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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 46% 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 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 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 mineral metabolism, including serum ionized calcium (iCa) and calcitonin (CT), were obtained before PTx. Patients aged < 18 years and patients treated with cinacalcet were excluded from the study. Chief cells (CC), OC and transitional oxyphil cells (TOC) were evaluated by means of a semiquantitative assessment in all the histological specimens; patients were considered positive if OC and/or TOC were present in more than 5% of examined area and at least in one gland.
Results: The 65 patients were subdivided into three groups, according to cell distribution: group 1 (only CC), group 2 (CC+OC), and group 3 (CC+OC+TOC). There were no significant differences either in the demographic characteristics or parathyroid hormone (PTH), alkaline phosphatases (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).

MP518 Table 1. Demographic and biochemical characteristics of the patients

	Group1 (CC)	Group2 (CC+OC)	Group3 (CC+OC+TOC)	Statistical significance *
number	20	23	22	
Age, years	40±10	52±14	54±13	NS
HDvintage,months	124±82	113±55	98±60	NS
M/F	12/8	11/12	8/14	NS
PTH, pg/ml	1690 ± 587	1653 ± 718	1376± 501	NS
ALP, mU/ml	295 ± 213	291 ± 186	253 ± 125	NS
CT, pg/ml	10.1 ± 5.6	18.4 ± 9.5	27.9 ± 16	p <0.01
tCa, mg/dl	10.2 ± 0.6	10.52 ± 0.5	10.8 ± 0.7	p <0.01
iCa, mmol/L	1.21 ±0.2	1.32 ± 0.11	1.35 ± 0.1	p <0.001
Albumin, g/dl	3.99 ± 0.4	3.97 ± 0.38	3.87 ± 0.5	NS
P, mg/dl	6.0 ± 1.5	6.0 ± 1.3	6.1 ± 1.1	NS

* ANOVA test; NS = not significant

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

MP519 DIFFERENCES IN MICROARCHITECTURE PARAMETERS OF BONE QUALITY IN LOW AND HIGH TURNOVER RENAL OSTEODYSTROPHY ASSESED BY HR-pQCT

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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 prevalent hemodialysis (HD) postmenopausal women were recruited for measurements of bone microarchitecture at the distal radius (DR) and tibia (TB). HD patients were matched for age, dialysis vintage and time since menopause and were divided in two groups according to their serum iPTH: Low bone turnover (LBT) iPTH <200 pg/ml (n:7; mean age 52.8 ± 4 y; iPTH 124 ±55) and High Bone turnover (HBT) iPTH >500 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 than HBT (N: 13 ± 2.5%; LBT 6.4 ± 3.8%; HBT 9.8 ± 3.7 p=0.05); trabecular thickness (TbTh) was slightly decreased in LBT and significantly increased in HBT (N: 0.06 ± 0.01 mm; LBT: 0.046 ± 0.01; HBT: 0.070 ± 0.01; p=0.01) . Cortical Thickness (CtTh) was decreased in LBT but much more in HBT (N: 0.69 ± 0.18 mm; LBT: 0.47 ± 0.07; HBT: 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; HBT: 719 ± 120 mg HA/cm3. %dif -11,4% p=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 HBT. The lower cortical volumetric density probably reflects higher bone porosity in the HBT patients.

MP520 PARATHYROID HORMONE PROFILING FOR OPTIMIZATION OF CALCIUM CONTENT IN DIALYSATE IN SEVERE HYPERPARATHYROIDISM, IN TAILORED, INCREMENTAL HEMODIALYSIS

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Introduction and Aims: Severe hyperparatyroidism is still a challenge in hemodialysis. The definition of dialysate Calcium (Ca) is a pending issue, coming of age in case of tailored dialysis schedules and of portable home dialysis machines (NxStage), with low flow dialysate. Direct measurement of Ca mass transfer is complex; Ca levels at start and end of dialysis are a poor measure of Ca balance. This study aims at describing intradialyitic Parathyroid Hormone (PTH), Ca and Phosphate (P) profiling for the definition of the Ca content in the dialysate, in patients with severe hyperparathyroidism on daily and incremental hemodialysis.
Methods: The study was performed in a Dialysis Unit dedicated to home hemodialysis and critical patients, with wide use of daily and tailored hemodialysis. Ca-P-PTH profile gathered Creatinine, Urea, Ca total and ionised, Albumin, Na, K, P, PTH (conventional laboratory methods) at start, mid and end of dialysis. Severe hyperparatiroidism was defined as PTH>300 pg/ml for at least 3 months. Four schedules of treatment were tested: 1. NxStage (Ca 1.5 mEq/L); 2. and 3. Conventional dialysis, polysulphone filter 1.8-2.1 m2, Ca 1.5 or 1.75 mEq/L; 4. NxStage, plus intradialytic Ca infusion. Dialysis sessions were tailored at normalization of pre-dialysis Ca and P (CaxP<50). In the case of severe hyperparathyroidism, therapy with vitamin D, Calcium, Phosphate binders, Calcium mimetic agents are adjusted monthly.
Results: 48 Ca-P-PTH profiles are collected, 38 in severe hyperparatiroidism (9 patients).Phosphate is efficiently reduced by all techniques. Ca levels are not modified on treatment 1, and increase in the other schedules. PTH levels are not modified on treatment 1 and significantly decrease in the other schedules, ($p<0.05$). The differences in "delta" start to end of dialysis are significant on treatment 1 vs other treatments ($p<0.05$).
Conclusions: PTH profiles may be of use in defining an appropriate Ca content in dialysate in severe hyperparathyroidism. The role of smaller surfaces and of lower flows on NxStage could be elucidated by use of larger filters and modulation of the Ca content in the dialysate. Our data support the need for tailored dialysate also on "low-flow" home dialysis, to increase its therapeutic potentials.

