CKD-MBD II

**MP516** KDIGO-RECOMMENDED PTH LEVEL ACCELERATES AORTIC CALCIFICATION IN PATIENTS NEW TO HEMODIALYSIS

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**Introduction and Aims:** Vascular calcification is an important factor influencing cardiovascular complications and the vital prognosis in hemodialysis patients. However, a target level of PTH and a guide for medical practice to prevent vascular calcification are not clearly defined in the KDIGO’s guidelines and are controversial. We investigated the development and progression of aortic calcification in the early stage of hemodialysis initiation.

**Methods:** We performed a retrospective cohort study in 102 patients who initiated hemodialysis for end-stage kidney disease between July 2004 and June 2009 and could be followed-up for three years in our hospital. We compared the extent of calcification in the aortic arch at the time of hemodialysis initiation and three years later by reviewing postero-anterior chest X-ray. We defined an outcome as an increase in the extent of calcification by 50% and examined the factors related to this outcome using multiple logistic regression analysis.

**Results:** Aortic arch calcification was observed 66% of patients at baseline and increased to 80% during the three-year study period. In addition, forty-eight of the 102 patients achieved the outcome. The mean daily dose of calcium carbonate (1,000-mg units) for three years (odds ratio: 2.2 [95% CI 1.5 - 3.4]), an iPTH level of 180 pg/ml or above (3.9 [1.6 - 10.6]), and age (1.5 [1.0 - 2.3]) were significantly associated with progression of aortic calcification. On the other hand, the presence of diabetes, use of activated vitamin D and statin, mean levels of serum calcium and phosphorus and factors related to lipid for three years were not associated with the progression of aortic calcification.

**Conclusions:** The KDIGO’s guideline recommend PTH level is maintained in the range of two to nine times the upper normal limit in patients with CKD stage5D, regarding the relative risk of death. However, in view of vascular calcification, it is important to control the PTH levels more strictly from the early stage of dialysis initiation, in addition to reducing the doses of calcium-containing phosphate binders as far as possible.

**MP517** VARIATION IN NHS SERVICES AND ACHIEVEMENT OF TARGETS IN THE MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM IN PATIENTS WITH END-STAGE RENAL DISEASE UNDERGOING DIALYSIS IN THE UK NHS

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**Introduction and Aims:** Secondary hyperparathyroidism (SHPT) is widely prevalent in patients undergoing dialysis and is associated with significant morbidity and mortality. There are several differing target ranges set by the renal association, KDIGO and KDOQI with anecdotal evidence of significant variation in practice across UK renal units. The aim of this study was to examine the achievement of targets for calcium, phosphate and PTH according to the various available guidelines and relate this to staffing and services across 8 UK renal units.

**Methods:** A retrospective multi-centre study was undertaken in 8 UK renal units purposely selected to include a variety of sizes and geographical locations. Calcium, phosphate and PTH results were extracted from renal unit databases and data regarding renal unit service structure and local policies related to SHPT management was obtained through a key informant questionnaire and review of written policies. Results: 2361 patients were included from 8 UK renal Units. Number of dialysis patients from each centre ranged from 110 to 636. Geographical locations ranged from Dundee in Scotland to Exeter in the South of England. Overall achievement of targets was low with 11% of all patients with all 3 biomarkers within the Renal Association and KDOQI targets and 23% within the KDIGO targets. Reported staffing varied between the units ranging from 27 patients per consultant to 91 patients per consultant. Dietician and renal pharmacist input also varied from 55 patients per dietician to 154 patients and 110 patients per renal pharmacist to no renal pharmacist. The 2 units with the highest number of patients achieving target range for calcium, phosphate and PTH differed considerably in staffing (27 vs 91 patients per consultant, 75 vs 159 patients per dietician and 195 vs 636 patients per renal pharmacist for the 2 sites respectively).

**Conclusions:** Achievement of targets for calcium, phosphate and PTH are low across all dialysis centres, not helped by differing target ranges and a lack of consensus as to what constitutes best practice in SHPT management. In line with this observation, this study confirms there to be no clear association between reported staffing levels and achievement of targets.

**MP518** THE NUMBER OF OXYPHIL CELLS INCREASES IN SECONDARY HYPERPARATHYROIDISM

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**Introduction and Aims:** The number of oxyphil cells (OC) increases in the parathyroid glands (PTG) of patients affected by secondary hyperparathyroidism (HPT), especially if they are treated with vitamin D and/or calcium/supplements. Furthermore, the incubation of PTG with a high calcium medium has been shown to lead to the formation of OC, consistent with the hypothesis that calcium-sensing receptor (CaSR) stimulation may increase the OC number. This hypothesis has been not tested in the clinical setting. Aim of this study was to verify whether the cell populations in the PTG can be influenced by disorders of mineral metabolism as measured before parathyroidectomy (PTx).

**Methods:** A retrospective study on 65 consecutive patients submitted to a first PTx, either total or subtotal, in our hospital in the last 4 years was performed. Biochemical parameters of PTG with a high calcium medium has been shown to lead to the formation of OC, consistent with the hypothesis that calcium-sensing receptor (CaSR) stimulation may increase the OC number. This hypothesis has been not tested in the clinical setting. Aim of this study was to verify whether the cell populations in the PTG can be influenced by disorders of mineral metabolism as measured before parathyroidectomy (PTx).

**Results:** The number of oxyphil cells (OC) increases in the parathyroid glands (PTG) of patients affected by secondary hyperparathyroidism (HPT), especially if they are treated with vitamin D and/or calcium/supplements. Furthermore, the incubation of PTG with a high calcium medium has been shown to lead to the formation of OC, consistent with the hypothesis that calcium-sensing receptor (CaSR) stimulation may increase the OC number. This hypothesis has been not tested in the clinical setting. Aim of this study was to verify whether the cell populations in the PTG can be influenced by disorders of mineral metabolism as measured before parathyroidectomy (PTx).

**Conclusions:** Achievement of targets for calcium, phosphate and PTH are low across all dialysis centres, not helped by differing target ranges and a lack of consensus as to what constitutes best practice in SHPT management. In line with this observation, this study confirms there to be no clear association between reported staffing levels and achievement of targets.
Conclusions: The morphologic prevalence of OC and TOC in HPT was associated with statistically significant increases in serum iCa and iCa serum levels, that could provoke an increase in the CT serum levels. Uremic patients affected by HPT, being exposed to higher iCa levels, may have a shift in the phenotype of parathyroid cell populations.

Differences in microarchitecture parameters of bone quality in low and high turnover renal osteodystrophy assessed by HR-pQCT

Introduction and Aims: Abnormal bone turnover is common in CKD, but its effects on bone quality remains unclear. The aim of this study was to identify differences in bone microarchitecture between patients with low vs. high bone turnover by HR-pQCT.

Methods: Twenty-two patients with severe hyperparathyroidism (PTH > 300 pg/ml for at least 3 months) were included in the study. The patients were divided into two groups according to their serum iPTH: Low bone turnover (LBT) iPTH < 200 pg/ml (n=7; mean age 52.8 ± 6.1; iPTH 124 ± 55) and high bone turnover (HTBT) iPTH > 300 pg/ml (n=15; mean age 51.6 ± 7.9; iPTH 1142 ± 669). Thirty healthy volunteers served as controls.

