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 phosphate 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 stage 5D, 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 calcimimetics. 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:** No significant differences either in the demographic characteristics or parathyroid hormone (PTH), alkaline phosphates (ALP), albumin and phosphate (P) serum levels among the three groups. Interestingly, total serum calcium (tCa), iCa and CT serum levels were significantly different and increased steadily from group 1 to group 3 (Table).

<table>
<thead>
<tr>
<th>Group1 (CC)</th>
<th>Group2 (CC+OC)</th>
<th>Group3 (CC+OC+TOC)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>number</td>
<td>20</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Age, years</td>
<td>40±10</td>
<td>52±14</td>
<td>54±13</td>
</tr>
<tr>
<td>HD vintage, months</td>
<td>12±4±82</td>
<td>113±55</td>
<td>98±60</td>
</tr>
<tr>
<td>M/F</td>
<td>12/8</td>
<td>11/12</td>
<td>8/14</td>
</tr>
<tr>
<td>PTH, pg/ml</td>
<td>1690±587</td>
<td>1653±718</td>
<td>1576±101</td>
</tr>
<tr>
<td>ALP, mU/mL</td>
<td>295±213</td>
<td>291±186</td>
<td>253±125</td>
</tr>
<tr>
<td>CT, pg/ml</td>
<td>10.1±5.6</td>
<td>18.4±9.5</td>
<td>27.9±16</td>
</tr>
<tr>
<td>iCa, mg/dl</td>
<td>10.2±0.6</td>
<td>10.52±0.5</td>
<td>10.8±0.7</td>
</tr>
<tr>
<td>Ca, mmol/L</td>
<td>1.21±0.2</td>
<td>1.32±0.11</td>
<td>1.35±0.1</td>
</tr>
<tr>
<td>Albumin, g/dl</td>
<td>3.99±0.4</td>
<td>3.97±0.38</td>
<td>3.87±0.5</td>
</tr>
<tr>
<td>P, mg/dl</td>
<td>6.0±1.5</td>
<td>6.0±1.3</td>
<td>6.1±1.1</td>
</tr>
</tbody>
</table>

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Conclusions: The morphologic prevalence of OC and TOC in HPT was associated with statistically significant increases in serum Ca and iCa 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.

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.

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 HBT. The lower cortical volumetric density probably reflects higher bone porosity in the HBT patients.

Introduction and Aims: Parathyroid hormone (PTH) is one of the important hormones regulating calcium and phosphate homeostasis in the management of bone metabolism. Methods that are currently used for its determination can measure both the complete molecule 1-84 as well as its degradation fragments the non 1-44 (PTH). Both molecules have different and sometimes opposite effects. This study is performed to determine whether patients are having a low bone turnover using the marketed automated methods. The third generation measuring PTH 1-84(PHTbio). Methods: The study was performed in 147 patients on hemodialysis with the determination of PTH, PTHbio, PTH ratio (PTHbio / PTHbio), Ca, P, FGF23, 25OHvitD3, before hemodialysis. PTH and PTHbio were measured using roche elects. Results: The mean age of the study population was 66.1 ± 14.59 years, 76 men and 71 women, the mean time on HD was 5.2 ± 4.79 years.13 patients were on HDF online, and 134 on standard HD. Other studied mean values were: Ca 9.21±0.74 mg/dl, P 5.34 ± 1.5 mg/dl, PTHbio 174.9±217.18 pg/ml, PTH1-84/PTH7-84: 1.723±3.285, FGF23 2855.0±4246.8 RU/ml, 25 OH vitD 35.55 ng/ml. There is correlation between FGF23 and PTH1,PTHbio and the ratio PTH1-84/PTH7-84, but not with the 25OHvitD. In the univariate model PTH1-84/PTH7-84 ratio correlates positively with FGF23 (p<0.04) such that a 1% increase in the ratio of an increase of 1.6% of PTH23. PTHbio/PTH7-84 also correlate with FGF23. The ratio does not correlate with the Ca or P, or years in HD or age. Conclusion: 1. It is very important to know the values of 1-84 and non 1-44 fragments in our patients. 2. The values of PTH 1-84 are significantly lower than those used now. 3. All measured forms of PTH correlate well with each other but indicate different aspects of the disease. - The expression a sample of high turnover bone and correlates with the FGF23.
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 fibrosa 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 and medical records 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) quartiles were <132.5 pg/ml, ≥132.5 <261.0, ≥261.0 <510.4, and ≥510.4 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 respectively. Post hoc analysis of these 4 groups revealed that only Group 1 and Group 2 were significantly different. The NEADLS scores were significantly lower in Group 1 (Intact-PTH <25th) than Group 2, 3 and 4 (Intact-PTH >25th).