PTH pg/ml	Average at start (st.d.)	Average at mid (st.d.)	Average at end (st.d.)	ΔPTH (mid - start) (p-value*)	ΔPTH (end - start) (p-value*)	ΔPTH (treatments - Nx Stage) (p-value#)
Nx Stage (5)	563 (303)	437 (227)	538 (327)	-126 (0.3)	-25 (0.8)	
HDB Ca 1.5 mg/dl (11)	630 (345)	214 (86)	267 (110)	-416 (0.03)	-363 (0.002)	338 (0.01)
HDB Ca 1.75 mg/dl (25)	759 (483)	261 (282)	197 (132)	-497 (0.0002)	-562 (0.000002)	537 (0.000003)
NxStage + Ca gluc (7)	804 (384)	227 (95)	283 (165)	-577 (0.01)	-521 (0.01)	436 (0.04)
Ca mg/dl	Average at start (st.d.)	Average at mid (st.d.)	Average at end (st.d.)	ΔCa (mid - start) (p-value*)	ΔCa (end - start) (p-value*)	ΔCa (treatments - Nx Stage) (p-value#)
Nx Stage (5)	9.2 (1.13)	9.4 (0.93)	9.7 (1.02)	0.2 (0.7)	0.5 (0.3)	
HDB Ca 1.5 mg/dl (11)	9.13 (0.92)	10.35 (0.74)	10.78 (0.69)	1.21 (0.01)	1.64 (0.00003)	-1.15 (0.005)
HDB Ca 1.75 mg/dl (25)	9.06 (0.96)	10.3 (0.81)	10.93 (0.87)	1.25 0.00003)	1.87 (0.0000001)	-1.37 (0.000003)
NxStage + Ca gluc (7)	7.29 (2.24)	9.76 (0.67)	8.93 (2.6)	2.47 (0.02)	1.64 (0.01)	1.14 (0.04)
P mg/dl	Average at start (st.d.)	Average at mid (st.d.)	Average at end (st.d.)	ΔP (mid - start) (p-value*)	ΔP (end - start) (p-value*)	ΔP (treatments - Nx Stage) (p-value#)
Nx Stage (5)	4.56 (1.02)	2.66 (0.67)	2.3 (0.53)	-1.9 (0.002)	-2.26 (0.006)	
HDB Ca 1.5 mg/dl (11)	5.31 (1.03)	2.47 (0.66)	2.45 (0.36)	-2.84 (0.00004)	-2.86 (0.0000004)	0.60 (0.03)
HDB Ca 1.75 mg/dl (25)	5.16 (0.97)	2.68 (0.55)	2.56 (0.46)	-2.48 (0.0000001)	-2.6 (0.0000001)	0.34 (0.0001)
NxStage + Ca gluc (7)	4.93 (0.95)	2.7 (0.74)	2.22 (0.86)	-2.23 (0.000009)	-2.71 (0.0002)	0.45 (0.06)

MP520

MP521 THE IMPORTANCE OF DIFFERENTIATION BETWEEN PARATHYROID HORMONE 1-84 (iPTH) AND NON 1-84 FRAGMENTS IN THE DISORDERS OF BONE AND MINERAL METABOLISM

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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 1-84 (PTHi). 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 of the third generation measuring PTH 1-84(PTHbio).
Methods: The study was performed in 147 patients on hemodialysis with the determination of PTH, PTHbio, PTH ratio (PTHbio / PTH-PTHbio), Ca, P, FGF23, 25OHvitaminD, before hemodialysis. PTH and PTHbio were measured using roche **elecsys®**,FGF23 Immunotopics.
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 ±2.3 mg/dl, PTHi 298.04±306.53 pg/ml, PTHbio 174.94±172.18 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 PTHi,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 FGF23. PTHbio iPTH and also correlate with FGF23. The ratio does not correlate with either the Ca or P, or years in HD or age. In the univariate analysis model the PTH1-84/PTH7-84 ratio correlates positively with FGF23 (p 0.04) such that a 1% increase in the ratio represents an increase of 1.6% of FGF23. PTHbioand iPTH also correlate with FGF23. The ratio does not correlate with either the Ca or P, or years in HD or age.
Conclusions: 1. - It is very important to know the values of 1-84 and non1-84 fragments 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 4. - The ratio expresses a sample of high turnover bone and correlates with the FGF23.

MP522 THE RELATIONSHIP BETWEEN INTACT PARATHYROID HORMONE LEVELS AND DAILY PHYSICAL ACTIVITY IN HEMODIALYSIS PATIENTS

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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 were recorded for all patients. Depressive symtoms, 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 (P:0.009). Post hoc analysis of these 4 groups revealed that only Group 1 and Group 2 (P:0.012), and Group 2 and Group 4 (P:0.034) were different with respect to NEADLS scores.
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.

MP523 ATTENUATED MEGALIN EXPRESSION CONTRIBUTES TO THE PATHOGENESIS IN HYPERFUNCTIONING PARATHYROID TUMORS

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Introduction and Aims: Megalin is a multiligand endocytotic 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 enhances the secretion of parathyroid hormone (PTH) from parathyroid tumors in primary hyperparathyroidism (PHPT) and secondary hyperparathyroidism of uremia (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 therapeutic parathyroidectomies. The study was approved by the institutional ethics committees and was conducted in accordance with the principles of the Declaration of Helsinki.

Results: The megalin expressions decreased 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 hyperplasias. 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-sRAP. The distribution of megalin overlaps with that of His-sRAP in the membrane region.
Conclusions: The incorporation of His-sRAP suggested megalin has a crucial role 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.

