



NEWSLETTER # 6 (2), 2016

CKD-MBD related publications in the ERA-EDTA journals

The ERA-EDTA acknowledges the high clinical and scientific relevance of the syndrome CKD-MBD, 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 2016, **26 CKD-MBD related articles** have been published; 21 in [Nephrology Dialysis and Transplantation](#) (including 2 PRO-CON debates) and 5 in [Clinical Kidney Journal](#).

- 1) The potential indication of **phosphate (P)-binders** in chronic kidney disease (CKD) stage 3-4 was a matter of an interesting PRO-CON debate between Drs **A. Bellasi** ([Nephrol Dial Transplant 31:184-188](#); [Nephrol Dial Transplant 31: 194-195](#)) and **B. Kestenbaum** ([Nephrol Dial Transplant 31: 189-194](#); [Nephrol Dial Transplant 31: 188-189](#)). Dr Bellasi defended the central importance of P balance in stage 3–4 chronic kidney disease considering that, until new evidence becomes available, it is reasonable to lower P burden (possibly avoiding calcium overloading) in hyperphosphatemic CKD patients. On the other hand, Dr Kestenbaum considered that no intervention to lower serum P concentrations in CKD should be applied until evidence is produced that the same intervention produces benefits and does not cause any harm. **Drs C. Zoccali and F. Mallamaci**, as moderators, concluded that “phosphate binders in CKD patients: a clear ‘No’ at the moment, but stay tuned” ([Nephrol Dial Transplant 31: 196-199](#)) because novel information in regard to this field is expected soon (COMBINE, ANSWER studies). Moderators underlined that, in essence, both contenders agreed that there is still insufficient knowledge to recommend the use of P-binders in pre-dialysis CKD patients, particularly because the risk of harm cannot be safely excluded. A full-review on the challenge of controlling P in CKD was published later by Dr **J.B. Cannata-Andía and K. J. Martin** ([Nephrol Dial Transplant 31: 541-547](#)). Finally, **L. Tran et al** ([Nephrol Dial Transplant 31:636-645](#)), reported an interesting association between higher phosphorus levels (≥ 3.5 mg/dL) and a greater likelihood for anemia in a huge population [155,974 individuals with early CKD and normal kidney function (>30 mL/min/1.73 m²)], and **G. Rosa-Díez et al** ([Clin Kidney J 9:481-485](#)) described that hemodialysis patients receiving sevelamer show higher serum magnesium levels and a reduced risk of hypomagnesemia. This effect could contribute to the still controversial superiority of sevelamer in preventing vascular calcifications.
- 2) Another interesting PRO-CON debate was published on the use of *nutritional vs active vitamin D* replacement in CKD by Dr **D. Goldsmith** ([Nephrol Dial Transplant 31:698-705](#); [Nephrol Dial Transplant 31: 713](#)) and Drs **R Agarwal and P.I. Giorgianos** ([Nephrol Dial Transplant 31: 706-713](#); [Nephrol Dial Transplant 31: 705](#)). Dr Goldsmith considered that it is more prudent to start ‘the fight against bone disease’ using cheap, natural and safe interventions, such as ergocalciferol and cholecalciferol, at the very first signs of PTH elevation. On the other hand, the opponent’s included an updated meta-analysis and considered that vitamin D supplementation restores the levels but not the vitamin D deficiency in CKD; consequently, using *activated* vitamin D would be the right way to go. Moderators, **Drs C. Zoccali and F. Mallamaci** ([Nephrol Dial Transplant 31: 714-716](#)) considered that whether inactive forms of vitamin D remain biologically and clinically ineffective in advanced CKD or whether replenishing vitamin D stores in these patients may

have protective effects beyond those afforded by adequate amounts of active vitamin D will likely remain an untested question, at least in the short and medium terms. They also provided an interesting box on milestones in vitamin D knowledge. Finally, Drs **S. Mazzaferro and M. Pasquali** ([Nephrol Dial Transplant 31: 23-30](#)) reviewed both the dynamic biologic evolution and chemistry of the vitamin D system, providing an increased understanding of its biological complexity and envisaging why therapies with vitamin D are still a matter of debate.