Conclusions: 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.

MP524 TRENDS IN MEDICAL AND SURGICAL MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM (SHPT) AMONG HEMODIALYSIS PATIENTS: REALITY VS OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS)

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Introduction and Aims: SHPT is highly prevalent among patients on chronic hemodialysis (HD), and parathyroid hormone (PTH) levels have risen over the past decade. Treatment options for SHPT include pharmacological agents and surgical removal of parathyroid glands (parathyroidectomy (PTX)). We describe trends in PTH levels and SHPT treatments in the DOPPS, to evaluate the hypothesis that PTX rates have decreased over the time period since the availability of cinacalcet therapy.

Methods: 39,499 participants in DOPPS phase 2-4 (2002-2012) without a prior PTX were included. Incident PTX rates were calculated as the sum of PTX hospitalizations divided by follow-up time. PTH levels, cinacalcet, and vitamin D prescriptions were collected at study enrollment. Poisson, logistic, and linear regression were used to calculate the trend over DOPPS phase in PTH rate, PTH level, and medication prescription respectively.

Results: Trends over time in PTH levels and SHPT treatments are shown in Table 1. In Eur-A/NZ and in N America, median PTH increased but the prevalence of very high PTH (>800 pg/mL) remained stable. In Japan, median PTH remained relatively stable, but the prevalence of PTH >800 decreased. PTX rates decreased in Eur-A/NZ and in N America, median PTH increased but the prevalence of very high PTH rate had increased. PTX rates decreased in Eur-A/NZ and in N America, median PTH increased but the prevalence of very high PTH rate had increased. PTX rates decreased in Eur-A/NZ and in N America, median PTH increased but the prevalence of very high PTH rate had increased.

Conclusions: In the international DOPPS cohort, SHPT treatment changed over the past decade, with a decrease in PTX and increase in cinacalcet and vitamin D prescription. Given the proven efficacy of calcimetics, the rise in median PTH levels observed outside of Japan was likely due to higher target PTH levels (as reported by medical directors at DOPPS facilities, not shown). The prevalence of very high PTH (>800 pg/mL) has changed little in Japan and decrease in PTX, probably because cinacalcet is now prescribed for this condition.

MP525 ATTENUATED MEGLIN EXPRESSION CONTRIBUTES TO THE PATHOGENESIS IN HYPERFUNCTIONING PARATHYROID TUMORS

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Introduction and Aims: Megalin is a multiligand endocytic receptor involving in the reabsorption of 25-hydroxyvitamin D (25OHD) and vitamin D binding protein (DBP) in renal proximal tubules. Decrement of vitamin D receptor (VDR) expression in hyperfunctioning parathyroid tumors (ShPT), however, little is known about the role of 25OHD in these hyperfunctioning parathyroid diseases.

Methods: To assess the megalin expression, parathyroid tumors were obtained from PHPT and SHPT patients, and normal parathyroid glands from thyroid carcinoma patients. A polyclonal antibody for megalin was used for the assessment of its expression by immunohistochemistry. To assess the role of megalin in incorporation of ligand, histidine-tagged soluble recombinant protein for the soluble form of 39-kD receptor-associated protein (His-sRAP), which binds to the ligand-binding domain of megalin, was administered to primary cultured parathyroid cells obtained by megalin, was administered to primary cultured parathyroid cells obtained by

Results: In the international DOPPS cohort, SHPT treatment changed over the past decade, with a decrease in PTX and increase in cinacalcet and vitamin D prescription. Given the proven efficacy of calcimetics, the rise in median PTH levels observed outside of Japan was likely due to higher target PTH levels (as reported by medical directors at DOPPS facilities, not shown). The prevalence of very high PTH (>800 pg/mL) has changed little in Japan and decrease in PTX, probably because cinacalcet is now prescribed for this condition.