MP524 TRENDS IN MEDICAL AND SURGICAL MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM (SHPT) AMONG HEMODIALYSIS PATIENTS: RESULTS FROM THE DIALYSIS 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 regressions were used to calculate the trend over DOPPS phase in PTX 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 Japan while remaining relatively unchanged in N America. Patients with PTH>800 had a higher PTX rate after adjusting for region and phase (p<0.01). Cinacalcet prescription increased from DOPPS phase 3 to 4 in all regions. During the same time period, vitamin D prescription increased in Eur-A/NZ and North America. In Japan, prescription of any vitamin D remained stable, however use of IV vitamin D became more common in recent years.
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 calcimimetics, 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 despite an increase in median PTH and decrease in PTX, probably because cinacalcet is now prescribed for this condition.

Trends in medical and surgical management of SHPT, by DOPPS region

	DOPPS Phase (year)			
Treatment/Lab by Region	2 (2002)	3 (2006)	4 (2009)	p for trend[a]
Europe-A/NZ[b]				
PTH, pg/mL - median [IQR][c]	163(76,329)	204(107,380)	242(132,409)	<.01
PTH > 800 pg/mL, %	5.5	6.5	6.2	0.25
PTX rate, per 1000 pt yrs (95% CI)	16.7(15.3,18.1)	11.6(10.6,12.7)	8.8(8.0,9.5)	<.01
Cinacalcet[d], %	-	3.9	16.9	<.01
Vitamin D[e] (Any), %	31.6	50.4	50.5	<.01
IV, %	10.2	10.3	15.7	0.05
Oral, %	23.0	41.3	36.2	<.01
North America				
PTH, pg/mL - median [IQR][c]	203(101,382)	242(135,427)	269(170,437)	<.01
PTH > 800 pg/mL, %	6.9	9.0	9.0	0.14
PTX rate, per 1000 pt yrs (95% CI)	10.0(8.9,11.2)	10.5(9.1,12.0)	8.4(7.3,9.7)	0.16
Cinacalcet[d], %	-	11.4	20.4	<.01
Vitamin D[e] (Any), %	51.7	61.6	65.8	<.01
IV, %	43.6	51.0	62.2	<.01
Oral, %	9.7	11.7	6.6	0.32
Japan				
PTH, pg/mL - median [IQR][c]	143(62,261)	154(78,270)	132(74,217)	0.19
PTH > 800 pg/mL, %	2.8	2.1	0.7	<.01
PTX rate, per 1000 pt yrs (95% CI)	12.2(10.4,14.3)	14.2(12.3,16.4)	2.8(2.4,3.3)	<.01
Cinacalcet[d], %	-	0.1	8.5	<.01
Vitamin D[e] (Any), %	55.7	55.5	60.5	0.23
IV, %	11.1	17.9	27.8	<.01
Oral, %	47.0	38.9	35.7	<.01

a. Logistic regression was used to calculate p-values for trend over DOPPS phase for binary variables. Linear regression was used to calculate p-values for trend over DOPPS phase for continuous variables. Models accounted for facility clustering.
b. Europe-A/NZ includes Belgium, France, Germany, Italy, Spain, Sweden, United Kingdom, Australia and New Zealand.
c. PTH was log transformed before testing for trend over DOPPS phase.
d. Cinacalcet did not become widely available in the DOPPS countries until after DOPPS phase 2.
e. Calcitriol or one of its synthetic analogues included; nutritional vitamin D was not included.

MP524

MP525 THE CALCIMIMETIC CALINDOL PREVENTS HIGH PHOSPHATE-INDUCED VASCULAR CALCIFICATION BY UPREGULATING MATRIX GLA PROTEIN

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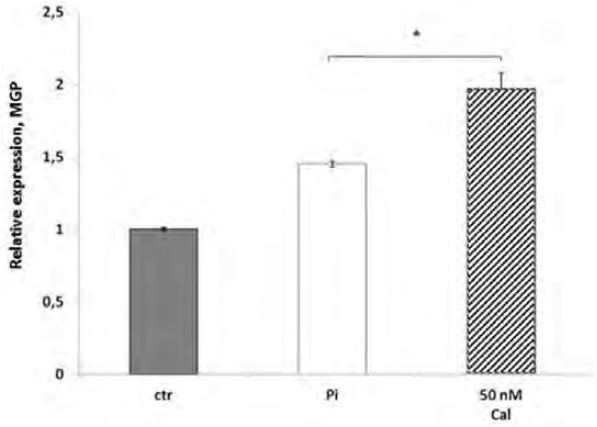
Introduction and Aims: High serum phosphate (Pi) levels represent a major issue in dialysis patients, because associate with secondary hyperparathyroidism (SHPT), vascular calcification (VC), and cardiovascular outcomes. In this population, calcimimetics are used to control SHPT, hyperphosphatemia, and, more recently, to delay the progression of VC. The aim of this *in vitro*study was to investigate the direct effects of the calcimimetic calindol 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 calindol were investigated on vascular calcium (Ca) deposition and VSMC osteoblastic differentiation.
Results: Calindol inhibited Ca deposition concentration-dependently with a maximal inhibition of 64.0±5.2% achieved at 100 nM. Furthermore, calindol was able topartially prevent the high Pi-induced Bone Morphogenic Protein 2 (BMP-2) expression upregulation (32.4 ± 4.6% of inhibition; p<0.01). Interestingly, the pretreatment with calindol enhanced the Matrix Gla Protein (MGP) gene expression significantly, compared to high Pi-treated cells (40.2 ± 6.6 % of increase, p<0.01).
Conclusions: In conclusion, we demonstrated that the calcimimetic calindol prevents high Pi-induced VC, by affecting osteoblastic differentiation *in vitro*. In particular, the inhibitory effect of calindol on VC is probably due to its stimulatory role on Ca Sensing Receptor, leading to an increase in the synthesis of MGP by VSMCs.