Results: At the DR, cancellous bone volume (BV/TV) was greatly decreased in LBT vs. HTBT (N: 13 ± 2.5%; LBT 64.3 ± 3.8%; HTBT 98.7 ± 3.7; p<0.05); trabecular thickness (TbTh) was slightly decreased in LBT and significantly increased in HTBT (N: 0.06 ± 0.01 mm; LBT: 0.046 ± 0.01; HTBT: 0.070 ± 0.01; p<0.01). Cortical Thickness (CTth) was decreased in LBT but much more in HTBT (N: 0.69 ± 0.18 mm; LBT: 0.47 ± 0.07; HTBT: 0.36 ± 0.20). Similar trends were seen for all parameters at the tibia except for a borderline significant difference in cortical volumetric density (LBT: 811 ± 69 mg HA/cm3; HTBT: 719 ± 120 mg HA/cm3; %diff: -11.4% ± 0.08).

Conclusions: We conclude that microarchitecture parameters of bone quality varies albeit by different mechanisms with different levels of bone turnover, trabecular parameters being more compromised in LBT and cortical parameters in HTBT. The lower cortical volumetric density probably reflects higher bone porosity in the HTBT patients.
Introduction and Aims: Poor physical activity and decreased daily activities are commonly seen in hemodialysis (HD) patients. Along with the progression of chronic kidney disease (CKD), various abnormalities of mineral and bone metabolism develop such as osteitis fibrosis and adynamic bone disease which are related with intact parathyroid hormone (Intact-PTH). Surprisingly scarce data exists regarding the relationship between intact-PTH and daily physical activity in HD patients.

Methods: This cross sectional included HD patients who regularly attending in a state hospital. Demographics, clinical parameters, laboratory data were recorded for all patients. Depressive symptoms, quality of life and daily activities of HD patients were measured by Beck Depression Inventory, SF-36, and Nottingham Extended Activities of Daily Living Scale (NEADLS) respectively.

Results: In total 114 patients were enrolled. The value of Intact-PTH for <25th (Group 1), <25th-50th (Group 2), 50th-75th (Group 3) and >75th (Group 4) were 132.5 ± 26.1, 132.5 ± 26.1, 51.0 ± 10.4 and 51.0 ± 10.4 respectively. The NEADLS scores were 25.3 ± 10.8, 35.0 ± 9.4, 27.2 ± 13.9 and 26.4 ± 12.9 as going from Group 1 to Group 4 patients with lowest and highest quartiles of Intact-PTH. PTH and daily activity is not linear and daily physical activity was lower only in group. However the post hoc analysis demonstrated that the association between intact-PTH and daily activity was not linear and daily physical activity was lower only in patients with lowest and highest quartiles of Intact-PTH.

Results: The megalin expressions decreased in tumors with PHPT and SHPT compared to normal parathyroid tissues. In SHPT, its expression was particularly depressed in nodular areas, compared with strong expression in normal parathyroid tissues. In hyperfunctioning parathyroid tumors, the expression of megalin may contribute vitamin D resistance and hyper-secretion of PTH in the hyperfunctioning parathyroid tumors.

Results: In total 114 patients were enrolled. The value of Intact-PTH for <25th (Group 1), <25th-50th (Group 2), 50th-75th (Group 3) and >75th (Group 4) were 132.5 ± 26.1, 132.5 ± 26.1, 51.0 ± 10.4 and 51.0 ± 10.4 respectively. The NEADLS scores were 25.3 ± 10.8, 35.0 ± 9.4, 27.2 ± 13.9 and 26.4 ± 12.9 as going from Group 1 to Group 4 patients with lowest and highest quartiles of Intact-PTH.

Conclusion: Intact-PTH levels were inversely associated with daily activities in whole group. However the post hoc analysis demonstrated that the association between intact-PTH and daily activity is not linear and daily physical activity was lower only in patients with lowest and highest quartiles of Intact-PTH.
**Abstracts**

**MP525**  
**CINACALCET DECREASES PLASMA FGF-23 CONCENTRATION IN HEMODIALYSED PATIENTS WITH CHRONIC KIDNEY DISEASE AND SECONDARY HYPERPARATHYROIDISM**  
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**Introduction and Aims:** Results of recently published clinical studies suggest that increased plasma fibroblast growth factor-23 (FGF-23) concentration in chronic kidney disease is a cardiovascular risk factor. The aim of this study was to assess influence of six months treatment with cinacalcet in hemodialysed chronic kidney disease (HD) patients with secondary hyperparathyroidism (sHPT) on plasma FGF-23 concentration.  

**Methods:** In 58 HD patients (30 males and 23 females, mean age 53.8 years) with sHPT (PTH >300) PTH (electrochemiluminescence Roche, Germany), FGF-23 (ELISA; Immunopectics, USA), calcium and phosphate concentrations were assessed before the first dose of cinacalcet and then after 3 and 6 months of treatment. The results are shown as means and 95% confidence index.  

**Results:** Serum PTH concentration was significantly decreased after 3 and 6 months of treatment from 1138 (931-1345) to 772 (551-992); p=0.0001 and 635 (430-839) pg/ml; p=0.0001, respectively. Plasma FGF-23 concentration decreased after 3 and 6 months of treatment from 593 (457-730) to 513 (380-645); p=0.099 and 433 (304-561) pg/ml; p<0.0001, respectively. Plasma FGF-23 concentration decreased after 3 and 6 months of treatment. The results are shown as means and 95% confidence index.  

**Conclusions:** 1. Treatment with cinacalcet decreases plasma FGF-23 concentration in hemodialysed chronic kidney disease patients with secondary hyperparathyroidism. 2. Clinical consequences of decreased plasma FGF-23 during the therapy with cinacalcet need to be elucidated.

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**MP528**  
**ANALYSIS OF I-KLOTHO, FIBROBLAST GROWTH FACTOR-, VITAMIN-D AND CALCIUM-SENSING RECEPTOR IN 70 PATIENTS WITH SECONDARY HYPERPARATHYROIDISM**  
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**Introduction and Aims:** Secondary hyperparathyroidism (sHPT) is known as a very common complication in patients with chronic kidney disease, and G-protein-coupled calcium-sensing receptor (CaSR), Vitamin D receptor (VDR) and Fibroblast growth factor receptor (FGFR) Klotho complexes seem to be involved in its development.  

**Methods:** Hyperplastic parathyroid glands from 70 sHPT patients and normal parathyroid tissue from 7 patients were obtained during parathyrectomy. Conventional morphological and immunohistochemical analysis of parathyroid glands was performed after dividing each slide in a 3x3 array.  

**Results:** The presence of lipocytes in the normal parathyroid gland and tissue architecture (nodal in patients with sHPT) allows for discrimination between normal parathyroid glands and parathyroid glands of patients with sHPT. Protein expression of Klotho, FGFR, CaSR and VDR was higher in the normal parathyroid glands compared to the sHPT group (p=0.001, p=0.07, p=0.01 and p=0.001). The variability of each protein expression within each tissue slide was high. Therefore correlations between the different immunohistochemical variables were analyzed for each of the nine fields and then analyzed for all patients. Using this analysis, a highly significant positive correlation could be found between the expression of FGFR and VDR (r=0.004). Interestingly, in terms of VDR we found a shift to a more mixed nuclear/cytoplasmic staining in the sHPT group compared to normal parathyroid gland cells, which showed solid nuclear staining for VDR (p=0.005).  

**Conclusions:** CaSR, VDR and an impaired Klotho-FGFR-axis seem to be the major players in the development of sHPT. Whether the detected correlation between FGFR and VDR and the shift to a more mixed nuclear/cytoplasmic staining of VDR will yield new insights into the pathogenesis of the disease has to be evaluated in further studies.
**SCLEROSTIN AND 1 YEAR SURVIVAL AMONG PATIENTS UNDERGOING HEMODIALYSIS**

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**Results:** Patients with 25-hydroxy vitamin D3 levels greater than median value and receiving calcitriol therapy (Group 2), patients with 25-hydroxy vitamin D3 levels lower than median value and not receiving calcitriol therapy (Group 3) and finally patients with 25-hydroxy vitamin D3 levels lower than median value and not receiving calcitriol therapy (Group 4) (Log-rank: p=0.0049). Increased sclerostin quartiles are associated with decreased survival (Log-rank: p<0.025). Highest sclerostin quartile (>2282 pg/ml) was associated with a 22% increase in the multivariable adjusted risk of death, as compared with the lowest quartile (<370 pg/ml) adjusted also for both calcitriol therapy and serum 25-hydroxy vitamin D3 levels.