Conclusions: The megalin expression decreases in tumors with PHPT and SHPT compared with strong expression in normal parathyroid tissues. In SHPT, its expression was particularly depressed in nodular areas, compared with adjacent diffuse hyperplasia. In the primary cultured parathyroid cells, the expression of megalin was observed at the membrane region. The expression of His-RAP was observed in the membrane region and cytosol 15 min after the administration of His-RAP. The distribution of megalin overlaps with that of His-RAP in the membrane region.

Conclusions: The incorporation of megalin was demonstrated in incorporation of 25OHD in parathyroid cells. The decrement of the megalin expression may contribute vitamin D resistance and hyper-secretion of PTH in the hyperfunctioning parathyroid tumors.

MP525 THE CALCIIMIMETIC CALINDEL PREVENTS HIGH PHOSPHATE-INDUCED VASCULAR CALCIFICATION BY UPREGULATING MATRIX GLA PROTEIN

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Introduction and Aims: High serum phosphate (Pi) levels represent a major issue in dialysis patients, because associate with secondary hyperparathyroidism (SHPT), vascular calcification (VC), and cardiovascular outcomes. In this population, calcimimetics are used to control SHPT, hyperparathyroidism, and, more recently, to delay the progression of VC. The aim of this in vitro study was to investigate the direct effects of the calcimimetic calindel on the progression of high Pi-induced VC.

Methods: Rat vascular smooth muscle cells (VSMCs) were incubated with high Pi concentrations, and the effects of calindel were investigated on vascular calcium (Ca) deposition and VSMC osteoblastic differentiation.

Results: Calindel inhibited Ca deposition concentration-dependently with a maximal inhibition of 64.0±5.2% achieved at 100 nM. Furthermore, calindel was able topotentially prevent the high Pi-induced Bone Morphogenetic Protein (BMP) 2 expression upregulation (32.4 ± 4.6% of inhibition; p <0.01). Interestingly, the pretreatment with calindel enhanced the Matrix Gla Protein (MGP) gene expression significantly, compared to high Pi-treated cells (40.2 ± 8.6% of increase; p <0.01).

Conclusions: In conclusion, we demonstrated that the calcimimetic calindel prevents high Pi-induced VC, by affecting osteoblastic differentiation in vitro. In particular, the inhibitory effect of calindel on VC is probably due to its stimulatory role on Ca Sensing Receptor, leading to an increase in the synthesis of MGP by VSMCs.
**MP527**

**COMPARISON OF CINACALCET PLUS PARICALCITOL TO CINACALCET PLUS CALCITRIOL THERAPY IN HEMODIALYSIS PATIENTS WITH SEVERE HYPERPARATHYROIDISM**

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Introduction and Aims: Secondary hyperparathyroidism is a complication of hemodialysis and severe SHPT is associated with high mortality. Clinical guidelines support the combination therapy with cinacalcet and VDRA treatment in patients with SHPT; however, there is no consensus on the most effective type and dose of combination. The aim of this study is to evaluate and compare the effectiveness of cinacalcet and paricalcitol or calcitriol treatment of MHD patients with severe SHPT.

Methods: This multicenter observational clinical study was conducted between July 2011 and August 2012. 146 patients with severe SHPT on chronic hemodialysis were enrolled into the study. Patients with serum calcium ≤ 10.5 mg/dL, Ca × P < 75 and PTH level ≥ 1000 pg/mL were divided into two groups either who received cinacalcet plus intravenous paricalcitol (Group CP) or cinacalcet plus intravenous calcitriol (Group CC) for the treatment at least one year.

Results: 78 patients in group CP and 68 subjects in group CC were evaluated. Demographic and clinical characteristics and laboratory data of two groups were similar at baseline. In group CP, mean PTH values in 1st and 12th month were 1257.6 ± 668.4 pg/mL and 928.8 ± 497.3 whereas in group CC, mean PTH values in 1st and 12th month were 1226.9 ± 595.6 pg/mL and 1210.9 ± 574.8 (p<0.003). At baseline two groups’ phosphorous levels were similar however for a period of 5 months of the following up period in group CP phosphorous levels were significantly lower than the group CC (p<0.02, respectively). At baseline both groups’ alkaline phosphatase levels were similar however at the end of the study in group CP, ALP levels were significantly lower than the group CC (p<0.002). Both initial and completion cinacalcet doses were similar in both groups. Despite the mean dose of vitamin D administration was significantly higher in paricalcitol group (14.98 ± 9.06 mcg/week/12 months) than the calcitriol group (10.8 ± 8.85 mcg/week/12 months) we observed less hyperparathormia and elevated Ca×P in group CP (p<0.01, p<0.05 respectively).