MP525

MP526 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; Immutopics, 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=0.015, respectively. Serum calcium and phosphate concentration remained stable during the observation [calcium: 2.15 (2.07-2.22) before treatment, 2.11 (2.04-2.17) after 3 months of treatment and 2.08 (2.0-2.15) mmol/l after 6 months of treatment]; [phosphate: 2.02 (1.87-2.18), 1.97 (1.81-2.14) and 1.9 (1.74-2.05) mmol/l; p=0.20 respectively].
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.

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 < 10.5mg/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 929.8 ± 497.3 whereas in CC group, 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 follow-up period in group CP phosphorus 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 hyperphosphatemia and elevated CaxP in group CP (p<0.01, p<0.05 respectively). Duration of vitamin D cessation because of high phosphorus levels were significantly shorter in group PC group CC (3(6) vs. 4(5) months, p<0.011).
Conclusions: This observational study showed that combination therapy with paricalcitol and cinacalcet is superior in terms of PTH response to treatment, less hyperphosphotemia 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.

MP528 ANALYSIS OF Î-KLOTHO, FIBROBLAST GROWTH FACTOR-, VITAMIN-D AND CALCIUM-SENSING RECEPTOR IN 70 PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

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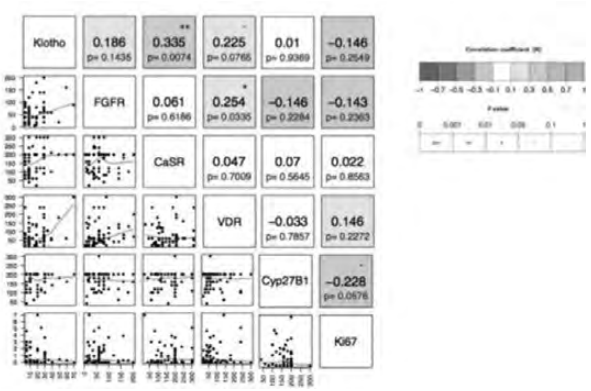
Introduction and Aims: Secondary hyperparathyroidism (sHPT) is known as a very common complication in patients with chronic kidney disease, and G-protein-coupled calcium-sensing receptor (CaSR), Vitamin D receptor (VDR) and Fibroblast growth factor receptor (FGFR)/Klotho complexes seem to be involved in its development.
Methods: Hyperplastic parathyroid glands from 70 sHPT patients and normal parathyroid tissue from 7 patients were obtained during parathyroidectomy. 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 than analyzed for all patients.Using this analysis, a highly significant positive correlation could be found between the expression of FGFR and VDR (p=0.0004). 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).
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.



MP528

MP529 SCLEROSTIN AND 1 YEAR SURVIVAL AMONG PATIENTS UNDERGOING HEMODIALYSIS

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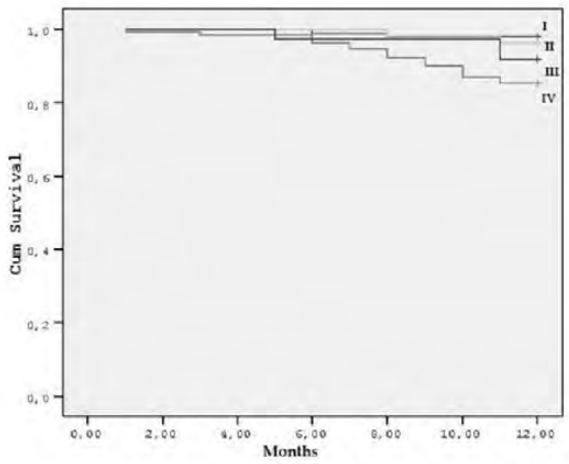
Introduction and Aims: Sclerostin, a protein expressed by osteocytes, has recently been shown to be a good predictor for bone formation in chronic kidney disease patients. Serum sclerostin levels are increased in these patients and whether sclerostin affects patient survival is unknown.
Methods: We examined 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 (7,42‰) died. Patients who died were elder (67,8±9 vs 56,5±13 years, p=0.013), 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 (21,6 ng⁄ml; Group 1) were associated with an increase in survival when compared to 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.



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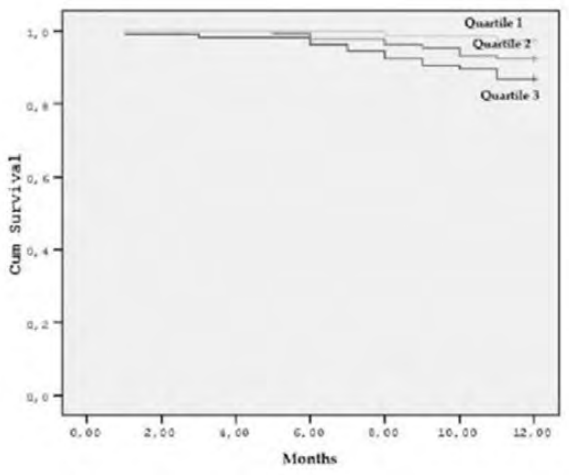

MP529

MP530 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 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 and 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 %), hemodialysis: 88,6% (AD: 85,9 %, 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<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 %) following in group VOLD (28,8 %) and AD (27,3 %). Serum iPTH level was lower in patients with DM compared to pts without DM patients in all age groups (AD: p<0,01; OLD: p<0,001; VOLD: p=0,646). Calcimimetic (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 levels and laboratory target achievements 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.