**Conclusions:** Increased sclerostin levels seem to be independently associated with mortality among prevalent hemodialysis patients.

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**DIETARY TRENDS AND MANAGEMENT OF HYPERPHOSPHATAEMIA AMONG DIALYSIS PATIENTS**

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**Introduction and Aims:** Achieving recommended levels of protein intake while maintaining guideline levels of serum phosphorus (P) is associated with the best outcomes in patients undergoing dialysis. Hyperphosphataemia management (using dietary modification and binders to reduce intestinal P absorption) can be complicated if patients consume drinks and processed food that are rich in P-containing additives. We conducted a survey to examine dietary trends among patients with chronic kidney disease (CKD) and the problems associated with P content.

**Methods:** Renal care professionals responsible for providing dietary advice in renal units in the Netherlands, Spain, Sweden and the UK were asked to complete an online questionnaire. The information requested included responder demographics, patient numbers, nutritional trends and problems associated with dietary P restriction. Results from the 4 countries were pooled.

**Results:** The questionnaire was completed by 48 dietitians, 35 nurses and 1 physician (>60% response rate) representing clinics with >15 000 dialysis patients in total. Since entering clinical practice a mean of 15 years ago, 29 (35%) responders had noticed a decrease in the consumption of food prepared from fresh ingredients, 47 (56%) had noticed an increase in consumption of fast food, and 40 (48%) had noticed an increase in consumption of foods rich in F-containing additives; 50 (60%) felt that CKD patients now have greater awareness of the P content of food. Haemodialysis (HD) patients were reported as being most likely to have difficulty restricting P: 32 (40%) responders reported that the majority of their HD patients found it hard to follow advice on P restriction; younger patients (<45 years) were thought to have the most difficulty. When asked about the relative importance of restricting P in maintaining protein intake in HD patients, 42 (50%) considered them equally important and 30 (36%) favoured maintaining protein intake.

**Conclusions:** This survey suggests that, despite increased awareness of the P content of food, many patients have problems restricting dietary P. There is a trend towards greater consumption of processed foods in which P-containing additives may be used to extend shelf life, improve colour or flavour, or increase water retention. P from these additives is absorbed more easily than P from natural protein-rich foods. The renal community must lobby for labelling of food and drink to show use of P additives and, ideally, P content per portion. This would enable patients to avoid or limit their intake of unnecessary P from additives and help maintain adequate protein intake within the limits imposed by dialysis and an acceptable binder regimen.

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**AGE DEPENDENT MINERAL AND BONE DISEASES CHARACTERISTICS AND TREATMENT PRACTICE OF DIALYSED PATIENTS IN HUNGARY - RESULTS FROM NATIONWIDE CLINICAL AUDIT**

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**Introduction and Aims:** Achieving laboratory targets of CKD-MBD, which depends on several factors, can be highly challenging in clinical practice. Recently, an unintentional age dependent treatment practice was reported in CKD patients. Therefore, we analysed CKD-MBD related laboratory target achievements and drug prescriptions in CKD-5D patients in order to test whether in across age groups there is unintentional age dependent treatment practice was reported in CKD patients. We conducted a survey to examine dietary trends among patients with chronic kidney disease (CKD) and the problems associated with P control.

**Methods:** It is a multicentre, nation-wide, retrospective, cross-sectional, observational study in Hungarian dialyzed CKD patients. 5008 patients CKD-MBD related data was collected within the timeframe from Q2 2010. The patients were allocated by their ages (years) into three groups (AD:<65; OLD: 65-80; VOLD: >80). (AD = adult; OLD = old; VOLD = very old).

**Results:** Mean age: 63.4±14.2 years old, male proportion: (n=2644) 52.8% (AD: 58.8 %, OLD: 48.2 %, VOLD: 43.0 %), haemodialysis: 88.6% (AD: 85.9 %, OLD: 90.8 %, VOLD: 92.9 %). Total serum median PTH level was 178.0 pg/ml (IR: 75.8-361.5) and it significantly (p<0.001) deviated among groups (AD: 223.4 pg/ml (IR: 83.0-494.0); OLD: 163.8 pg/ml (IR: 73.2-318.5); VOLD: 122.4 pg/ml (55.7-274.0)). Achieved laboratory targets of serum Ca and P were the highest (66.9 % and 53.2 %) in group OLD following group VOLD (OLD vs VOLD: p=NS and p=NS) and AD (AD vs OLD:
p<0.001 and p<0.05]. There was significant (p<0.001) difference in all laboratory (iPTH/Ca/P) target achievement between group AD (15.8%) and OLD (20.2%). Prevalence of type 2 diabetes mellitus (DM) was the highest (p<0.001) in group OLD (39.9%) followed by group VOLD (28.8%) and OLD (27.3%). Serum sMg levels were lower in patients with DM compared to those without DM in all patient groups in all age groups: AD: p<0.01; OLD: p<0.001; VOLD: p=0.666. Calcimetric (p<0.001), phosphate binders (p<0.01) and vitamin D (p<0.01) prescription was the highest in the AD group in comparison to OLD and VOLD groups. Percentage of patients without these medication was the highest in group VOLD (38.4%).

Conclusions: In CKD-5D patients laboratory values and target achievement of serum iPTH, Ca and P as well as treatment practice of mineral and bone metabolism are significantly different from each other across age groups. Serum iPTH level continuously and significantly decreased with increasing age and it further decreased in case of T2DM. Further research needs to more elucidate these age related clinical differences in CKD-MBD patients in Hungary.

**Results:**

- Patients aged 71 (56–89), were on PPI, omeprazole, 20 mg once daily, already for 25 (14–48) months.
- Eleven patients received dialysis for 118.5 (22–348) months were included in the study.
- There were 16 hemodialysis and 25 peritoneal dialysis patients.
- The ratio of vitamin D deficiency was 78% in the PPI group and 17% in the no-PPI group.
- Vitamin D deficiency in addition to anemia, may contribute to sexual dysfunction.
- There were significant differences in sMg levels between PPI and no-PPI groups.
- sMg levels were lower in PPI group throughout the study compared to no PPI group and this difference was statistically significant in months 1, 5 and 10 (2.19±0.24 vs 2.51±0.30 mg/dL, p=0.002, 10.63±0.33 vs 12.0±0.24 mg/dL, p=0.002 and 2.11 vs 2.41±0.29 mg/dL, p=0.02, respectively), whereas no significant difference was found in other studied parameters, including Ca and PTH. In both groups, no significant changes were detected in the study in all measured parameters, except for PTH that was sig each other acer by the end (282.50±111.65 vs 551.67±215.10 pg/mL, p=0.002 for PPI group and 178.21±114.14 vs 453.62±288.80 pg/mL, p<0.01 for no PPI group).
- The difference in sMg and vitamin D levels between the two groups was significant according to sex (male/female), HD modality (conventional HD/HDF) and calcium or paricalcitol use.

**Conclusions:**

- Long-term PPI use was associated with variable low sMg levels in HD patients, with significant differences in serum Ca and PTH levels. This association appears to be independent of factors such as sex, HD adequacy and modality as well as calcitriol or paricalcitol use.