Conclusions: This observational study showed that combination therapy with paricalcitol and cinacalcet is superior in terms of PTH response to treatment, less hyperparathyromia and decrease in alkaline phosphatase levels to combination calcitriol and cinacalcet in dialysis patients with severe SHPT. We suggest that paricalcitol and cinacalcet combination should be preferred in resistant cases.

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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) have significant roles in the development of sHPT. Whether the detected correlation between FGFR/FGFR-Klotho complexes seem to be involved in its development.

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

Results: The presence of lymphocytes 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, VDR and an impaired Klotho-FGFR-axis seem to be the major players in the development of sHPT.

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 a highly significant positive correlation could be found between the expression of FGFR and VDR (p=0.004).

Interestingly, in terms of VDR we found a shift to a more mixed nuclear/cytoplasmic staining in the HPT group compared to normal parathyroid gland cells, which showed solitary nuclear staining for VDR (p>0.05).

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 (p=0.004).

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.
Abstracts

Nephrology Dialysis Transplantation

MP529 SCLEROSTIN AND 1 YEAR SURVIVAL AMONG PATIENTS UNDERGOING HEMODIALYSIS
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Introduction and Aims: Sclerostin, a protein expressed by osteocytes, has recently shown to be a good predictor for bone formation in chronic kidney disease patients. Serum sclerostin levels are increased in these patients and whether sclerostin affects patient survival is unknown.

Methods: We examined 1 year survival according to serum sclerostin levels in a prospective cohort of 350 prevalent hemodialysis patients (164 males, 186 females, mean age: 57±13 years, mean hemodialysis vintage: 58±32 months).

Results: During follow-up, 26 hemodialysis patients (7.4%) died. Patients who died were 4(15.4%) younger, had lower 25-hydroxy vitamin D3 (19.6 ±9.1 vs 29.8±11 ng/ml, p=0.024) and higher sclerostin levels (2143±1327 vs 1469±1373 pg/ml, p=0.017). 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 receiving calcitriol (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.

MP530 DIETARY TRENDS AND MANAGEMENT OF HYPERPHOSPHATEMIA 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 control.

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 P-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 (18–45 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.

MP531 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 any difference in diseases related clinical practice and characteristics.

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%; mean age: 57±13 years, mean hemodialysis vintage: 58±32 months). (AD: 68.7%, OLD: 90.8%, VOLD: 92.9%). Total serum median iPTH 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<NS and p<0.001). Adequacy of FSH and PTH levels were the lowest (19.7% and 15.0%) in group AD (AD vs OLD: p<0.001 and p<0.001). A total of 77% patients are on P inhibitor therapy (AD: 80.1%, OLD: 74.2%, VOLD: 69.0%).
RELATIONSHIP BETWEEN VITAMIN D AND SEXUAL DYSFUNCTION IN DIALYSIS PATIENTS

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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.

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 of 85.4%, anxiety rate of 22.7%, depression rate of 50% Sexual Dysfunction rates in women and in men were 95.4% and 75%, respectively. There was a significant difference in terms of sexual dysfunction between vitamin D groups (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).

In hemodialysis patients ASEX total score was significantly worse than continuous ambulatory peritoneal dialysis patients. There was a positive correlation between ASEX total score and age (p = 0.456, p = 0.0003).

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.

PROTON PUMP INHIBITOR-INDUCED HYPOMAGNESEMA IN HEMODIALYSIS PATIENTS AND ITS PREDICTIVE FACTORS

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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 hemodialysis (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 71.8 ± 4.9 years, were on PPI, omeprazole, 20 mg once daily, already for 25 (14-30) months at 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 cinacalcet 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±0.28 vs 2.51±0.30 mg/dL, p=0.002, 1.63±0.19 vs 2.01±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 during 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±141.14 vs 453.62±288.80 pg/mL, p=0.01 for no PPI group). URR >75% and spKt/V >1.5 were found in PPI group, while in no PPI group >70% and >1.4, respectively, throughout the study. No significant differences were noted in sMg and the other studied parameters between two groups when analyzed according to sex (male/female), HD modality (conventional HD/HDF) and cinacalcet or paricalcitol use.