MP532 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. Patients were divided into 3 groups according to the level of 25-hydroxyvitamin D: 25-hydroxyvitamin D level ≤ 5 ng / ml group1, 6-15 ng / ml group 2,16-30 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.Values greater than cut-off point were evaluated as anxiety and depression, respectively .
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 was 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 (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). 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 (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.

MP533 PROTON PUMP INHIBITOR-INDUCED HYPOMAGNESAEMIA 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 (56-89), were on PPI, omeprazole, 20 mg once daily, already for 25 (14-48) 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±0.54 mg/dL, p=0.002, 1.91±0.33 vs 2.40±0.24 mg/dL, p=0.002 and 2.11±0.20 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 significantly higher by the end (282.50±121.65 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). 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 HD-HDF patients without 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.

MP534 MAGNESIUM REGULATES PARATHYROID FUNKTION IN NORMAL RAT GLANDS *IN VITRO*

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Introduction and Aims: Parathyroid cells have cell-surface calcium-sensing receptors (CaSR) to respond to small changes in serum calcium (Ca^{2+}) levels. 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 orhigh Ca^{2+} levels, the effect of Mg^{2+} on PTH inhibition was minor or absent. With excessively high Mg^{2+} concentration (5.0 mM), maximal inhibition of PTH secretion was observed. After six hours incubation at a Ca^{2+} concentration of 1.0 mM, the expression of parathyroid receptors CaSR, VDR, FGFR1 and Klotho (at both mRNA and protein levels) was significantly increased with a 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.

MP535 MAGNESUM 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 . 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 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 0.6 %Mg supplementation treatment.
Conclusions: An increase in dietary of Mg promotes the reversion of vascular calcification and hyperparathyroidism.

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	Aorta Ca	Aorta P	P plasma	PTH	Mg plasma
2w Nx	55±12.4	28±7.1	14.9±1.1	284±23.3	7.2±0.8
2w Nx+2w Mg	32±4.80	18±3.4	10.3±0.9	103±17.9	9.4±0.3

MP536 LOWER DIALYSATE CALCIUM CONCENTRATION FOR HOME HEMODIALYSIS 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 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 (Japan Home Hemodialysis Registry: 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 files. Ca concentration of dialysate was made dichotomous, i.e. dialysate with Ca of 2.5mEq/L (LoCa) and 3.0mEq/L (HiCa). Patients treated by acetate-non-containing and citrate-added dialysate were excluded, because citrate could interfere with plasma ionized Ca concentration. Relationship between calcium concentration of dialysate 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 HHD patients in Japan. Total numbers of HHD patients were 327, 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 dialysate types were 46 (22%), 145 (69%), and 18 (9%) for LoCa, HiCa, and acetate non-containing dialysate, 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 9.13±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 iPTH: 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, iPTH 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 HHD 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.

MP537 DIFFERENCE IN FACTORS ASSOCIATED WITH BONE FRAGILITY 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 (tHcy) 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=0.04). In male patients, plasma tHcy 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 nonenzymatic cross-links. Hyperhomocysteinemia, a frequent complication in HD patients, might play a role in bone fracture in this population.

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	Male (n=32) Fracture			Female (n=22) Fracture		
	+	-	P	+	-	P
n	9	23		12	10	
Age (year)	66 ± 15	65± 10	0.44	69± 11	67± 12	0.89
Duration on HD (month)	96± 73	136 ± 103	0.37	139 ± 12	98 ± 91	0.95
Albumin (g/dL)	3.9 ± 0.3	3.8 ± 0.2	0.40	3.7 ± 0.3	3.8 ± 0.3	0.34
Adjusted calcium (mg/dL)	9.1 ± 0.2	8.9 ± 0.7	0.37	9.3 ± 0.6	9.0 ± 0.5	0.26
Phosphate (mg/dL)	5.0 ± 0.7	4.9 ± 0.7	0.77	4.7 ± 0.7	5.2 ± 1.0	0.18
Intactparathyroid hormone(pg/mL)	128 ± 71	99 ± 47	0.25	98 ± 48	144 ± 62	0.09
Alkaline phosphatase (U/L)	254 ± 125	272 ± 105	0.41	327 ± 123	286 ± 100	0.29
Total homocysteine (μmol/L)	61 ± 43	38 ± 18	0.04	31 ± 8.9	39 ± 14	0.24
High sensitivity C-reactive protein (mg/dL)	0.029 ± 0.026	0.070 ± 0.096	0.36	0.10 ± 0.17	0.04 ± 0.04	0.62
Lateral spine (L2-L4), BMD (g/cm^2)	0.77 ± 0.17	0.65 ± 0.17	0.18	0.45 ± 0.09	0.57 ± 0.09	0.02
Lateral spine (L2-L4), YAM (%)	84 ± 19	71 ± 19	0.19	58 ± 12	74 ± 13	0.02

MP538 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 reciprocal development pathways but exhibit opposite effects. Here we investigated the relationship between the Treg and Th17 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% ±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.