**Introduction and Aims:**

- Sexual dysfunction is very common in dialysis patients. It impairs the quality of life. This work was done in order to assess the relationship between serum vitamin D levels with sexual dysfunction in dialysis patients.
- Methods: 25-hydroxyvitamin D level of 41 dialysis patients were evaluated. 25-hydroxyvitamin D levels <30 ng / ml were accepted as vitamin D deficiency.
- Patients were divided into 3 groups according to the level of 25-hydroxyvitamin D: 25-hydroxyvitamin D level ≤ 5 ng / ml group, 16-15 ng / ml group 2.6-10-30 ng / ml group 3. We applied the Hospital Anxiety and Depression Scale (HADS), and Arizona Sexual Experiences Scale (ASEX) to all patients. ASEX for the total score was used as cut-off point 11. Values ≥ 11 were considered as sexual dysfunction. HADS anxiety subscale scores was taken as the cut-off point 10 and HADS depression subscale was taken as the cut-off point 7.
- Results: The mean age of patients was 51.8 ± 16.9 years, 51% male, 49% were female.
- There were 16 hemodialysis and 25 peritoneal dialysis patients.
- The ratio of vitamin D level under 15 ng / ml was 87.8%. Sexual dysfunction rate was 93.8%.
- Sexual Experiences Scale (ASEX) to all patients. ASEX for the total score was used as cut-off point 11.
- There was a significant difference in terms of sexual dysfunction between vitamin D groups (group 2 versus 3 and group 1 versus 3, p=0.05).
- Vitamin D levels were positively correlated with the level of hemoglobin and albumin (r = 0.349, p = 0.025, r = 0.419, p = 0.006).
- Sexual dysfunction rate was 93.8% in hemodialysis patients and 80% in peritoneal dialysis patients (p<0.05).
- There was a positive correlation between ASEX total score and age (r = 0.456, p = 0.003).

**Conclusions:**

- Vitamin D deficiency in addition to anemia, may contribute to sexual dysfunction in hemodialysis patients. Sexual dysfunction is more common than peritoneal dialysis patients. Advanced age, malnutrition and vitamin D deficiency have negative impact on sexual life.

**Introduction and Aims:**

- Long-term use of proton pump inhibitors (PPIs) has been reported in association with low serum magnesium (sMg) levels, which may cause serious adverse events. Furthermore, clinical studies have shown that hypomagnesaemia is associated with vascular calcification and cardiovascular mortality among patients with end-stage renal disease (ESRD). However, limited data are available regarding the impact of extensively used PPIs on sMg in ESRD patients on dialysis (HD). The present study was performed to prospectively evaluate this association and detect potential predictive factors.

**Methods:**

- Eighteen stable HD patients, (male/female: 13/5), aged 68.5 (39-89) years, dialyzed for 118.5 (22-348) months were included in the study. Eleven patients received conventional HD and 7 hemodiafiltration (HDF). Thrice weekly HD session length was 4.5 hours. Dialysate Mg concentration was 0.5 mEq/L. Ten out of 18 patients, age 71 (68-89), were on PPI, omeprazole, 20 mg once daily, already for 25 (15-38) months (baseline (PPI group) and the remaining patients, age 61.5 (39-78), were PPI free (no PPI group). Follow-up period was 14 months. No patient was on Mg-containing phosphate binders.
- Half of study patients in both groups were on calcitriol and equal number of patients was receiving paricalcitol throughout follow-up. Biochemistry measurements including sMg, serum calcium (Ca), phosphorus (P), parathyroid hormone (PTH) and alkaline phosphatase (ALP) were performed monthly and HD adequacy was determined at the same intervals by urea reduction ratio (URR) and single-pool Kt/V (spKt/V).

**Results:**

- sMg levels were lower in PPI group throughout the study compared to no PPI group and this difference was statistically significant in months 1, 5 and 10 (2.19±0.24 vs 2.51±0.30 mg/dL, p=0.002, 10.63±0.33 vs 12.0±0.24 mg/dL, p=0.002 and 2.11 vs 2.41±0.29 mg/dL, p=0.02, respectively), whereas no significant difference was found in other studied parameters, including Ca and PTH. In both groups, no significant changes were detected in the study in all measured parameters, except for PTH that was sig each other acer by the end (282.50±111.65 vs 551.67±215.10 pg/mL, p=0.002 for PPI group and 178.21±114.14 vs 453.62±288.80 pg/mL, p<0.01 for no PPI group).
- The difference in sMg and vitamin D levels between the two groups was significant according to sex (male/female), HD modality (conventional HD/HDF) and calcium or paricalcitol use.

**Conclusions:**

- Long-term PPI use was associated with variable lower sMg levels in HD patients, with significant differences in serum Ca and PTH levels. This association appears to be independent of factors such as sex, HD adequacy and modality as well as calcitriol or paricalcitol use.

**Introduction and Aims:**

- Parathyroid glands have cell-surface calcium-sensing receptors (CaSR) to respond to small changes in serum calcium levels (Ca 2+). Other divalent cations such as magnesium (Mg 2+) are also able to activate CaSR. The aim of our study was to determine in vitro the effect of Mg 2+ on PTH secretion as well as on the expression of parathyroid receptors (CaSR, vitamin D receptor (VDR), fibroblast growth factor receptor 1 (FGFR1) and Klotho).

**Methods:**

- Intact parathyroid glands were obtained from normal rats. For secretion studies, tissue was sequentially incubated in increasing concentrations of Ca 2+ (0.8, 1.0, 1.2, and 1.5 mM) and Mg 2+ (0.5, 1.0, 2.0, and 5.0 mM). PTH secreted to incubation medium was measured by using an ELISA kit. For mRNA or protein studies, glands were incubated in the presence of 1.0 mM Ca 2+ and physiological (0.5 mM) or high (2.0 mM) Mg 2+ levels. CaSR, VDR, FGFR1 and Klotho mRNA levels were determined by real time RT-PCR. Protein levels were assessed by immunohistochemistry.

**Results:**

- When PTH secretion was stimulated by low Ca 2+, only Mg 2+ concentrations of 2.0 and 5.0 mM reduced PTH secretion by 38% and 68%, respectively. However, Mg 2+ did not decrease PTH values below those observed with normal Ca 2+. Concentration with normal or high Ca 2+ levels, the effect of Mg 2+ on PTH inhibition was minor or absent. We observed a significant (p<0.001) difference in all laboratory measurements including sMg, serum calcium (Ca), phosphorus (P), parathyroid hormone (PTH) secreted to incubation medium was measured by using an ELISA kit. For mRNA or protein studies, glands were incubated in the presence of 1.0 mM Ca 2+ and physiological (0.5 mM) or high (2.0 mM) Mg 2+ levels. CaSR, VDR, FGFR1 and Klotho mRNA levels were significantly increased with Mg 2+ concentration of 2.0 as compared to 0.5 mM.

**Conclusions:**

- Our results show that high Mg 2+ concentrations (2.0 mM or above) inhibit PTH secretion only when Ca 2+ levels are low. Mg 2+ also modulates parathyroid function through up-regulation of the key receptors CaSR, VDR, FGFR1 and Klotho.
(Mg) containing phosphate binders are effective in controlling serum phosphate. A moderate increase in serum Mg concentration has been observed in patients treated with Mg containing phosphate binders. The impact of a moderate increase in serum Mg in HC is not clear. Previous experimental works have shown that high Mg concentration reduces calcification of vascular smooth muscle cells in vitro. However, there are no in vivo studies where the effects of high concentrations of Mg were evaluated. The present study was designed to evaluate whether a dietary supplementation of Mg can revert HC in rats with renal failure induced by 5/6 nephrectomy (Nx) + calcitriol (CTR) and high phosphorous (P, 1.2%) diet.

