NEWSLETTER 2014

CKD-MBD related publications in the ERA-EDTA journals

Starting from this newsletter, as a contribution of ERA-EDTA communication team, we are going to report on the most recent papers published on the journals of our society and dealing with CKD-MBD. We summarize here the content of a first group of papers providing a link to their abstracts.

From January to June 2014, 19 CKD-MBD related articles have been published, 15 in Nephrology Dialysis and Transplantation and 4 in the Clinical Kidney Journal. Only two experimental studies were published in this period.

1) A full review on circulating biomarkers to monitor bone turnover in CKD hemodialysis (HD) patients (hypothesis and facts) was published by P. Delanaye et al (Nephrol Dial Transplant 29: 997-1004) and the different effects of paricalcitol- or cinacalcet-centred therapies on markers of bone disease in HD patients with secondary hyperparathyroidism (2HPT) was reported by M. Cozzolino et al (Nephrol Dial Transplant 29: 899-905).

In the first review, it is stated that PTH is still the most widely used but is in sensu stricto not the best bone biomarker, whereas bone alkaline phosphatase (AP) can be considered a true bone biomarker. The potential interest of other molecules is thoroughly discussed. The second publication reports secondary results from the IMPACT-SHPT study (Ketteler M et al. Nephrol Dial Transplant 27:3270-3278, 2012), and shows that paricalcitol-centred therapy reduced circulating bone turnover markers such as AP and bone-AP and increased FGF-23 levels as compared with cinacalcet-centred therapy.


Importantly enough, it is shown that the variability of C-terminal FGF-23 for 2-years is small, and confirms FGF-23 as an important predictor of major clinical events in patients with CKD. Moreover, single measurements seem to reliably represent individual’s FGF-23 status over time as long as kidney function remains stable.

3) An important summary on the basic principles of arterial hemodynamics and various methodologies to assess arterial stiffness and the latest recommendations for clinical applications has been published by P. Boutouyrie et al (Nephrol Dial Transplant 29: 232-239). It includes methodological considerations for validation and entry into the European Renal and Cardiovascular Medicine registry.

4) Several publications deal with different forms of phosphate (P) control. F. Locatelli et al (Nephrol Dial Transplant 29: 1239-1246) reports a posthoc analysis of the CONVESTUDY, examining P levels in patients treated with low-flux HD, pre-dilution haemofiltration and haemodiafiltration. In this study, convective techniques did not significantly affect serum P levels and P variability was mainly explained by a center effect. In a different study, J. Zaritsky et al (Nephrol Dial Transplant 29: 437-441) reported lower C-terminal FGF-23 levels in short daily HD patients despite similar serum calcium, P and PTH levels in patients treated with conventional HD. In a 1-year prospective randomized study, F. Locatelli et al (Nephrol Dial Transplant 29: 1061-1073) reported that colestilan, a new anion-exchange resin that binds both P and bile acids in the gastrointestinal tract, is effective and safe in HD patients and achieves similar P and cholesterol reductions/responder rates than sevelamer. Finally, N. Chen et al (Nephrol Dial Transplant 29: 152-160) published their randomized, double-blind, placebo-controlled study of sevelamer carbonate over 8 weeks in Chinese HD.
patients.

5) Regarding **PTH control**, a single dose of Velcalcetide (AMG 416), a novel IV peptide agonist of the calcium-sensing receptor (CaSR), reduced serum PTH and FGF-23 in healthy male subjects in a phase 1 study conducted by **K. J. Martin et al** (Nephrol Dial Transplant 29: 385-392) supporting current studies evaluating velcalcetide as a treatment for 2HPT in HD patients. **P. Molina et al** (Nephrol Dial Transplant 29: 97-109) reported that 666 IU/day of cholecalciferol in non-dialysis CKD patients not only decreased PTH and induced a mild rise in P levels but also a beneficial effect in decreasing albuminuria was observed.

6) **J. Wagner et al** (Nephrol Dial Transplant 29: 146-151) observed an increase in hospitalized central and peripheral **bone fracture rates** from 1992 to 2004 among elderly United States HD patients analyzing the USRDS datasets, specially in elderly white female patients. This trend abated with stabilization, but remained high, between 2004 and 2009. Overtreatment, increased burden of illness and comorbidities were postulated as potential explanations for these observations.

7) Chronic **hypercalcemia** from inactivating mutations of vitamin D 24-hydroxylase (CYP24A1) was described by **G. Colussi et al** (Nephrol Dial Transplant 29: 636-643) indicating not only that CYP24A1 is a key physiologic regulator of calcitriol and calcium levels but also that a balanced reduction in calcitriol and the glomerular filtration rate are instrumental for CKD. A clinical report of metabolic acidosis-induced hypercalcemia in an azotemic patient with primary hyperparathyroidism in a sepsis context was described by **M. Rastegar et al** in the Clin Kidney J 7: 299-302.

8) **M.E. Rodríguez-Ortiz et al** (Nephrol Dial Transplant 29: 282-289) have shown that **magnesium** (Mg) reduces PTH secretion by incubating intact rat parathyroid glands in different calcium and Mg concentrations **in vitro**. This observation was mainly observed when a moderate-low clinically relevant calcium concentration was present. Mg also upregulated all key cellular receptors at the mRNA and protein levels. In clinical grounds, both Mg and FGF-23 levels were independent predictors of **pulse pressure** in a report of 80 type 2 diabetic patients with CKD stages 2 to 4 (A. Fragoso et al, Clin Kidney J 7: 161-166). Other cardiovascular risk markers such as β₂-microglobulin, FGF-23, IL-8, IL-18, IL2-RA or TNF-R1 were associated with coronary **artery calcification**, abdominal and/or thoracic aortic calcification in patients with CKD stage 3-4 according to **C.I.K. Weber et al** (Clin Kidney J 7: 167-173).

9) **A. Amblee et al** (Clin Kidney J 7: 186-189) published an interesting clinical report of a giant cell tumor in the right foot causing **tumor-induced osteomalacia** with **normal** systemic FGF-23 levels (but elevated FGF-23 values on the right femoral vein)

10) Finally, an experimental study by **D. Rubel et al** (Nephrol Dial Transplant 29: 1012-1019) shows the known antifibrotic, nephroprotective effects of paricalcitol versus calcitriol on top of ACE-inhibitor therapy in the distinct COL4A3 knockout mouse model for progressive renal fibrosis.