Effects of Parathyroidectomy on Plasma Different Parathyroid Hormone Fragments Levels in Chronic Kidney Disease Patients
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Background:
Intact parathyroid hormone (iPTH) measured by the second generation assays include not only (1-84)PTH, but also (7-84)PTH. Now the third generation PTH assays have been shown specific test for (1-84)PTH. Here we investigated the levels of plasma iPTH, (1-84)PTH, (7-84)PTH in stage 5 chronic kidney disease (CKD) patients, and evaluate the effects of parathyroidectomy(PTX) on above parameters in severe secondary hyperparathyroidism(SHPT) subgroups.

Methods:
We included 252 CKD patients divided by baseline plasma iPTH levels. Thirty-one PTX patients were followed up with median time of 7.1 months. Serum iPTH and (1-84)PTH were measured and (7-84)PTH levels were calculated by subtracting the (1-84)PTH values from the iPTH values.

Results:
Plasma iPTH, (1-84)PTH, (7-84)PTH levels were closely related with each other, while (1-84)PTH/iPTH gradually reduced with upregulated iPTH levels. For CKD subgroups with plasma iPTH level>800 pg/ml, (1-84)PTH/iPTH furtherly decreased to 0.5(Fig1). After PTX, plasma different PTH fragments levels were decreased obviously and (1-84)PTH/iPTH were increased in severe SHPT patients(Table 1).

Conclusion: PTX can diminish abnormal increased iPTH, (1-84)PTH,(7-84)PTH levels and upregulate (1-84)PTH/iPTH for severe SHPT patients. Blood iPTH value may overestimate the severity of SHPT. Measurement of (1-84)PTH is suggested for accurate diagnosis and treatment in chronic kidney disease-mineral and bone disorder(CKD-MBD) patients.

Key words: Chronic kidney disease; mineral and bone disorder; (1-84)PTH; (7-84)PTH; Secondary hyperparathyroidism; Parathyroidectomy
Management of bone and mineral metabolism disorders before the dialysis stage remains still perfectible. Data from the French Phosphorus and Calcium Survey « Photo-Graphe »

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Background: Only limited data is available on the management of the chronic kidney disease-associated bone and mineral metabolism disorder (CKD-MBD) in the pre-dialysis stages of CKD in France. A better knowledge of current management habits could lead to an improvement in the implementation of international recommendations (KDIGO).

Methods: The 3rd version of the French Phosphorus and Calcium Survey “Photo-Graphe” (Sanofi) included a cohort of CKD stage 4 and 5 patients, whose aim was to examine the prevalence of CKD-MBD and the quality of its management in patients under the care of 62 nephrologists from over 20 geographical regions in France. The study started in October 2011, i.e. one year after patient enrollment. We examined in particular the prevalence therapeutic inertia, defined as the percentage of patients presenting with laboratory parameter abnormalities indicative of CKD-MBD who were not receiving adequate treatment.

Results: A total of 456 patients with CKD stage 4 and 154 with CKD stage 5 were studied. Their mean age was 72.9 ±14.2 years, and male/female ratio was 58/42. KDIGO targets of serum PTH for CKD stages 4 and 5 were not achieved in respectively 80 and 84% of the patients, for serum calcium in 8 and 22% and for serum phosphate in 12 and 46%. As a potential explanation, therapeutic inertia was estimated to account for respectively 45 and 60% of insufficiently controlled secondary hyperparathyroidism, and for 36% of persistent hyperphosphatemia in stage 5. It should be noted that 55.5 and 57.5 % of patients were receiving native vitamin D.

Conclusion: In this national Observatory, the management of CKD-MBD stages 4 and 5 appears suboptimal, especially as regards the control of secondary hyperparathyroidism which remained untreated in nearly 50% of the patients. Hyperphosphatemia was also common and inadequately controlled in CKD stage 5. To improve the management of CKD-MBD, nephrologists need to be more aware of the importance of aiming for recommended laboratory targets and how this can be achieved.
Comparative analysis of serum fgf-23, klotho, sclerostin, phosphorus, PTH levels, as well as EGFR and central systolic blood pressure as factors associated with cardiovascular calcification in chronic kidney disease Russian patients