Conclusions: Long-term PPI use was associated with variably lower sMg levels in HDF patients and 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 cinacalcet or paricalcitol use.

MAGNESIUM REGULATES PARATHYROID FUNCTION IN NORMAL RAT GLANDS IN VITRO

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Introduction and Aims: Parathyroid cells have cell-surface calcium-sensing receptors (CaR) to respond to small changes in serum calcium (Ca2+) levels. Other cations such as magnesium (Mg2+) are also able to activate CaR. The aim of our study was to determine in vitro the effect of Mg2+ 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 Ca2+ (0.8, 1.0, 1.2, and 1.5 mM) and Mg2+ (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 Ca2+ and physiological (0.5 mM) or high (2.0 mM) Mg2+ 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 Ca2+, only Mg2+ concentrations of 2.0 and 5.0 mM reduced PTH secretion by 38% and 68%, respectively. However, Mg2+ did not decrease PTH values below those observed with normal Ca2+ concentration. With normal or high Ca2+ levels, the effect of Mg2+ on PTH inhibition was not greater or absent. With exceptionally high Mg2+ concentration (5.0 mM), maximal inhibition of PTH secretion was observed. After six hours incubation at a Ca2+ concentration of 1.0 mM, the expression of parathyroid receptor CaSR, VDR, FGFR1 and Klotho (at both mRNA and protein levels) was significantly increased with a Mg2+ concentration of 2.0 as compared to 0.5 mM.

Conclusions: Our results show that high Mg2+ concentrations (2.0 mM or above) inhibit PTH secretion only when Ca2+ levels are low. Mg2+ also modulates parathyroid function through up-regulation of the key receptors CaSR, VDR, FGFR1 and Klotho.

MAGNESIUM REVERSES VASCULAR CALCIFICATION IN UREMIC RATS

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Introduction and Aims: Cardiovascular disease is associated with high mortality in chronic kidney disease (CKD) patients. Vascular calcification (VC) is a frequent complication and a strong predictor of mortality in these patients. Hyperphosphatemia is a major pathogenic factor for VC. Recent clinical studies indicate that magnesium...
(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 VC 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 VC 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. 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 plasmatic 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.

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**LOWER DIALYSATE CALCIUM CONCENTRATION FOR HOME HEMODIALYSIS CAN AFFECT CALCIUM BALANCE DURING DIALYSIS SESSION AND BONE METABOLISM**

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1Working Group for Patient Registry Japanese Society for Home Hemodialysis

**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 dialysate 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 (JHHDR).

**Methods:** At the end of the year 2011, we sent questionnaires to the facilities where home hemodialysis (HHD) is provided. Anonymous data were collected as electronic analyses.

**Results:** The total numbers of HHD patients were 327, which was surveyed by 16 centers. Total numbers of HHD patients who treated by acetate-non-containing home hemodialysis (HHD) is provided. 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) level but not in BMD between the two groups. Multiple logistic regression analysis showed that in females, BMD was independently associated with a history of fracture (p=0.04). In male patients, plasma Hcy level was marginally 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 non-enzymatic cross-links. Hyperhomocysteinemia, a frequent complication in HD patients, might play a role in bone fracture in this population.

**DIFFERENCE IN FACTORS ASSOCIATED WITH BONE FRAILTY 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) level 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=0.04). In male patients, plasma Hcy level was marginally significantly associated with a history of bone fracture (p=0.07).

**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 non-enzymatic 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: T helper (Th) lymphocytes play critical roles in the immune activation and inflammation in the chronic hemodialysis (HD) patients and mineral bone disorders including hyperparathyroidism and hyperphosphatemia 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 the inflammatory effects. Interleukin-17 producing effector memory T (Th17) cells and activation and inflammation in the chronic hemodialysis (HD) patients 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 phorbomlyristate acetate (PMA) and ionomycin in different time point. The Th17 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% ± 10.2%) 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 Treg 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.