Methods: VC was generated in male wistar rats through Nx, CTR administration (80 ng/kg) and high P diet (1.2%) for 2 weeks (control group). The effect of dietary Mg on VC was evaluated by dietary supplementation (0.6% Mg). Rats were distributed in the following groups: Nx + CTR + P + 1.2% and Nx + CTR + P + 1.2% + 2 additional weeks of 0.6% Mg diet. Calcium (Ca) and P contents in plasma, aorta, lung and stomach were analyzed. Plasma levels of creatinine, Mg and PTH were also measured. Finally, van Kossa staining was performed in aorta.

Results: Aortic Ca levels as well as aortic, stomach and placental levels of P decreased after 2 additional weeks with 0.6% Mg supplementation vs. rats without Mg. These levels were similar or lower than in the control group. Mg and CTR levels increased in rats fed with 0.6% Mg diet while PTH levels decreased significantly with respect to the control group. Van Kossa staining and plasma levels of P were also lower than those of rats fed without Mg diet or control group. Finally, mortality decreased drastically (50%) after Mg supplementation treatment.

Conclusions: An increase in dietary of Mg promotes the reversion of vascular calcification and hyperparathyroidism.

| Abstracts | Nephrology Dialysis Transplantation |

| MP535 | LOWER DIALYSE CALCIUM CONCENTRATION FOR HOME HD CAN AFFECT CALCIUM BALANCE DURING DIALYSIS SESSION AND BONE METABOLISM |
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Introduction and Aims: Many clinical reports of frequent or long hemodialysis have recently demonstrated dramatic clinical benefits in terms of morbidity or mortality. Such treatments bring enhanced ultrafiltration capacity due to prolonged treatment period per week, as well as improved solute removal. There is a concern that even subtle differences in dialyse composition can cause larger consequences than ordinary in-center hemodialysis. Above all, negative calcium (Ca) balance through larger fluid removal can lead to decrease in bone mineral density. In order to elucidate this hypothesis, we investigated the data obtained through the registry that was developed by Japanese Society for Home Hemodialysis (Japan Home Hemodialysis Registry: JHHDR).

Methods: At the end of the year 2011, we sent questionnaires to the facilities where home hemodialysis (HHHD) is provided. Anonymous data were collected as electronic files. Ca concentration of dialyse was made dichotomous, i.e. dialyse with Ca of 2.5mmol/L (LoCa) and 3.0mmol/L (HiCa). Patients treated by acetate non-containing and citrate-added dialyse were excluded, because citrate could interfere with plasma ionized Ca concentration. Relationship between calcium concentration of dialyse and other clinical parameters were compared. Missing values were excluded from the analyses.

Results: In total, data for 202 patients were collected, which comprises 61.8% of total HHHD patients in Japan. Total numbers of HHHD patients were 337, which was surveyed by Japanese Society for Dialysis Therapy. Age of entire population was 52.0±10.1 years old. Male was 80.1%. Chronic glomerulonephritis and diabetic nephropathy as primary diagnoses were 47.6% and 14.2%, respectively. Dialysis vintage was 9.2±7.7 years. Numbers of the patients according to dialyse types were 46 (22%), 145 (69%), and 18 (9%) for LoCa, HiCa, and acetate non-containing dialyse, respectively. Predialytic corrected Ca level (9.37±0.06 vs 9.12±0.11, p=0.04) and postdialytic corrected Ca level (10.17±0.14 vs 9.36±0.20, p=0.001) were lower for LoCa group. Vitamin D (Vit D), either oral or as an injection, usage (66.7% vs 82.2%, p=0.04) and Ca carbonate usage (30.4% vs 57.8%, p=0.001) were higher among LoCa group, while numbers of the patient on cinacalcet did not differ between two groups. Intact parathyroid hormone (iPHT) tended to be higher (Log iPHT: 2.08 vs 2.16, p=0.24) among LoCa group, though the difference did not reach statistical significance.

Conclusions: In LoCa group, Ca levels were lower despite higher proportion of vit D or Ca carbonate prescription. Moreover, iPHT tended to be higher despite higher proportion of vit D usage and comparative cinacalcet use. These results indicated that Ca balance was negative during LoCa dialysis use on HHHD patients and eventually can lead to bone mineral loss. Therefore, such LoCa should be used with caution in the supplementation of vit D and Ca carbonate.

| Abstracts | Nephrology Dialysis Transplantation |

| MP537 | DIFFERENCE IN FACTORS ASSOCIATED WITH BONE FRACTURE BETWEEN MALE AND FEMALE PATIENTS ON HEMODIALYSIS |
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Introduction and Aims: In the general population, osteoporosis is more frequently found in females, and is commonly evaluated by change of bone mineral density (BMD). In clinical practice of hemodialysis (HD), however, bone fracture sometimes occurs in male patients with normal BMD. The aim of this study was to examine the difference in clinical factors associated with bone fracture between male and female patients on HD.

Methods: In this study, we included 54 patients (male : female = 32 : 22, age 66 ± 11 years, HD duration 123 ± 105 months) treated with HD for more than 1 year. The patients were classified into 2 groups: one with a history of bone fracture after HD initiation (n=21), and the other without the history (n=33). Between the groups, we compared clinical factors including blood biochemical tests and BMD by dual-energy X-ray absorptiometry in both sexes separately.

Results: Nine of the male patients and 12 of the females had a history of bone fracture after HD initiation. In the female patients, there was a significant difference in BMD and the young adult mean (YAM) of lateral lumbar spine between the two groups (Table). In contrast, in the male patients, there was a significant difference in plasma total homocysteine (Hcy) levels but not in BMD between the groups. Multiple logistic regression analysis showed that in females, BMD was independently associated with a history of fracture (p<0.004). In male patients, plasma Hcy level was significantly associated with a history of bone fracture (p<0.07). Table. Comparison between patients with and without fracture.

Conclusions: Bone strength depends on both bone quantity and quality, and collagen cross-links are determinants of bone quality. Recent studies have indicated that hyperhomocysteinemia reduced bone strength via a reduction of enzymatic cross-links and an increase of nonenzymatic cross-links. Hyperhomocysteinemia, a frequent complication in HD patients, might play a role in bone fracture in this population.

| Abstracts | Nephrology Dialysis Transplantation |

| MP538 | FRAGILITY BETWEEN MALE AND FEMALE PATIENTS ON HEMODIALYSIS (125069) |

Introduction and Aims: In the general population, osteoporosis is more frequently found in females, and is commonly evaluated by change of bone mineral density (BMD). In clinical practice of hemodialysis (HD), however, bone fracture sometimes occurs in male patients with normal BMD. The aim of this study was to examine the difference in clinical factors associated with bone fracture between male and female patients on HD.

Methods: In this study, we included 54 patients (male : female = 32 : 22, age 66 ± 11 years, HD duration 123 ± 105 months) treated with HD for more than 1 year. The patients were classified into 2 groups: one with a history of bone fracture after HD initiation (n=21), and the other without the history (n=33). Between the groups, we compared clinical factors including blood biochemical tests and BMD by dual-energy X-ray absorptiometry in both sexes separately.

Results: Nine of the male patients and 12 of the females had a history of bone fracture after HD initiation. In the female patients, there was a significant difference in BMD and the young adult mean (YAM) of lateral lumbar spine between the two groups (Table). In contrast, in the male patients, there was a significant difference in plasma total homocysteine (Hcy) levels but not in BMD between the groups. Multiple logistic regression analysis showed that in females, BMD was independently associated with a history of fracture (p<0.004). In male patients, plasma Hcy level was significantly associated with a history of bone fracture (p<0.07). Table. Comparison between patients with and without fracture.