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BACKGROUND: Cardiovascular calcification (CVC) is a major contributor to cardiovascular risk in CKD. Early CVC markers are actively sought now to improve prognosis of CKD patients. We have conducted a cross-sectional study of the main factors suggested associated with CVC, including serum Klotho (sKlotho), FGF-23 and sclerostin in CKD. METHODS: 130 CKD stage 2-5D Russian patients were examined. In addition to routine tests, sKlotho (human soluble alfa-Klotho Assay, IBL-Takara), FGF-23 (FGF-23 ELISA, Merk Millipore, kit using monoclonal antibodies to the native human FGF-23 molecule), sclerostin (human sclerostin ELISA kit, Biomedica, Vienna) were measured; augmentation indices, central blood pressure (BP) - by «Sphygmacor» (Australia); valvular calcification - by Echocardiography, semiquantitative scale, and aortic calcnosis - by abdominal aorta radiography in lateral projection, were done. All procedures were performed in accordance with Helsinki Declaration. RESULTS: The association of studied factors (serum FGF-23, sKlotho, sclerostin along with phosphorus, PTH, central systolic BP, eGFR) with CVC was carried out in three models (1st-augmentation index, 2nd-valvular calcification and 3rd-aorta calcification) in univariate (UVA) and multivariate (MVA) analyses. In UVA, all studied factors were associated with valvular and vascular calcification in all three models. After MVA, associated with CVC remained sKlotho (in two models), central systolic BP (in two models), sclerostin, phosphorus, eGFR – in one model. CONCLUSIONS: In CKD 2-5D stages patients the most associated with CVC factors are sKlotho and central systolic BP.

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Cardiac Troponin I and FGF-23 in ckd patients

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Abstract:

BACKGROUND: Serum FGF-23 increases in early CKD stages (2-3A) and suggested damages myocardium, but exacted mechanisms of it have not been determined yet. At the same time detectable cardiac troponins serum levels are often observed in CKD patients, even in asymptomatic cardiovascular disease. The aim of the study was to investigate the possible associations of FGF-23 and high-sensitivity cardiac troponin I (TPI) serum levels in CKD patients.

METHODS: In addition to routing laboratory examination, serum FGF-23 (Human FGF-23 ELISA, with monoclonal antibodies to native human FGF-23 molecule, Merk Millipore), TnI (high-sensitive human TnI ELISA assay, Biomerica) and instrumental examination: Echocardiogram, central arterial blood pressure (CBP) and blood supply of endocardium (BSE) by "Sphygmacor" (Australia) were measured in 130 stable patients with non-dialysis CKD stages 2-5.

RESULTS: In univariate analysis serum TPI correlated with: FGF-23 \( r = 0.536; p<0.01 \), PTH \( r = 0.446; p<0.05 \), LVMMI \( r = 0.449; p<0.05 \), diastolic dysfunction of the left ventricle \( r = 0.523; p<0.05 \), BSE \( r = 0.543; p<0.01 \), central diastolic BP levels \( r = 0.546; p<0.01 \), eGFR \( r = -0.497; p<0.01 \). The multivariate analysis, including FGF-23, PTH, eGFR, central diastolic BP levels, LVMMI, has showed the independent association of TPI only with FGF-23 levels in the CKD patients \( \beta = 1.256; p = 0.019 \).

CONCLUSIONS: In this study, according to multivariate analysis, minimally-moderate elevated TPI serum levels were associated with elevated FGF-23 levels in the stable non-dialysis CKD 3-5 stages patients. So FGF-23 may be the cause of the detectable TPI serum levels observed in CKD patients.

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Glycoprotein sclerostin and vascular calcification in Russian patients with chronic kidney disease

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BACKGROUND: Sclerostin is actively studied now as novel cardiovascular calcification (CVC) participant in chronic kidney disease (CKD), but results are conflicting. The aim of the study was to examine the association of serum sclerostin with CVC in CKD Russian patients.

METHODS: In addition to routing investigations, serum sclerostin levels (ELISA, Biomedica, Vienna), central blood pressure (CBP), pulse wave velocity (PWV) - by «Sphygmacor» device (Australia), EchoCG, X-ray of the abdominal aorta (Kauppila method) were measured in 130 CKD 2-5D stages patients

RESULTS: It was found serum sclerostin levels were increased as CKD advanced, starting at 3A stage, while serum phosphorus and PTH were increased from 4-5 CKD stages. In univariate analysis serum Sclerostin correlated with: systolic CBP \( r = 0.542; p<0.01 \), PWV \( r= 0.632; p<0.01 \), degree of heart \( r=0.612; p<0.01 \) and abdominal aorta calcification (AAC) \( r=0.523;p<0.01 \), LVMMI \( r=0.545; p<0.01 \). In the multivariate analysis, including sclerostin, FGF-23, phosphorus, eGFR and central systolic BP, independent associations of the heart calcification \( 0.011; p=0.032 \) and \( 0.079; p=0.001 \) as well as AAC \( 0.113; p=0.004 \) were obtained only for both serum sclerostin and central systolic BP. At the same time, we can see inversing of the sign of «beta» for sclerostin from «plus» - in univariate to «minus» - in multivariate analysis that may indicate protective role of sclerostin in CVC.