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, Ca×P product, CRP, cholesterol, triglycerides and BMD (bone mineral density) in Patienten Hemodialysis and Predialysis stages (stage 384).

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 pre-dialysis group (stage 384CKD), Group C:Control group, consists of 10 healthy no significant difference in survival rate between the high and low OCP groups in normal Ca × P patients, while significant difference (P < 0.001) was observed in high Ca × P group.

Conclusions: Serum OC levels may be a useful marker for predicting the emergence of new CVD events in maintenance HD patients.
volunteers who are age and sex matched to the patients. All groups were subjected to the following: full medical history, full clinical examination, total serum Calcium and total serum Phosphorus, C-Reactive Protein (CRP), total serum cholesterol and triglycerides, intact parathyroid hormone (iPTH), serum Osteoprotegerin (OPG) and measurement of BMD with DXA at lumbar spine L2-L4.

**Results:** There was highly statistical significant increase in OPG level measured for groups A, B compared with group C. In dialysis group, OPG showed a non significant correlation with calcium, but it showed a significant positive correlation with age. On the other hand, it showed a high significant positive correlation with iPTH, Phosphorus, Ca×Ph product, CRP, Cholesterol, Triglycerides, and stage 3 & 4 of CKD. It showed a significant positive correlation with age, iPTH, Phosphorus. On the other hand, it showed a significant negative correlation with Cholesterol. While a highly significant negative correlation was obtained with corrected serum calcium, and high significant negative correlation with BMD.

**Conclusions:** We conclude that the osteoprotegerin increased in patients with CKD even in the stages before the start of renal replacement therapy. We strongly suggest the annual determination of this marker as part of the biologic flow-up of these patients. Serum OPG may be a useful biomarker for early diagnosis of CKD-MBD, also OPG or one of its derivatives may be used in the future in the treatment of CKD-MBD.

**MP542 SATANUM 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 patients receiving lanthanum carbonate.

**Results:** In the unmatched cohort, the lanthanum-treated group had a significantly 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 concentrations of phosphate >6.0 mg/dl (HR 0.53; 95% CI 0.29 to 0.96; P = 0.035). Similarly, 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 0.50; 95% CI 0.27 to 0.91; P = 0.029).

**Conclusions:** Treatment with lanthanum carbonate was independently associated with survival benefit in maintenance haemodialysis patients with uncontrolled hyperphosphatemia. Randomized controlled trials are needed to determine whether lanthanum carbonate actually improves survival among patients receiving maintenance haemodialysis.

**MP543 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 iP absorption (Ap) is important for evaluating effect of diet and phosphate binders. Ap is considered to be equal to the amount of intradialytic iP removal (Rp) because the balance of absorption from intestine and elimination of iP 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 thrice a week. Their blood flow rate (Qb) was between 160-240 ml/min. Their serum iP concentration (Pa) at start of HD was 4.5±1.8mg/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=33.06QBt•(HD1)+24.5(489)(500)+0.51+1.75UNt•Ni•4.668Pa4+0.0694U(Pa+Pa4), where Qb (dl/min), Ht, and Ht = hematocrit at start and end of HD, UNt and Ni = serum urea nitrogen concentration at that, Pa4 and Pa0 = Pa 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 eRps in 3 sessions. eRpw was compared with eRP in HD1 (eRP1).

**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 eRps in each HD session was 35.8, 33.7 and 30.5%. Weekly amount of iP removal estimated by data from HD1 (eRPwHD1) was shown as eRPwHD1=2.793eRPs. This eRPwHD1 was extremely similar to the sum of Rp from three sessions (y=0.951x+138, R=0.947, P<0.001). (3) In 87 HD sessions, correlation between eRP and pre-HD Pa was observed (y=175x+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 175mg when Pa becomes 1mg/lower in conditions of this study. For reducing the Pa before HD, by 1mg, weekly amount of iP absorption should be restricted by 489 mg.