Conclusions: Bone strength depends on both bone quantity and quality, and collagen cross-links are determinants of bone quality. Recent studies have indicated that hyperhomocysteinemia reduced bone strength via a reduction of enzymatic cross-links and an increase of nonenzymatic cross-links. Hyperhomocysteinemia, a frequent complication in HD patients, might play a role in bone fracture in this population.
INTERLEUKIN-17 PRODUCING EFFECTOR MEMORY T CELLS AND CD4+CD25+FOXP3+ REGULATORY T CELLS CORRELATED WITH PHOSPHATE AND PARATHYROID HORMONE LEVELS IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction and Aims: The Th17 (Th) lymphocytes play critical roles in the immune activation and inflammation in the chronic hemodialysis (HD) patients and mineral bone disorders including hyperparathyroidism and hyperparathyphosphatemia contribute to the inflammatory effects. Interleukin-17 producing effector memory T (Th17) cells and CD4+CD25+ FOXP3+ regulatory T (Treg) cells both come from naive Th cells, share reciprocal development pathways but exhibit opposite effects. Here we investigated the relationship between the Th17 and Treg cells and mineral bone disorder in the chronic HD patients.

Methods: One hundred and five patients (age ≥35 years old) on chronic HD over 3 months were enrolled. Patients with systemic infection or malignancy, taking immunosuppressive medication were all excluded. The peripheral blood mononuclear cells were collected, cultured and stimulated by phytohemagglutinin-L (PHA-L), phorbolmyristate acetate (PMA) and ionomycin in different time point. The Treg cells and Th17 cells were then stained and analyzed by flow cytometry. Hematological and biological markers were detected. The relationship was analyzed by statistical analysis.

Results: The T cell differentiation were as follows: Th17 cells (mean ± standard deviation (SD): 25.61% ± 0.10% and Treg cells (8.45% ± 4.3%). In the mineral aspect, the Th17 cell differentiation correlated with phosphate (P) level (r = 0.211, p < 0.05) and intact parathyroid hormone (iPTH) level (r = -0.277, p < 0.05). The Th17 cell differentiation negatively correlated with P and iPTH levels (r = 1.97, p < 0.05 and r = -1.76, p < 0.05). Besides, the Th17/Treg cell ratio also correlated with the age and albumin levels (r = 0.25, p < 0.01 and r = 0.26, p < 0.05) but did not correlated with the calcium, alkaline-P or CRP levels as determined by statistical analysis. In the non-diabetes patients group (n = 53), the Th17 cells differentiation more predominant correlated with P and iPTH levels (r = 0.443, p < 0.001 and r = 0.384, p < 0.005).

Conclusions: The results indicate that the Th17/Treg imbalance in the chronic HD group. Higher phosphate level and intact parathyroid hormone level, and lower albumin level increase the Th17 cell differentiation, especially in the non-diabetes, chronic HD patients.

ELDECALCITOL (ELD) TREATMENT FOR LOW BONE MASS IN POSTMENOPAUSAL WOMEN RECEIVING MAINTENANCE HEMODIALYSIS

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Introduction and Aims: ELD, a new active vitaminD3 analog developed in Japan, has been recognized as an effective osteoporotic therapeutic drug in primary osteoporosis. We treated postmenopausal women receiving maintenance haemodialysis in our institution with ELD for 1 year, and evaluated the effects on lumbar spine bone mineral density (LS-BMD).

Methods: Twenty-one postmenopausal women receiving haemodialysis in our institution for at least 6 months were enrolled. Patients with two or more previous vertebral fractures, those receiving a metal-containing phosphate binder, and those with a mean serum albumin-corrected calcium (Ca(Alb)) level >9.5mg/dL were excluded. ELD treatment was started at 0.5µg/day. LS-BMD was measured at the lateral aspect of the L2-L4 vertebrae using the dual-energy X-ray absorptiometry method (DEXA) on a QDR2000 densitometer.

Results: Table 1 shows the changes in mean Ca(Alb), P, intact PTH, BAP, and TRACP-5b. Data shown as mean(SD). Mean Ca(Alb), P, and intact PTH levels were well-controlled before and after ELD treatment. ELD could be used safely without causing severe hypercalcemia. Mean BAP level was significantly decreased throughout this study (reference range; 31 to 123 U/L). Mean TRACP-5b level was significantly decreased after 6months ELD treatment, however the level had remained higher than normal range throughout this study (reference range;120 to 420 mU/dL). Table 2 shows the changes in mean LS-BMD. Data shown as mean(SD). Mean LS-BMD was significantly increased after 6 months, but then decreased after 1 year ELD treatment. t = p<0.05 vs before treatment.

Conclusions: Although our results are observational study at a single institution, they suggest that ELD could be safely used to increase bone mass in dialysis patients. However, ELD treatment may not be enough to improve low bone mass due to severely bone absorption such as postmenopausal women.

RELATIONSHIP OF OSTEOPROTEGERIN LEVEL AND CHRONIC KIDNEY DISEASE- METABOLIC BONE DISEASE (CKD-MBD)

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Introduction and Aims: The plasma level of Osteoprotegerin (OPG) in combination with intact parathyroid hormone (iPTH) can be used as a marker for noninvasive diagnosis of CKD-MBD (Chronic Kidney Disease- Metabolic Bone Disease) in hemodialysis and predialysis patients. The aim of the study to assess the level of (OPG) in end stage renal disease, and whether there is significant correlations between, iPTH, serum calcium, phosphorus, CaXph product, CRP, cholesterol, triglycerides and BMD (bone mineral density) in Patients Hemodialysis and Predialysis stages (stage 3&4).

Methods: Eighty one individuals were included in the study, classified into three groups GROUP A: 41 patients chronic kidney disease stage 5, GROUP B: 30 patients as pre-dialysis group (stage 3&4CKD), GROUP C:Control group, consists of 16 healthy individuals.

Conclusions: The study showed that Osteoprotegerin level was significantly increased in chronic kidney disease stage 5 patients when compared with group B, and significantly decreased in control group. These results indicate that Osteoprotegerin level is well correlated with chronic kidney disease stage 5 patients.
LANTHANUM CARBONATE AND SURVIVAL IN MAINTENANCE HAEMODIALYSIS PATIENTS

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Introduction and Aims: Lanthanum carbonate is a non-calcium phosphate binder that is effective for the treatment of hyperphosphatemia in patients undergoing dialysis. However, there are limited data on whether treatment with lanthanum carbonate affects survival. Methods: We retrospectively collected data on maintenance haemodialysis patients (n = 2,269) beginning in December 2008, a time immediately prior to the commercial availability of lanthanum carbonate in Japan. We compared all-cause mortality among patients who began treatment with lanthanum carbonate (n = 675) with those who remained untreated (n = 1,594). We also compared survival in a subcohort of treated patients who began treatment with lanthanum carbonate (n = 675) with those who remained untreated (n = 568) patients matched by the propensity score of availability of lanthanum carbonate in Japan. We compared all-cause mortality among the treated and untreated groups.

Results: Treatment with lanthanum carbonate was independently associated with lower mortality than the untreated group (HR 0.46; 95% CI 0.32 to 0.66; P < 0.0001). Multivariate-adjusted analyses showed no significant association between lanthanum carbonate and survival in the whole cohort (HR 0.72; 95% CI 0.48 to 1.07; P = 0.10) but there was a significant association in a subgroup of patients with baseline serum phosphate >6.0 mg/dl (HR 0.46; 95% CI 0.29 to 0.72; P = 0.029). Lanthanum carbonate was not associated with a significant survival benefit in the propensity score-matched cohort (HR 0.71; 95% CI 0.46 to 1.09; P = 0.12) but a significant association was found when the analysis was restricted to patients with baseline serum phosphate >6.0 mg/dl (HR 0.40; 95% CI 0.27 to 0.64; P = 0.0011). Stratified analysis did not show that Qb and body weight affect this correlation. These findings show that the eRp decreases by 175 mg when Pa decreases by 1 mg in conditions of this study. For reducing the Pa before HD, by 1 mg, weekly amount of i absorption should be restricted by 489 mg.

