CKD-MBD – An Official ERA-EDTA Working Group
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CKD-MBD related publications in the ERA-EDTA journals

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 July to December 2019, **23 CKD-MBD related articles**, including several editorial comments and experimental studies, have been published; 18 in Nephrology Dialysis and Transplantation and 5 in Clinical Kidney Journal.

- **Phosphate (P) control (i.e. through diet and/or P-binders)** remains as an iterative issue in many publications. **Salomo et al** (Nephrol Dial Transplant 34 (10):1691) found short-term favorable effects on the P axis (dramatic reduction of 24-h urinary P) using the New *Nordic Renal* Diet (realistic, feasible, unsupplemented whole-foods dietary pattern). An editorial devoted to this article and other "renal diets" (mainly on P physiology) is reviewed by **J.J. Scialla and P.-H. Lin** (Nephrol Dial Transplant 34 (10):1619). Two *post-hoc* analyses of phase 3 trials, **G.A. Block et al** (Nephrol Dial Transplant 34 (7):1115), on ferric citrate, and **M. Ketteler et al** (Nephrol Dial Transplant 34 (7):1163), on sucroferric oxyhydroxide and sevelamer, analyze their effects on CKD-MBD parameters. *Ferric citrate* reduced intact fibroblast growth factor-23 (FGF23) and C-terminal FGF23, partially via changes in iron balance (for *C-terminal* FGF23) and serum P (for *intact* FGF23) and partially via unknown/unmeasured mechanisms. Sucroferric oxyhydroxide *and* sevelamer also reduced serum FGF23 and increased bone formation marker levels. Short-term effects of sevelamer (carbonate) on FGF23 and pulse wave velocity (PWV) in patients with normophosphatemic stage 3 CKD were evaluated by **A.B. de Krijger et al** (Clin Kidney J 12 (5):678) and found that sevelamer did not improve PMV. However, in subgroup analysis it did improve in patients with no or limited abdominal aorta calcifications. A related editorial by **J. Bover and M. Cozzolino** (Clin Kidney J 12 (5):673) refers to this small steps towards the potential of "preventive" treatment of early P loading in CKD.

- **Wakasugi et al** (Nephrol Dial Transplant 34 (7):1207) described that functional impairment was significantly associated with 1-year mortality and attenuated the effect of hyperphosphatemia on mortality among prevalent dialysis patients. Calcemia and PTH were associated with mortality irrespective of the functional status. A related editorial (**P.A. Ureña-Torres and M. Cohen-Solal**; Nephrol Dial Transplant 34 (7):1077) analyzed this and other factors able to modify this association. On the other hand, in an *experimental* study, **Y. Sakaguchi et al** (Nephrol Dial Transplant 34 (8):1310) demonstrated that a low magnesium diet aggravates P-induced kidney injury and P metabolism (by impairing PTH secretion and down-regulating renal α-Klotho). **T. Oka et al** (Nephrol Dial Transplant 34 (7):1154) described that hypomagnesemia was a common electrolyte abnormality in patients with CKD and that renal magnesium tubular wasting was associated with proteinuria.

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- Regarding **vascular calcification**, in two experimental studies, **Bouabdallah et al** (Nephrol Dial Transplant 34 (7):1125) showed that P and indoxyl sulphate induced human aortic smooth muscle cell calcification, which was significantly exacerbated by *endothelial* cell-conditioned medium and highlighted the novel role of IL-8. **K. Belmokhtar et al** (Nephrol Dial Transplant 34 (12):2018) demonstrated that receptor for advanced glycation end-products (RAGEs), through the modulation of Pit-1 expression, is a key molecule in the genesis of vascular calcification in CKD. Clinically, **M.C. Lamarche et al** (Nephrol Dial Transplant 34 (10):1715) reported that in stages 3–5 CKD patients, coronary artery calcification (CAC) is an independent predictor of both end-stage renal disease (ESRD) and mortality *at 10 years*. Those who developed ESRD at the fastest rate either had the highest CAC score or the worst CKD-MBD derangements (lowest calcidiol, and highest serum P). Finally, **A. Galassi et al** (Clin Kidney J 12 (4):546) showed the improvement of wounds in a hemodialysis patient affected by calciphylaxis, treated by multipronged intervention including both *intravenous* and *intralesional* sodium thiosulphate.

- Several pleiotropic effects of FGF23 were analyzed in different studies. Experimentally, **A. Navarro-García et al** (Nephrol Dial Transplant 34 (11):1864) demonstrated that **FGF23** promotes rhythm alterations and contractile dysfunction in adult ventricular cardiomyocytes. Interestingly, both contraction dysfunction and pro-arrhythmic Ca^{2+} events induced by FGF23 were blocked by soluble Klotho. **M.R. Hanudel et al** (Nephrol Dial Transplant 34 (12):2057) analyzed the effects of erythropoietin on the production and metabolism of FGF23 in a translational study (mice and humans). **H. Xu et al** (Nephrol Dial Transplant 34 (12):2051) found, in contrast to the common notion that FGF23 causes clinically significant sodium retention, that FGF23 is independently associated with an *increased* FENa in non-dialysis CKD patients. Therefore, **C.A. Wagner et al** (Nephrol Dial Transplant 34 (12):1986) analyzed in an editorial what the role of FGF23 is in cardiovascular disease, and that it may be more complicated than initially anticipated. Finally, **J.M. Valdivieso et al** (Nephrol Dial Transplant 34 (12):2079) described that the presence of the allele T of the single nucleotide polymorphism rs495392 of the Klotho gene is associated with a decrease in the odds of progression of atheromatosis in CKD patients.

- **Miscellany: Rottembourg et al** (Clin Kidney J 12 (6):871) underlined the importance of early treatment of secondary hyperparathyroidism (SHPT) by retrospectively analyzing **parathyroid hormone (PTH)** control in French hemodialysis patients treated with cinacalcet. **T. Sato et al** (Clin Kidney J 12 (5):686) examined the relationship between renal tubular damage after **parathyroidectomy** and potential signaling pathways. **K. Hamada-Ode et al** (Nephrol Dial Transplant 34 (8):1426) described different kinetics of serum **Dkk1** and **sclerostin** in their Japanese patients with CKD, and that in stage 1-3 CKD, Dkk1 is a prognostic indicator for the progression of CKD. Finally, **M. Bonani et al** (Nephrol Dial Transplant 34 (10):1773) described the beneficial effect of denosumab not only on bone mineral density but also on the trabecular bone score (TBS) in the novo kidney transplant patients.

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