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

Methods: We recruited 52 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±3.0 years and 59.6±0.95 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±1.06 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 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 (KDIGO) foundation 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 ± 75 months. The treatment involved administration of calcium carbonate (17%), calcium acetate (17%), sevelamer (30%), alfalcidol (18%), cincalcet (11%), and cholecalciferol (9.1%). The mean daily rate of 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: 0.93–1.41 mmol/L) (r² = 0.6, p < 0.001; y = 0.55 + 1.4 and r = 0.35; p < 0.001; y = 0.78 + 1.3, respectively). The mean ratios of 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 values: iCa was 1.12 ± 0.07 mmol/L in males and 1.16 ± 0.08 mmol/L in females (p = 0.008). Serum bone markers, PTH values, aortic 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 hypercalcemia is highly prevalent in patients on HD (43%): the male predominance of this finding was not expected. Insufficient dietary calcium intake or insufficient supplementation may be the main cause for this finding. iCa appears superior to Alb-Ca in predicting hypercalcemia. Hypercalcemia is very uncommon and not predicted by tCa.
differences between both groups neither in phosphorous level nor in number of samples with serum phosphorous > 5.5 mg/dL.

**Conclusions:** An isolated dose of 3 mg of 25-Hydroxycholecalciferol keeps enough levels of 25(OH)D with decreased LFT for three months. The dose seems secure but the correction of 25(OH)D levels and their potentially beneficial effects require long-term follow-up studies.

### MP548

#### A RANDOMIZED, OPEN-LABEL, CROSSOVER DESIGN STUDY TO COMPARE THE SAFETY AND EFFICACY OF SEVELAMER CARBONATE VERSUS CALCIUM CARBONATE IN THE TREATMENT OF HYPERPHOSPHATEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON DIALYSIS

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**Introduction and Aims:** Hyperphosphatemia (HyperPO4) and chronic kidney disease: metabolic bone disease (CKD-MBD) is common in end stage renal disease (ESRD). Untreated hyperPO4 can lead to cardiovascular calcification and calciphylaxis. It is a recognised risk factor for cardiovascular disease (CVD) in CKD patients. Controlling hyperPO4 is paramount in retarding CKD-MBD and reducing CVD. Several phosphate (PO4) binders are approved to treat hyperPO4. Calcium-based PO4 binder is the most commonly used; however, it can cause hypercalcemia & increased cardiovascular calcification. Sevelamer, calcium-free PO4 binder is frequently associated with gastrointestinal (GI) disturbances. The aim of this study is to evaluate the efficacy and safety of Sevelamer Carbonate (SC) compared to Calcium Carbonate (CaCO) in Asian ESRD patients.

**Methods:** Fifty two (52) Asian ESRD patients were enrolled in this prospective randomized open-labelled crossover trial. After 2 weeks washout, subjects were randomly assigned to either SC or CaCO for 6 weeks. This followed by another 2 weeks washout & a crossover to the other drug for another 6 weeks. The dosage was titrated at week 2 & 4 with target phosphorus ≤ 1.78 mmol/L.

**Results:** Mean age was 52 ± 13.81 years; Male:Female = 28:24. Race; Malay: Chinese: Indian = 26(50%): 22(42.3%): 4 (7.7%). Mean MRT duration was 7.96 ± 5.51 years. Mean maximum daily dosage for SC & CaCO were 4.13 g (5.2 tablets) & 2.97 g (6 tablets) respectively. Significant reduction in phosphorus was observed at week 2 in both treatment groups (P < 0.02) & remained so at week 6. Phosphorus reduced from 2.01 ± 0.65 at baseline to 1.63 ± 0.52 mmol/L at week 6 with SC (P = 0.001), 1.96 ± 0.59 at baseline to 1.42 ± 0.71 mmol/L at week 6 with CaCO (P = 0.001). Calcium increased from 2.15 ± 0.28 to 2.23 ± 0.21 mmol/L during CaCO (P = 0.029), however no significant changes was observed during SC (2.16 to 2.14 mmol/L). Serum albumin increased significantly from 35.47 to 36.63 g/L during SC (P = 0.008) but not with CaCO. Calcium-phosphorus product reduced from 3.93 to 3.01 mmol²/L (P = 0.001) during SC, 3.63 to 2.75 mmol²/L (P = 0.001) during CaCO. Serum intact parathyroid hormone (iPTH) reduced from 332 to 279 pg/ml during SC whereas during CaCO increased from 296 to 344 pg/ml during CaCO. These were not significant. Three patients (5.8%) developed mild GI side effect (epigastric pain and bloated) during SC. All were resolved spontaneously and did not require any treatment.

