed to nicotinamide’s side effects. Finally, M. Wester et al (Nephrol Dial Transplant 32 (6): 951) showed in awake goats the effectiveness and low-risk profile of a regenerable potassium and P sorbent system to enhance dialysis efficacy and device portability.

2) S-J. Tan et al reported in Clin Kidney J 10(3): 397 on non–dialysis CKD patients and healthy volunteers, that abnormalities in P regulatory pathways are disturbed early in CKD. While intact FGF-23 was statistically associated with P excretion on univariate analyses, soluble Klotho could be a marker of P reabsorption due to its significant association, independent of intact FGF-23. Experimentally, M.A. de Jong et al (Nephrol
Dial Transplant 32 (1): 73) provided a proof of principle for crosstalk between the FGF23-klotho axis and the renin-angiotensin system (RAS). A high circulating level of FGF23 had been associated with an impaired response to RAS blockade-based therapy in clinical studies. Therefore, recombinant FGF23 was administered in a mouse model of renal fibrosis and demonstrated an important interaction between exogenous FGF23 and losartan. In a different study, T. Takenaka et al (Nephrol Dial Transplant 32 (5): 791) reported that klotho suppressed RAS in adriamycin nephropathy. Furthermore, klotho supplementation inhibited Wnt signaling, ameliorating renal angiotensin II, and klotho protein appeared to suppress epithelial-mesenchymal transition by inhibiting TGF-β and Wnt signaling. S. Bansal et al (Nephrol Dial Transplant 32 (6): 960) reported that only a acute on chronic exposure to lipopolysaccharide stimulates FGF23 production in a normal mouse model of inflammation, and that the spleen, under these conditions, contributed substantially to elevated circulating FGF23 levels.

3) CKD-MBD has been implicated in vascular calcification pathogenesis. In this regard, G. Cianciolo et al (Clin Kidney J 10 (3): 389) suggested that in CKD-MBD, endothelial-progenitor cells (EPCs) undergo an endothelial-to-procalcific shift, besides established phenotype switch of vascular smooth muscle cells, representing a risk factor for vascular calcification. A link between mineral disorders and vitamin D replacement therapy emerged. Data from the German registry on calciphylaxis was published by V.M. Brandenburg et al (Nephrol Dial Transplant 32 (1): 126). Approximately 50% of calciphylaxis patients used vitamin K antagonists, uncontrolled hyperparathyroidism was not the key determinant of calciphylaxis, and therapeutic strategies were heterogeneous. D. Arroyo et al (from the Spanish NEFRONA study) (Nephrol Dial Transplant 32 (3): 513) reported that asymptomatic peripheral artery disease is very prevalent in all CKD stages, but factors related to a low or high pathological ankle-brachial index differ in different stages of CKD. Diabetes, dyslipidaemia, inflammation and mineral-bone disorders play a role, P being especially important in earlier CKD, and LDL-cholesterol being an independent predictor only in stage 5D CKD. N. Huang et al (Nephrol Dial Transplant 32 (4): 677) performed a longitudinal analysis of community-dwelling elderly Icelandic adults from the Age, Gene/Environment Susceptibility Reykjavik Study. They evaluated the associations of pulse wave velocity, carotid pulse pressure and augmentation index with the change in eGFR and urine albumin/creatinine ratio, and showed that abnormalities in vascular health may play a role in larger declines in eGFR beyond traditional cardiovascular risk factors. Finally, in an experimental study, S.D. Rodenbeck et al (Nephrol Dial Transplant 32 (3): 450) demonstrated in a rat model that with progressive CKD there is an increase in resting intracellular calcium in vascular smooth muscle cells (VSMCs) due, in part, to increased...
store-operated calcium entry and impaired calcium extrusion from the cell. Such changes seem to predispose VSMCs to phenotypic changes that are a prerequisite to calcification.

4) Miscellaneous contents:
   a. A. Vik et al [Clin Kidney J 10 (1): 38] described that the association between osteoprotegerin and eGFR varies with age and renal function.
   b. C. Lim et al [Clin Kidney J 10 (3): 341] described that hypophosphatemia is common during renal replacement therapy in critically ill patients with acute kidney injury, and it is associated with adverse events and clinical outcomes.
   c. O.J. Ziff et al [Clin Kidney J 10 (3): 411] described the impact of seasonality on the dynamics of native vitamin D repletion in long-term renal transplant patients. Vitamin D repletion could safely and effectively be achieved in the majority of chronic stable renal transplant recipients using a 6-month bolus intermediate-dose schedule (either 240 000 IU or 360 000 IU cholecalciferol if pre-repletion serum vitamin D was between 20 and 50 nmol/L or <20 nmol/L, respectively). Winter repletion was associated with an inadequate response; however, all patients experienced a post-repletion fall towards deficiency in the absence of maintenance supplementation, irrespective of the season of repletion.
   d. K. Yokoyama et al [Nephrol Dial Transplant 32 (3): 534] described in a Japanese cohort that increasing frequency of monitoring was helpful when serum marker levels exceeded the target range, partially via adjustment in the therapeutic regimen, but they no evidence was found that frequent measurements are helpful when mineral levels are already within target ranges.

Finally, contents of the 2017 Madrid ERA-EDTA Congress can be found in the 2017 Nephrol Dial Transplant Supplement # 3.

Oral sessions on CKD-MBD and CKD-MBD in dialysis can be found following each one of these links, as well as Poster Sessions on CKD-MBD.
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