CONCLUSIONS: According to multivariate analysis, increased serum sclerostin as CKD advanced may be directed against CVC progression and may be useful as early marker protected cardiovascular system in CKD.
Possibilities of protein restriction diet supplemented with essential amino acids ketoanalogues for correction of FGF-23 and klotho disturbances in chronic kidney disease 3b-4 stages Russian patients

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Abstract:

BACKGROUND: FGF-23 and Klotho play an important role in cardiovascular complications in CKD. The aim of the study was to evaluate the effect of low protein diet (LPD) supplemented with essential amino acids ketoanalogues (KA) on serum FGF-23 and Klotho levels in CKD.

METHODS: 51 CKD stage 3B-4 patients were included in the study. The patients were divided into 2 groups depending on the diet type. The group 1 (n=25) got LPD-0.6 grams/kg of weight/day and KA (Ketosteril) -1 tabl/5 kg of weight/day during 12 studied months; the group 2 (n=26) matched to the 1st group, took LPD without KA. FGF-23 (FGF-23 ELISA, Merk Millipore), Klotho (soluble alpha-Klotho Assay, IBL-Takara) as well as Bioimpedance analysis, echocardiography and pulse wave velocity (PWV) by "Sphygmacor" were performed.

RESULTS: None of the group 1 patients was found any nutritional status disorders, while five patients of group 2 have decrease in body mass index (BMI) and muscle mass (p<0,05). Group 1 patients had lower serum FGF-23, PTH, phosphorus (p < 0,05) and higher Klotho and eGFR (p<0,05), than group 2. In the multivariate analysis independent factor correlated with higher serum Klotho was LPD+KA (beta=0,48;p=0,02), but not isolate LPD (beta=0,94;p=0,86). Cardiac calcification scores and PWV increase were detected more often [9% vs 16%, p=0,04 and 10% vs 21%, p =0,02, respectively] in 2nd group as well as the degree of mass miocardium indices increase (23% vs 12%).

CONCLUSIONS: Supplementation of KA to LPD in CKD patients provides not only stable nutritional status, but can correct FGF-23 and Klotho that totally contribute to reduction of cardiovascular risk in CKD patients.
Influence of calcium concentration on PTH level using citrate dialysate
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Background
The citrate dialysate (CD) is increasingly used. Calcium balance and hyperparathyroidism control could be altered due to the lower concentration of ionized calcium in dialysis fluid between acetate (AD) and CD. Randomized studies are not always transposable in the real life. The aim of this prospective study is to assess clinical and biological parameters after switch from acetate to citrate dialysate in 4 self-dialysis units.

Methods
56 HD patients (63±14 yrs, M/F: 36/20), treated in 4 self-dialysis units (one nephrologist visit and one biological evaluation per month) were switched from AD to CD. Calcium concentration was 1.5 mmol/l vs 1.75 to ensure same calcium mass balance based on literature review. Usual monthly biological evaluations (including PTH) were performed in 4 different laboratories (close to the unit, far from the main dialysis in-center) during 6-month follow-up.

Results
Calcemia was not different at 6 months over citrate dialysate (2.21mmol/l versus 2.24mmol/l at M6, p=0.26). PTH was significantly lower at 6 months (462pg/ml versus 306 pg/ml, p=0.0003). 3rd generation PTH assay changed in 2 laboratories. Upper limit of normal range is different between the 2 kits. Patients KDIGO classification could be different. Using an electronic patient database, the physician is not always aware of this change.

B2M decreases (30.76mg/l versus 27.01mg/l, p<0.001). Adverse events (muscles spasms, hypotension) seemed to be lower under citrate dialysate and no coagulation problem occurred.

Conclusion
Citrate dialysate with higher calcium concentration compare with acetate dialysate can decrease PTH blood level but the attention of physician could be drawn on PTH kit change.