- 3) **I.A. Andersen et al** ([Nephrol Dial Transplant 31: 767-772](#)) reported that patients with acute decompensated heart failure (HF) had markedly elevated plasma **fibroblast growth factor-23 (FGF23)** levels. Myocardial FGF23 gene expression was present in HF at a similar level as normal controls, and immunohistochemistry showed similar cellular distribution of FGF23 in HF and controls, suggesting that the myocardium did not contribute to the elevated FGF23 in HF. An associated editorial by **O.M. Gutiérrez** ([Nephrol Dial Transplant 31: 688-690](#)) underlined that Andersen's data suggest that while cardiomyocytes have the capability to synthesize and secrete FGF23, HF per se does not up-regulate this process and provide new incentives to further elucidate the spectrum of ways that excess FGF23 impacts cardiac function and how it may ultimately contribute to the pathophysiology of HF in CKD.
- 4) **Cardiovascular calcification (CVC)** in CKD was nicely updated by **G. Schlieper et al** ([Nephrol Dial Transplant 30: 31-39](#)) underlining that a plethora of factors contribute to the development of CVC in CKD. Different pathologies may have overlapping yet distinct mechanisms and vascular smooth muscle cells are actively involved in the process of media calcification. Therapy should aim at correcting the imbalance of promoters and inducers to prevent the initiation and progression of CVC. On the other hand, **E. Hecht et al** ([Nephrol Dial Transplant 31: 789-797](#)) describe *in vivo* and *in vitro* that gelatinases such as matrix-metalloproteinases 2 and 9 (MMP2 and MMP9) provide essential signals for phenotypic vascular smooth muscle cell conversion, matrix remodelling and the initiation of CVC. Consequently, their inhibition may be a promising strategy in the prevention of CVC. Finally, **G. Cianciolo et al** ([Clin Kidney J 9:280-286](#)) reviewed the role of calcifying circulating cells in CVC in CKD patients and **R. Caluwé et al** ([Clin Kidney J 9:273-279](#)) reviewed the ongoing randomized controlled trials on the effects of vitamin K supplements and antagonists on the progression of CVC. A case series on the multimodal treatment of calciphylaxis were published by **D. Russo et al** ([Clin Kidney J 9:108-112](#)).
- 5) **Miscellaneous contents:**
 - a. **J.B. Wetmore et al** ([Nephrol Dial Transplant 31: 103-111](#)) described the changes in **CKD-MBD-related parameters** (i.e. PTH, Ca, P) and medication use following **parathyroidectomy** in 1402 patients. In a different observational study, **A.S. Artan et al** ([Clin Kidney J 9:486-493](#)) described **sex differences** in serum P, PTH and vitamin D use in incident and prevalent male and female dialysis patients.
 - b. **M. Jadoul and T. Druke** ([Nephrol Dial Transplant 31: 507-509](#)) wrote an editorial updating **β_2 -microglobulin amyloidosis** after the report by **J. Hoshino et al**. ([Nephrol Dial Transplant 31: 595-602](#)). After the flood of publications in the late 1980s and early 1990s, and the shared view that the incidence and severity of the disease had greatly decreased thereafter, the field became nearly silent until this publication. The authors reported on the significance of the decreased risk of dialysis-related amyloidosis based on results of Japanese surveys.
 - c. A report from the ESPN/ERA-EDTA registry shows considerable variations in **growth hormone (rGH) policy and prescription in paediatric** ESRD across Europe. Along this publication by **M. van Huis et al** ([Nephrol Dial Transplant 31:609-619](#)) it is shown that in many countries the actual rGH prescription in growth-retarded ESRD children is low. Nutritional intake and metabolic bone disease were prioritized over starting rGH.

- 6) Finally, contents of the 2016 Vienna ERA-EDTA Congress can be found in the [2016 Nephrol Dial Transplant Supplement # 1](#).



Oral sessions on [Mineral Metabolism](#) and [CKD-MBD](#) can be found following each one of these links, as well as Poster Sessions on [Chronic Kidney Disease Bone Disease](#) and [Dialysis Bone Disease](#).

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on behalf of the ERA-EDTA WG