Conclusions: (1) The i absorption was not dependent on protein intake or parathyroid hormone level. (2) The amount of i absorption per week could be easily estimated. (3) Relationship between serum i concentration at start of weekly first HD and amount of i absorption was revealed.

EVALUATION OF WEEKLY PHOSPHATE REMOVAL IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Excess of phosphate (iP) is a risk for death in hemodialysis (HD) patients. Estimating the amount of i absorption (Ap) is important for evaluating effect of diet and phosphate binders. Ap is considered to be equal to the amount of intradialytic i removal (Rp) because the balance of absorption from intestine and elimination of i is generally maintained in HD patients. We established a formula for calculating estimated Rp (eRp) and reported in the 49th ERA-EDTA congress. For obtaining an easy method for providing estimated Ap (eAp) per week, we analyzed phosphate kinetics of entire week using this formula.

Methods: We studied 29 patients undergoing 4-hour HD twice a week. Their Blood flow rate (Qb) was between 160-240 ml/min. Their serum i concentration (Pa) at start of HD was 4.5±1.1mg/dl. Blood samples were drawn at start and end of HD in consecutive 3 HD sessions (the first (HD1), second (HD2) and third (HD3) HD sessions of the week). We calculated eRp using following formula as reported previously: eRp=3.06Qb*(1-Ht0+Ht4)/500(0.5+1.75UN0+0.33PA0+4.66PA4)+0.0694iP(Pa0+4.66PA4), where Qb (dl/min), Ht0 and Ht4=hematocrit at start and end of HD, UN0 and UN4= serum urea nitrogen concentration at that, Pa0 and Pa4=P at that, UF = amount of ultrafiltration (dl/session). (1) We compared iP and UN alteration within a week. (2) The total eRp per week (eRpw) was calculated by sum of eRp in three sessions. eRpw was compared with eRp in HD1 (eRps). (3) The Relationship between eRp and Pa was analyzed in 87 HD sessions.

Results: (1) Eight of 29 patients did not have the highest Pa before HD, although serum UN concentrations before HD, were the highest in all patients. The removal amount of iP was not associated with that of UN or parathyroid hormone level. (2) eRpw was 2648±579mg. The percentage of eRp in each HD session was 35.8, 33.7 and 30.5%. Weekly amount of i removal estimated by data from HD1 (eRps) was shown as eRp(HD1)=2.790eRps. This eRp(HD1) was extremely similar to the sum of Rp from three sessions (r=0.951 Ex+138, R=0.947, P<0.001). (3) In 87 HD sessions, correlation between eRp and pre-HD Pa was observed (r=0.756±0.102, R=0.806, P<0.001). Stratified analysis did not show that Qb and body weight affect this correlation. These findings show that the eRp decreases by 175 mg when Pa decreases by 1 mg in conditions of this study. For reducing the Pa before HD, by 1mg, weekly amount of i absorption should be restricted by 489 mg.

Conclusions: (1) The i absorption was not dependent on protein intake or parathyroid hormone level. (2) The amount of i absorption per week could be easily estimated. (3) Relationship between serum i concentration at start of weekly first HD and amount of i absorption was revealed.
known to mediate strong binding to bone hydroxyapatite crystals. During bone resorption the OC that is incorporated into the bone matrix is released into the circulation, and, hence, is considered as a marker of bone turnover, rather than a specific marker of bone formation. The marked elevation of OC in patients with renal failure has been regarded as a combination of impaired clearance and increased skeletal production. In subclinical vitamin K deficiency part of the OC in serum remains undercarboxylated (ucOC) and thus inactive in respect to bone metabolism. The objective of the present study was to assess the ucOC levels in postmenopausal hemodialysis (HD) patients with and without secondary hyperparathyroidism.

Methods: We recruited 53 menopausal women: 26 on HD and 26 controls similar to the HD patients along criteria such as food intake, physical activity, medication use and other risk factors for osteoporosis. The mean age was 65.1 ± 13.0 years and 59.0 ± 9.5 years respectively. Serum levels of ucOC [ng/ml] were measured by EIA kit of TAKARA Bio. Inc. (Japan) before the HD session. Intact parathormone (iPTH) [ng/L] were measured on Immulite 2000 using chemiluminescent (CLIA) kit. Statistical analysis was performed by Student’s t-test and Pearson’s correlation.

Results: Serum ucOC in HD patients (16.45 ± 1.62 mg/mL, n=26) was significantly increased in comparison with the levels on control group members (3.01 ± 0.36 mg/mL, n=26), p < 0.0001. Serum ucOC levels [ng/mL] in HD patients are presented in table 1: Correlations between ucOC and different parameters in HD patients are presented in table 2.

Conclusions: 1. Serum levels of ucOC in HD patients were significantly increased in comparison with the healthy controls and a strong positive correlation was found between ucOC and iPTH concentration as well as between ucOC and HD duration. 2. In the initial stages of secondary hyperparathyroidism (iPTH >300 ng/L), serum ucOC levels were the same as in the patients without secondary hyperparathyroidism. 3. The treatment of secondary hyperparathyroidism with cinacalcet and calcitriol leads to significant increase of ucOC, most probably due to increased bone turnover.

PREDIALYSIS IONIZED CALCIUM LEVEL MEASUREMENTS IN PATIENTS ON HAEMODIALYSIS

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Introduction and Aims: Blood calcium measurement is recommended in patients on haemodialysis (HD). The Kidney Disease: Improving Global Outcomes (KDOQI) formulation recommends the measurement of ionized calcium (iCa) levels, but in clinical setting total calcium (tCa) level concentration is preferred over that of albumin-corrected calcium (Alb-Ca) level. Aim: To identify the factors associated with predialysis levels of iCa and to compare the ability of tCa and Alb-Ca levels in predicting iCa cases.

Methods: The predialysis iCa and tCa levels were measured, at the actual pH, for all patients on HD at a single institution and also underwent usual mid-week biology. The data were analysed using Linear regression and Bland-Altman testing.

Results: A total of 169 HD patients were evaluated, with a mean age of 71.8 ± 14 years; 41.6% were female and the mean duration of dialysis was 67.8 ± 14 months. The treatment involved administration of calcium carbonate (17%), calcium acetate (13%), sevelamer (30%), alfalcaldiol (18%), cinacalcet (11%), and cholecalciferol (0.5%). The mean dialysate calcium concentration (DDC) was 1.51 mmol/L. The mean iCa was 2.2 ± 0.14 mmol/L (range, 1.86–2.65 mmol/L) and the mean Alb-Ca was 2.3 ± 0.13 mmol/L (range, 1.9–2.67 mmol/L). Both were correlated with the iCa (mean iCa level: 1.14 ± 0.07 mmol/L; range, 0.93–1.4 mmol/L) (r² = 0.6, p < 0.001; y = 0.55 ± 1.4x and r² = 0.53; p < 0.001; y = 0.78 ± 1.3x, respectively). The mean ratios of iCa/iCa and Alb-Ca/iCa were 1.93 and 2.02, respectively. iCa was correct in 84% of patients, and Alb-Ca, in 37% of patients, in predicting low iCa levels (<1.12 mmol/L; n = 64). iCa was correct in 82% of patients, and Alb-Ca, in 80% of patients, in predicting normal iCa levels (1.12–1.32 mmol/L; n = 93). iCa was not a predictive factor for hypercalcemia (iCa > 1.32 mmol/L, n = 3); Alb-Ca predicted hypercalcemia in 2/3 patients. Sex was associated with iCa levels: iCa was 1.2 ± 0.07 mmol/L in males and 1.16 ± 0.06 mmol/L in females (p = 0.008). Serum bone markers, FTT values, arterial calcification scores, and bone mineral density values were not associated with iCa quartiles.