MP539 SERUM LEVELS OF OSTEOCALCIN ARE ASSOCIATED WITH CEREBRAL AND CARDIAC VASCULAR DISEASES IN HEMODIALYSIS PATIENTS

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Introduction and Aims: Osteocalcin (OC) is known as a bone metabolic marker. Serum OC levels have a better correlation with results of bone biopsies than serum levels of ALP or PTH in hemodialysis (HD)population. Further, OC has been reported to affect vascular calcification. In the present study, we examine correlation of serum OC levels with cerebral and cardiac vascular diseases (CVD) and mortality in maintenance HD patients.
Methods: This study is a longitudinal observational cohort study conducted over a period of 5 years. One hundred twenty-six HD patients were enrolled.We defined CVD events as new onset of fatal or nonfatal myocardial infarction, angina pectoris, cardiac failure, cardiac arrest caused by arrhythmia, cerebral infarction, or cerebral hemorrhage. To evaluate the impact of serum OC levels on CVD events, the participants were divided into two groups based on the median serum OC level of 71.5 ng/ml (low-serum OC group: <71.5 ng/ml, high-serum OC group ≥71.5 ng/ml).
Results: CVD events were observed in 29 out of 126 patients (23.0%). The number of cumulative CVD events in the low-serum OC group was significantly higher than that in the high-serum OC group ($p < 0.005$). Multivariate Cox proportional hazards analysis demonstrated that a low level of serum OC is a significant predictor of a higher incidence of CVD events [hazard ratio, 2.925; $p = 0.0401$] after adjustment.There was no significant difference in survival rate between the high and low OC 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.

MP540 ELDECALCITOL (ELD) TREATMENT FOR LOW BONE MASS IN POSTMENOPAUSAL WOMEN RECEIVING MAINTENANCE HAEMODIALYSIS

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Introduction and Aims: ELD, a new active vitaminD_3 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 evaluted 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 L_2-L_4 vertebrae using the dual-energy X-ray absorptiometry method (DEXA) on a QDR2000 densitometer.
Results: Table 1 shows the changes in mean serum Ca(Alb), P, intact PTH, BAP and TRACP-5b. Data shown as mean(SD). Mean serum 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. † is $p<0.05$ v.s 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 be not enough to improve low bone mass due to severely bone absorption such as postmenopausal women.

MP541 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 Patientson 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 10 healthy

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	LS-BMD	T score	Z score
Before	0.501 (0.119)	-3.81 (1.77)	-0.69 (1.70)
6 months after	0.518 (0.117)†	-3.57 (1.75)†	-0.39 (1.70)†
1 year after	0.509 (0.110)	-3.71 (1.64)	-0.49 (1.67)

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	Ca(Alb) (mg/dL)	P (mg/dL)	intact-PTH (pg/dL)	BAP (U/L)	TRACP-5b (mU/dL)
Before	8.97 (0.34)	5.06 (0.48)	111.5 (59.2)	131.3 (67)	722.5 (394.4)
6 months after	9.30 (0.34)	5.07 (0.51)	89.8 (54.5)	83.2 (44.2)	484.3 (270.1)
1 year after	9.47 (0.48)	5.16 (0.52)	79.0 (42.7)	67.5 (31.4)	459.5 (240.0)

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 DEXA 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, CaxPh product, CRP, Cholesterol , Triglycerides, and high significant negative correlation with BMD. **In pre-dialysis group**, OPG showed a non significant correlation with CaxPh product, CRP, Triglycerides and stage 3 & 4 of CKD. But it showed a high 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 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 (n = 568) and untreated (n = 568) patients matched by the propensity score of 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 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 0.93; 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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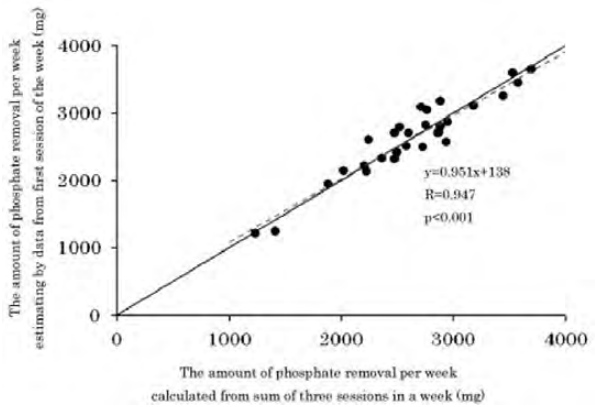
Introduction and Aims: Excess of phosphate (iP) is a risk for death in hemodialysis (HD) patients. Estimating the amount of iP absorption (Ap) is important for evaluating effect of diet and phosphate binders. Ap is considered to be equal to the amount of intradialytic iP removal (Rp) because the balance 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±1.0mg/dl. Blood samples were drawn at start and end of HD in consecutive 3 HD sessions (the first (HD_1), second (HD_2) and third (HD_3) HD sessions of the week). We calculated eRp using following formula as reported previously. $eRp=33.06Qb(1-(3Ht_0+2Ht_4)/500)(0.5+1.75(UN_4/UN_0)^{1/4})Pa_0+4.668Pa_4)+0.0689UF(Pa_0+Pa_4)$, where Qb (dl/min), Ht_0 and Ht_4=hematocrit at start and end of HD, UN_0 and UN_4 = serum urea nitrogen concentration at that, Pa_0 and Pa_4= 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 eRp in three sessions. eRpw was compared with eRp in HD_1 (eRp_1). (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_1 although serum UN concentrations before HD_1 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 iP removal estimated by data from HD_1 ($eRpw_{(HD1)}$) was shown as $eRpw_{(HD1)}=2.793eRp_1$. This $eRpw_{(HD1)}$ 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=0.800, 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 becomes 1 mg lower in conditions of this study. For reducing the Pa before HD_1 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.



