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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 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 2015, **27 CKD-MBD related articles**, including several editorial comments and experimental studies, have been published; 21 in Nephrology Dialysis and Transplantation and 6 in Clinical Kidney Journal.

1) **Phosphate (P)-related literature** has been shown to be prolific during this semester due to the importance of hyperphosphatemia in CKD patients, although P is an essential element for life and a rare element in the universe (editorial by **C.J. Ferro et al**, Nephrol Dial Transplant 30:163-168). **G. Block and T. Isakova** wrote another editorial ("Tip-toeing toward the finish line", Nephrol Dial Transplant 30: 1-3) based on the article published in the same January issue by **H. Komaba et al** (Nephrol Dial Transplant 30: 107-114) on the survival advantage associated with lanthanum carbonate for hemodialysis patients with uncontrolled hyperphosphatemia. It has been suggested for a long time now the potential survival advantage associated with P binder use, particularly with non-calcium based P binders, but in addition to patient-reported outcomes, randomized, controlled clinical trials are still needed to confirm or disprove this survival advantage. This is especially important taking into account the burgeoning cost and expanding number of "novel" P binders.

   A review on iron-based P binders (ferric citrate and sucroferric oxyhydroxyde) has been reported in Clin Kidney J 8: 161-167 by **A.L. Negri and P.A. Ureña-Torres**. Long-term (1 year) effects of sucroferric oxyhydroxyde as compared to sevelamer were published by **J. Floege et al** (Nephrol Dial Transplant 30:1037-1046). The important issue of drug adherence (including management of hyperphosphatemia and hyperparathyroidism management in CKD patients) was reviewed by **M. Burnier et al** (Nephrol Dial Transplant 30:39-44). Finally, indirectly related to P removal by dialysis, clearances of urea, creatinine and P (equivalent continuous clearance) as a P adequacy parameter were analyzed by **M. Debowska et al** (Nephrol Dial Transplant 30:129-136).

2) **Cardiovascular calcifications** were debated in a NDT polar-view controversy. **J. Bover et al** on behalf of the CKD-MBD EDTA working group defended the position that CV calcifications are clinically relevant (Nephrol Dial Transplant 30: 345-351; opponent's comments Nephrol Dial Transplat 30: 351-352). Although hard-outcome data is limited, screening for CV calcifications in selected patients seems reasonable, especially considering that *progression* of CV calcification seems to decrease or might be favored by certain CKD-MBD-related drugs. On the other hand, **C. Zoccali and G. London** stated that CV calcification is a surrogate marker, but not the cause of ongoing vascular disease, and it is not a treatment target in CKD (Nephrol Dial Transplant 30:352-357; opponent's comments Nephrol Dial Transplant 30: 357). **C. Wanner**, as moderator, concluded that treatment of CV calcification is a physical impossibility, so far

(Nephrol Dial Transplant 30: 358-359). Interestingly, *high* estimated GFR has been associated with coronary artery calcification in middle-aged Korean men *without* CKD (**H.M. Choi et al**, Nephrol Dial Transplant 30:996-1001) and thus, similar to other risk factors in nephrology, GFR is bidirectionally associated with CV disease. **I.E. Emrich and G.H. Heine** wrote a related editorial wondering whether "too much kidney function will kill you: just as none at all" (Nephrol Dial Transplant 30: 869-870).

3) A new **meta-analysis** on the effect of **vitamin D analogs** on mortality and CV outcomes among adults with CKD, including dialysis patients, has been published by **M.C. Mann et al** (Clin Kidney J 8: 41-48). This meta-analysis did not provide sufficient or precise evidence that vitamin D affects mortality or CV risk in CKD. However, as is stated by **L.F. Morrone and M. Cozzolino** (Clin Kidney J 8: 38-40), it is not the time to state that interventions based on vitamin D may reduce mortality in patients with CKD, but the opposite cannot be said yet beyond reasonable doubt. In different studies, **A. Pisani et al** (Nephrol Dial Transplant 30:661-666) showed that added-on **paricalcitol** in Fabry disease patients was effective in reducing proteinuria, and **A.C. Baxmann et al**, Clin Kidney J 8:49-53) described that overweight and body fat were predictors of hypovitaminosis D in renal transplant patients.

4) An ERA-EDTA position statement on the prescription of **calcimimetics** in dialysis patients with biochemical evidence of secondary hyperparathyroidism was published by **D. Goldsmith et al** (Nephrol Dial Transplant 30: 698-700). It is *not* recommended the routine use of calcimimetic therapy *to improve survival* in these patients, and that there is insufficient evidence whether parathyroidectomy or medical intervention with cinacalcet or standard care or a combination thereof should be preferred to control secondary hyperparathyroidism.

5) An interesting case-report on the treatment with **teriparatide** of a dialysis patient with recurrent bone fractures and biopsy-proven adynamic bone disease was described by **P. Giamalis et al** (Clin Kidney J 8:188-190).

6) Results from the NECOSAD study by C**. Drechsler et al** (Nephrol Dial Transplant 30: 288-293) show that *high* levels of serum **sclerostin** are associated with lower short-term cardiovascular mortality in dialysis patients. The importance of **calcitonin** ("the forgotten hormone") and its potential effects on osteocyte products, among other actions, has been recently reviewed by **A.J. Felsenfeld** and **B.S. Levine** (Clin Kidney J 8:180-187).

7) **S.L. Barker et al** (Nephrol Dial Transplant 30: 223-233), using an *immunoprecipitation-immunoblot* assay, measured both serum and urinary levels of full-length **soluble αKlotho** in humans, and established that human CKD is associated with αKlotho deficiency in serum and urine with this new technique. **K. Eckberg et al** (Nephrol Dial Transplant 30: 630-635) described the impact of living in a more westernized society on **FGF-23** levels among individuals of African ancestry. It is shown that "westernalization" may be associated with greater net phosphate absorption, as reflected by higher urinary phosphate excretion and higher FGF23 levels.

8) **M.V. Arcidiacono et al** described in two basic-science articles that the induction of C/EBPβ contributes to vitamin D inhibition of ADAM17 expression (attenuates the severe ADAM17/TGFa synergy) which drives **parathyroid hyperplasia** and high PTH in kidney disease (Nephrol Dial Transplant 30: 423-433). Additionally, they have shown that parathyroid EGFR activation is essential for parathyroid hyperplasia and VDR loss in CKD in a transgenic mouse model (Nephrol Dial Transplant 30:434–440).

9) Finally, **P. Evenepoel et al** (Nephrol Dial Transplant 30: 843-848) demonstrated that prevalence rates of microscopic **nephrocalcinosis** increase with increasing CKD stage to reach more than 50% in end-stage renal disease patients, and suggest that acid–base and mineral metabolism disturbances are implicated in its pathogenesis.

Some contents of the 2015 London ERA-EDTA Congress can be found in the Nephrol Dial Transplant Supplement # 3

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on behalf of the ERA-EDTA WG