Conclusions: Despite vitamin D supplementation and a mean DCC of ≥1.5 mmol/L, predialysis hypocalcemia is highly prevalent in patients on HD (43%); the male predominance of this finding was not unexpected. Insufficient dietary calcium intake or insufficient supplementation may be the main cause for this finding. iCa appears superior to Alb-Ca in predicting hypocalcemia. Hypercalcemia is very uncommon and not predicted by tCa.

ADMINISTRATION OF A SINGLE, LARGE ORAL DOSE OF 25-HYDROXYCALCIFEROL IN HEMODIALYSIS PATIENTS: EFFECTS ON THE MINERAL METABOLISM MARKERS

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Introduction and Aims: Vitamin D deficiency is common in patients with chronic kidney disease and dialysis, low levels have been associated with increased cardiovascular risk, and mortality. We evaluated the administration of a high and single, oral dose of 25(OH)calciferol (3 mg of Hydrocalutrol®, 180 000 IU) Serum levels of D vitamin and mineral metabolism markers have been analyzed.

Methods: Chronic hemodialysis patients with 25(OH)D < 30ng/ml were included. Patients with serum calcium > 10 mg/dl or PTH > 800 mg/ml were excluded. The patients were randomized in two groups: treated group and control group. Time follow-up was 16 weeks. The usual treatment for controlling Ca/P levels neither the treated group and the control group.

Results: A higher level of 25(OH)D was observed in the treated group and was maintained for 16 weeks. This fact was associated with a significant decrease of PTH levels in the 8 post-treatment weeks. Small and transitory increased levels of 25(OH)D levels were observed in the controlled group, associated to the summer period. The levels of 25(OH)D were even higher in the treated group and controlled one. Serum calcium was > 10 mg/dl in 16 of 252 (6%) performed samples in the treated group and only 1 of 264 (0.4%) samples were over 10 in the controlled group. Only two cases in the treated group showed serum calcium > 10.5 mg/dl. There were no significant changes of PTH levels in the treated group and control group.
Results: A randomized, open-label, crossover design study to compare the safety and efficacy of sevelamer carbonate versus calcium carbonate in the treatment of hyperphosphataemia in patients with chronic kidney disease on dialysis

N.B. SC:LC dose-relativities from approximately 2.1 have been reported as similar doses.

Introduction and Aims: Hyperphosphatemia (HyperPO4) and chronic kidney disease-metabolic bone disease (CKD-MBD) is common in end stage renal disease (ESRD). Untreated hyperPO4 is a leading cause of death in these patients. Calcium-based phosphate binders are inexpensive and commonly used as first-line therapy to manage hyperphosphataemia. However, their use is restricted in some patients because of the possibility of increased risk of hypercalcemia, vascular calcification and adynamic bone disease due to suppression of parathyroid hormone. We used a Markov model to compare the cost-effectiveness of the non-calcium phosphate binders lanthanum carbonate (LC) and sevelamer hydrochloride (SH) as second-line treatments. Yearly transitions between states were obtained from the European Dialysis and Transplant Association annual report. Efficacy data were taken from a randomized head-to-head phase 3 study performed in ESRD patients undergoing dialysis. Both ‘intention to treat’ (ITT) and completer populations were analysed. In accordance with Spanish healthcare service perspective, only direct costs (pharmaceutical and CVD management) were included. Medical costs (2012 prices in euros) were obtained from diagnosis-related groups. Drug costs were derived from ex-factory prices, adjusted to allow for a 7.5% mandatory rebate. Costs and outcomes were discounted at 3%. Deterministic and probabilistic sensitivity analyses (PSA) were conducted.

Methods: Three health states (alive without CVD, alive with CVD, dead) were included in the model used to assess the incremental cost-effectiveness ratio (ICER) of LC versus SH as second-line treatments. Yearly transitions between states were obtained from the European Dialysis and Transplant Association annual report. Efficacy data were taken from a randomized head-to-head phase 3 study performed in ESRD patients undergoing dialysis. Both ‘intention to treat’ (ITT) and completer populations were analysed. In accordance with Spanish healthcare service perspective, only direct costs (pharmaceutical and CVD management) were included. Medical costs (2012 prices in euros) were obtained from diagnosis-related groups. Drug costs were derived from ex-factory prices, adjusted to allow for a 7.5% mandatory rebate. Costs and outcomes were discounted at 3%. Deterministic and probabilistic sensitivity analyses (PSAs) were conducted.

Results: In a 10-year projection, LC achieved 3.81 (ITT) and 3.84 (completer) quality adjusted life-years (QALYs). With SH, 3.79 (ITT) and 3.78 (completer) QALYs were gained. Global costs for LC therapy were €18 680 (ITT) and €18 776 (completer), whereas for SH they were €18 517 (ITT) and €18 482 (completer). ICERs of LC versus SH were €6306/ QALY (ITT) and €4644/QALY (completer). CVD management cost was the most influential parameter in the model. Assuming a €38000/QALY threshold, LC was cost-effective compared with SH in 99.9% of PSA simulations.

Conclusions: In Spain, LC is cost-effective compared with SH for the second-line treatment of hyperphosphataemia in patients with ESRD undergoing dialysis.

Compared to sevelamer carbonate (SH), sevelamer hydrochloride (SH) is less cost-effective in the treatment of hyperphosphataemia in patients with end-stage renal disease (ESRD) undergoing dialysis.

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[sevelamer(S), sevelamer carbonate(SC) and lanthanum carbonate(LC)] are the drugs most commonly used to reduce the serum concentration of phosphorus(P). They are associated with gastrointestinal intolerance. The aim of our study was to compare these drugs in vivo and in vitro.

**Methods:** One tablet of SC 800mg, one of S 800mg and a tablet of LC 750mg were dissolved in solutions at pH2 corresponding to stomach-pH, following the USP dissolution II paddle method at a rotation speed of 50rev/min in 900ml of dissolution medium at a stable temperature of 37±0.01°C, maintained by a Haake cryostat. The dissolution profile obtained before and after addition of trehalose, a disaccharide used to stabilize pharmaceutical products for its effect on H-binding structures, was graphically reproduced using software TableCurve2D®. To calculate the amount of phosphoric acid stoichiometrically engaged by each single tablet, we followed the variation of pH of a phosphoric acid solution 4.00X10⁻⁹Mol. We also calculated the amount of CO₂ produced from each tablet and evaluated gastric-pH in vivo using 24h esophago-gastric pH measurement with and without administration of PB and Proton pump inhibitors (PPis) in CKD patients and in a control group.

**Results:** The amount of CO₂ produced by LC is 56ml, that of SC is 30ml; S does not produce CO₂. The complete solubilization of a tablet of LC occurs in 60 min, while that of S and SC in 10 min. The dissolution of PB increases the pH of solution (p<0.0001), this action is linked to the ability of these drugs to bind protons. The addition of trehalose increases the density of medium, but not generate any significant variation in the profile of drugs solubility. Engaged by the amount of phosphoric acid there was a best action of SC (R undertakes 4.00X10⁻⁹mol/L, LC 3.99X10⁻⁹mol/L, S 3.95X10⁻⁹mol/L). The pH increases even more after administration of PPis.

**Conclusions:** The action of PB is linked to their ability to uptake protons, so is preferable to take them after meal and especially after PPis; reducing the stomach acidity the protons detected are those of phosphoric acid. SC has a greater capacity to uptake phosphorus, S is the most tolerated because it doesn’t produce CO₂, LC is the less soluble.