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MP544 UNDERCARBOXYLATED OSTEOCALCIN AND SECONDARY HYPERPARATHYROIDISM IN POSTMENOPAUSAL PATIENTS ON HEMODIALYSIS

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Introduction and Aims: Osteocalcin (also known as non-collagenous bone matrix gla protein)(OC), is a vitamin K-dependent Ca^{2+}-binding protein, produced by osteoblasts. OC biosynthesis is tightly regulated by 1,25-dihydroxy-vitamin D_3. OC carries three gamma-glutamic acid residues (Gla) at positions 17, 21, and 24, which are target for vitamin K-dependent carboxylation and OC activation. Carboxylated OC is

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1	2	3	4
Control group	HD patients without secondary hyperparathyroidism (SHPT)	HD patients with SHPT, not treated with cinacalcet and calcitriol	HD patients with SHPT treated with cinacalcet and calcitriol
3.01±0.36 n=26	12.318±8.106 n=6	14.630±7.824 n=10	23.723±6.911 n=7
	2:1 p<0.001	3:2 p-NS	4:3 p<0.02

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Parameter	Pearson r	p
Parathormone	0.52	0.008
HD duration	0.77	0.0001
Age	-0.49	0.01

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 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±1.30 years and 59±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) levels [ng/L] were measured on Immulite 2000 using chemiluminiscent (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 ng/mL, n=26) was significantly increased in comparison with the levels in control group members (3.01±0.36 ng/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.

MP545 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 values.
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 160 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%), alfacalcidol (18%), cinacalcet (11%), and cholecalciferol (91.5%). The mean dialysate calcium concentration (DDC) was 1.51 mmol/L. The mean tCa 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) ($r^2 = 0.6$; $p < 0.001$; $y = 0.55 + 1.4x$ and $r^2 = 0.53$; $p < 0.001$; $y = 0.78 + 1.3x$, respectively). The mean ratios of tCa/iCa and Alb-Ca/iCa were 1.93 and 2.02, respectively. tCa was correct in 84% of patients, and Alb-Ca, in 37% of patients, in predicting low iCa levels (<1.12 mmol/L, n = 64). tCa 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). tCa was not a predictive factor for hypercalcaemia (iCa > 1.32 mmol/L, n = 3); Alb-Ca predicted hypercalcaemia in 2/3 patients. Sex was associated with iCa values: iCa was 1.12 ± 0.07 mmol/L in males and 1.16 ± 0.06 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 hypocalcaemia 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. tCa appears superior to Alb-Ca in predicting hypocalcaemia. Hypercalcaemia is very uncommon and not predicted by tCa.

MP546 SERUM 25-HYDROXYVITAMIN D ON CHRONIC KIDNEY DISEASE STAGE 5D- EFFECTS OF SUPLEMENTATION WITH CALCIFEROL

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Introduction and Aims: Chronic kidney disease(CKD)shows high incidence of Hypovitaminosis D(HyD)contributing to raise the risk of morbi-mortality.**Aims:**1-To study evolution of(HyD),in CKD stage5D, on patients undergoing Hemodialysis(HD) or Peritoneal Dialysis(PD)supplemented with oral doses individualized(to reach serum levels of 30ng/ml it was administered 100UI/0,7ng/ml)of calciferol(D3) at times:3mo;6mo;9mo.2-To compare incidence of HyD baseline(BL) and outcome on PD and HD.
Methods: 69 patients were evaluated,45 HD-62.2% male and 24 PD-62.5% male.The mean age on PD was 68.3±14.1 years on HD 53±16.9. Serum 25-hydroxyvitamin D (25OHD) was normal in 1(4.77%) patient on PD, and 6(13.3%) on HD. Serum levels of parathormone(PTH), Calcium(Ca), alkaline phosphatase(AP), phosphorus(P) and 25OHD was expressed as mean±SD. Mineral bone disease(MBD) was present as:PD group: adinamic bone disease (ABD)29.2% and secondary hyperparathyreoidism (SHP)20.8%;HD group: ABD 31.1%; SHP 35.6%.
Results: HD:25 patients were supplemented: 48% male, with mean age 53±16.9 years and BL values: 25OHD 22.6±6.8; Ca 9.8±0.8; P 5.4±1.5; AP 199.6±105.1; CaxP 51.9 ±14.5; PTH 285.6±234.7. Control group were constituted by 14 patients. **PD**: 3 controls,15 supplemented patients, 62.5% male, mean age 68.5±12.3 years; BL values: 25OHD 17.6±6.3; Ca 9.6±0.8; P 5.0±1.0; CaxP 48.9±12.1; PTH 266.8±249.9; AP 164.8 ±105.8. **PD:**0% of control and 38% of supplemented reached 25OHD normal values after 6 mo of treatment; increasing at 9mo comparing to BL (p<0.03); mainly on males (p<0.003) and older only 9mo(p<0.04). Ca at 9mo was lower than BL(p<0.04). **HD:**20%of control group and 26% supplemented reached normal levels increasing from BL (p<0,004) mainly on males(p<0.03) and older (p<0.04), although it showed an increase of PTH BL-9mo and 3-6mo(p<0.04).Ca BL to 6 mo decreased(p<0.05). CaXP values decreased (p<0.002); increased on supplemented patients at 9mo comparing to control (p<0.004). P decreased (p<0.003); increased on supplemented comparing to controls (p<0.007). PTH values increased (p<0.003).The main source of 25OHD is synthesis effected by ultraviolet radiation and low sun exposure contributes to HyD on HD e PD, as confirmed, in winter, by decreased values of 25OHD: 20% on PD and 55% on HD supplemented patients. **PD x HD**: PD: BL- 25OHD showed lower levels than on HD-BL (p<0.03), as well PTH 6mo (p<0.04) and PTH 9mo (p<0.02).
Conclusions: CKD stage 5D has high prevalence of HyD, which can manifest itself more seriously in PD, justified by older age. This study was performed in a region with high level of ultraviolet radiation, consequent it may have been minimized HyD. Considering the incidence of BMD and based on these results, we suggest: 1-Supplementation of 25OHD should have a different approach from general population, individualizing doses. 3-To find out a minimal dose for maintenance therapy. 2- six mo controls after standardization of 25OHD, having a measure preceding winter.4- Special care on females, PD, older and monitoring carefully patients with high P or PTH.