**Conclusions:** Sevelamer Carbonate was well tolerated & effective in controlling hyperphosphatemia as well as reducing calcium-phosphorus product in Asian ESRD patients. Increased in serum albumin could be related to reduce inflammatory markers that was noted in other studies.

### MP549

#### ANALYSIS OF THE COST-EFFECTIVENESS OF SWITCHING FROM SEVELAMER CARBONATE TO LANTHANUM CARBONATE MONOTHERAPY IN THE EUROPEAN UNION

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**Introduction and Aims:** Recent data from the USA demonstrated that the dose-relativity between sevelamer and lanthanum carbonate (LC) increases in parallel to each other. Increasing in serum albumin could be related to reduce inflammatory markers. The aim of this study is to evaluate the efficacy and safety of switching phosphorus binder therapy from SC to LC offers potential cost savings, a reduced daily tablet burden (3 vs 4 tablets/day), and effective serum phosphate control.

**Methods:** mp549 table:

<table>
<thead>
<tr>
<th>LC dose (mg/day)</th>
<th>SC dose (mg/day)</th>
<th>LC cost (€/day)</th>
<th>SC cost (€/day)</th>
<th>Dose-relativity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>4800</td>
<td>7.86</td>
<td>7.38</td>
<td>1.06</td>
</tr>
<tr>
<td>3000</td>
<td>5600</td>
<td>7.86</td>
<td>8.61</td>
<td>1.13</td>
</tr>
<tr>
<td>3000</td>
<td>6400</td>
<td>7.86</td>
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<td>2.11</td>
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<tr>
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<td>7.86</td>
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<td>9600</td>
<td>7.86</td>
<td>14.76</td>
<td>3.21</td>
</tr>
</tbody>
</table>

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

**Conclusions:** LC 3000 mg/day was more cost-effective than SC ≥ 5600 mg/day, but not lower SC doses ≤ 4800 mg/day. Patient chart data (2012) indicated that 40% of patients in Germany receive ≥ 5600 mg/day monotherapy, of which 37% receive doses ≥ 4600 mg/day. The annual cost savings with a switching one patient from SC to LC 3000 mg/day ranged from €274/year (SC 5600 mg/day) to €2520/year (SC 9600 mg/day).

**Conclusions:** Our analyses indicate that LC 3000 mg/day is more cost-effective than SC ≥ 5600 mg/day, which may account for over 40% of ESRD patients in Germany. For these patients, switching phosphate binder therapy from SC to LC offers potential drug cost savings, a reduced daily tablet burden (3 vs 4 tablets/day), and effective serum phosphate control.

### MP550

#### COST-EFFECTIVENESS OF LANTHANUM CARBONATE VERSUS SEVELAMER HYDROCHLORIDE IN THE TREATMENT OF HYPERPHOSPHATEMIA IN END-STAGE RENAL DISEASE PATIENTS IN SPAIN

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**Introduction and Aims:** Hyperphosphatemia in patients with end-stage renal disease (ESRD) undergoing dialysis is associated with cardiovascular disease (CVD), which is a leading cause of death in these patients. Calcium-based phosphate binders are inexpensive and commonly used as first-line therapy to manage hyperphosphatemia. 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 treatment.

**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 ‘intent-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%.

**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 €630/QALY (ITT) and €464/QALY (completer). CVD management cost was the most influential parameter in the model. Assuming a €38 000/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 hyperphosphatemia in patients with ESRD undergoing dialysis.

### MP551

#### COMPARISON OF SEVELAMER, SEVELAMER CARBONATE AND LANTHANUM CARBONATE IN VITRO AND IN VIVO

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**Introduction and Aims:** Hyperphosphatemia is common in patients with chronic renal failure(CKD), particularly in advanced stages. The phosphate binders(PB)
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 pH 2 corresponding to stomach-pH, following the USP dissolution II paddle method at a rotation speed of 50 rev/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 4.00X10⁻⁹ M. We also calculated the amount of CO₂ produced from each tablet and evaluated gastric-pH in vitro 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 4.00X10⁻⁹ mol/L, LC 3.99X10⁻⁹ mol/L, S 3.95X10⁻⁹ mol/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.