MP547 ADMINISTRATION OF A SINGLE, LARGE ORAL DOSE OF 25-HYDROXYCHOLECALCIFEROL 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-OHcolecalciferol (3 mg of Hidroferol ®, 180,000 UI) Serum levels of D vitamine and mineral metabolism markers have been analized.
Methods: Chronic hemodialysis patients with 25(OH)VitD < 30ng/ml were included. Patients with serum calcium > 10 mg/dl or PTH > 800 pg/ml were excluded. The patients were randomized in two groups: treated group and controlled group. Time follow-up was 16 weeks. The usual treatment for controlling Ca/P levels neither the dialysis bath (calcium of 2.5 mEq/L) were modified. 86 patients ended the study, 42 patients in treated group and 44 in controlled group.
Results: A higher level of 25(OH)VitD 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) VitD were observed in the controlled group, associated to the summer period. The levels of 25(OH)VitD were even bigger in the treated group than in the 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

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-Hidroxycholecalciferol keeps enough levels of 25(OH)Vit D with a decreased level of PTH for three months. The dose seems secure but the corrrection of 25(OH)VitD 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 HYPERPHOSPHATAEMIA 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 & reducing CVD. Several phosphate (PO4) binders are approved to treat hyperPO4. Calcium-based PO4 binder is the most commonly used, however it can cause hypercalcaemia & exacerbate vascular 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 phosphate ≤ 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 RRT 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 phosphate was observed at week 2 in both treatment groups ($P < 0.02$) & remained so at week 6. Phosphate 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 ± 0.37 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 $mmol^2/L^2$ ($P< 0.001$) during SC, 3.63 to 2.75 $mmol^2/L^2$($P< 0.001$) during CaCO. Serum intact parathyroid hormone (iPTH) reduced from 332 to 279 pg/ml during SC however 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 required 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 with the dose of sevelamer required to control serum phosphate levels. Overall phosphate levels were similar when treated with LC or sevelamer. The aim of this evaluation was to calculate cost-effectiveness comparisons of switching end stage renal disease (ESRD) patients from sevelamer carbonate (SC) to LC monotherapy using local German cost inputs.
Methods: SC:LC dose-relativity was based on US real-world, phase 4 trial data evaluating the relative phosphate binder dosing levels required to maintain phosphate control in ESRD patients. The relative costs of daily clinical monotherapy doses of SC and LC were calculated using German drug prices (LC 1000 mg: €2.62; SC 800 mg: €1.23; Sanofi prices, excluding value added tax).Although the average dose of LC monotherapy used in Germany is reported to be around 2500 mg/day, this evaluation looked at the cost-effectiveness of the slightly higher dose of LC 3000 mg/day against commonly used SC doses. This is a conservative approach since all comparisons of LC 2500 mg/day to sevelamer doses would be more cost-effective than those assessed here.
Results: Cost analysis of daily clinical doses, based on dosing levels required to treat phosphate levels to target from a US study (Table), revealed that LC 3000 mg/day is 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 SC ≥5600 mg/day monotherapy, of which 37% receive doses ≥6400 mg/day. The annual cost saving of 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 doses ≥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 ≥7 tablets/day), and effective serum phosphate control.

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LC dose (mg/day)	SC dose (mg/day)	LC cost (€/day)	SC cost (€/day)	Dose-relativity
3000	4800	7.86	7.38	1.6
3000	5600	7.86	8.61	1.9
3000	6400	7.86	9.84	2.1
3000	7200	7.86	11.07	2.4
3000	8000	7.86	12.30	2.7
3000	9600	7.86	14.76	3.2

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

MP550 COST-EFFECTIVENESS OF LANTHANUM CARBONATE VERSUS SEVELAMER HYDROCHLORIDE IN THE TREATMENT OF HYPERPHOSPHATAEMIA IN END-STAGE RENAL DISEASE PATIENTS IN SPAIN

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Introduction and Aims: Hyperphosphataemia 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 hyperphosphataemia. However, their use is restricted in some patients because of the possibility of increased risk of hypercalcaemia, 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%. 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 €30000/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.

MP551 COMPARISON OF SEVELAMER, SEVELAMER CARBONATE AND LANTHANIUM CARBONATE *IN VITRO* AND *IN VIVO*

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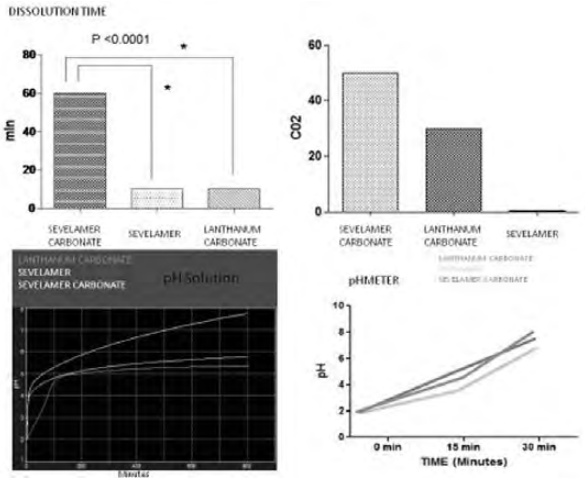
Introduction and Aims: Hyperphosphatemia is common in patients with chronic renal failure(CKD),particularly in advanced stages. The phosphate binders(PB)

[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 ours study was to compared 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 IIpaddle 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 his 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 $4.00X10^{-9}$Mol.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 inhibitor(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 pHmeter shown that gastric-pH increases significantly after administration of the tablets, especially with SC($p<0.0001$).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.



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