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Bone metabolism - Osteoporosis

Cod: M288

THE EFFECT OF PDE5 INHIBITORS ON BONE AND OXIDATIVE DAMAGE IN OVARIECTOMY-INDUCED OSTEOPOROSIS

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Osteoporosis is a major public health problem associated with many factors, and it affects more than 50% of women over 50 years old. In our study, we aimed to investigate the effect of PDE5 inhibitors on osteoporosis via the NO/cGMP/PKG signalling pathway. A total of fifty female albino Wistar rats were separated into five groups. The first group was appointed as the healthy control group with no ovariectomy. All animals in the other groups were bilaterally ovariectomized. Six month after the ovariectomy, vardenafil, udenafil and tadalafil were given to the third, fourth and fifth groups, respectively, but were not administered to the positive control group (10 mg/kg per day for 2 months). The BMD values were determined using a densitometry apparatus for all groups pre-and-post ovariectomy and after treatment. The level of NO, eNOS, ADMA, cGMP, PKG, PDE5, PYD, DPD, CTX and PICP were determined using an ELISA. The levels of MDA, 8-OHdG, dG and CoQ10 were determined by an HPLC assay. Additionally, the right femoral trabecular bone density and the epiphyseal plate were measured in all groups. Angiogenesis was histologically observed in the bone tissue. PDE5 inhibitors increased bone tissue angiogenesis through the NO/cGMP/PKG signalling pathway. Thus, we determined that the inhibitors caused a positive impact on the reduction of BMD and increased bone resorption markers. We also observed the positive effects of these inhibitors on oxidative stress. In conclusion, these PDE5 inhibitors increase angiogenesis in bone tissue and increase the re-formation rate of bone in rats with osteoporosis.

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Cod: M289

FREE 25 VITAMIN D AND CHRONIC KIDNEY DISEASE

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Background
Most chronic kidney disease (CKD) patients suffer from 25OH vitamin D (25OHvitD)deficiency,which might contribute to adverse health outcomes.Because vitamin D binding is altered during CKD, it has been proposed that serum free 25OHvitDbetter reflects vitamin D metabolism than total 25OHvitD. We aim to evaluate whether serum free 25OHvitD varies regarding the different stages of CKD, in comparison with total 25OHvitD.
Methods
We prospectively assessed 34 CKD patients during a glomerular filtration rate measurement (GFR) byinulinclearance. We measured serum free 25OHvitD by ELISA (DiaSource, Leuven, Belgium) and total 25OHvitD byimmunoluminometry(DiaSorin, Italy).
Results
Patients were aged 54.7 ±13.6yr, 44%were males. Mean GFR was 59 ±26 ml/min/1.73m2, serum total 25OHvitDwas 59.9±27.5ng/ml and serum free 25OHvitD 5.45 ±1.96 pg/ml.We found a strong association between free 25OHvitDand total 25OHvitD ($r=0.88$, $p<0.001$). Therewas no correlation between free 25OHvitD and GFRwhereas total 25OHvitDsignificantly declined with GFR decrease($r=-0.34$, $p=0.048$). Of interest, the ratio free/total 25OHvitD strongly decreased with the decline of kidney function ($r=0.55$ $p<0.001$).Wedid not find any relationshipbetween free 25OHvitDnor total 25OHvitD and measures of mineral metabolism.
Conclusion
This pilot study suggests that vitamin D bioavailability may be reduced in advancedCKD. The serum level of total 25OHvitDmay indeed mask low free 25OHvitD and inadequate correction of vitamin D deficiency.Free 25OHvitD may represent a new target for treatment adaptation.

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Cod: M290

NEW INSIGHTS ON THE NEW AUTOMATED DETERMINATION OF FGF23 ON THE DIASORIN LIAISON XL

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Introduction. Fibroblast growth factor 23 (FGF23), is a hypophosphatemic hormone produced by the osteocytes, that also decreases 1,25-(OH)2D levels. FGF23 increases early during the course of CKD. Increased FGF23 levels are associated with increased mortality in patients entering dialysis. Active FGF23 peptide is cleaved in the circulation and assays available on the market either measure the "intact" peptide or the "C-terminal" peptide. Here, we studied the stability of the peptide, provided reference ranges in a healthy population, and evaluated FGF23 concentrations in the different CKD stages for the automated DiaSorin assay on Liaison.
Materials and Methods. 5 hemodialyzed patients (HD) and 5 healthy volunteers had 8 EDTA samples which were processed as follows: one was immediately assessed after centrifugation, 4 samples were left 1, 4, 7 and 24 hours at room temperature (RT), centrifuged and kept at -80°C until determination and 4 samples were immediately centrifuged and frozen at -20°C. After 1, 4, 7 and 24 hours, aliquots were transferred at -80°C until analysis. After 2 days, all samples were thawed and run in duplicate in the same batch. Reference ranges were established in 910 healthy adults, and 44 samples per CKD stage (5D, 5, 4, 3a and 3b) were obtained to evaluate the impact of decreasing GFR on FGF23 values.
Results. The mean value was 60.8±19.4 and 1848±600 ng/L in the healthy and the HD population, respectively. The CV on the duplicates was 1.4%. We did not observe any decrease in FGF23 levels whatever the population or conservation condition. The distribution of the values obtained in the healthy population was Gaussian and the mean±SD was 57.9±17.5 ng/L. There were no differences between men and women and the 2.5 and 97.5 percentiles were 23.2 and 95.4 pg/mL. Patients in the 3a stage tended to have lower values than the 3b one (Median (IQR): 98.4 (53.5-128.7) vs 116.3 (73.6-147.5 ng/L) whereas there was a clear significant ($p<0.0001$) increase in FGF23 values according to CKD stage (Stage 4: 206 (131-305); Stage 5: 345(173-516) and 5D: 1015(385-4344).
Conclusions. We have evaluated the stability of FGF23, the reference range in a large population of healthy individuals and provided the first results of this new assay in a CKD population.

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Bone metabolism - Osteoporosis

Cod: M291

VITAMIN D DEFICIENCY AND ANTIEPILEPTIC DRUGS IN PEDIATRIC POPULATION WITH EPILEPSY

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Background: Chronic use of antiepileptic drugs (AEDs) especially with enzyme inducers, is associated with decreased bone mineral density and disorders of bone metabolism. Serum 25(OH)D3 concentration is the most commonly used index of vitamin D status, which is essential for the proper development and maintenance of bone, and reduced levels are seen in patients taking AEDs. Aim: To assess the effect of "old" or first generation AEDs (FGADs: phenyntoin (PHT), phenobarbital (PB), carbamazepine(CBZ) and valproic acid (VPA)) and "new" or second generation AEDs (SGADs: lamotrigine, gabapentin, levetiracetam, oxcarbazepine) on serum 25(OH)D3 levels and bone mineral metabolism markers in epileptic children. Materials and Methods: 154 children of a mean age 9,65±4,62, under long-term treatment with AEDs were divided in two groups: 65 (42 boys/23 girls) on FGADs and 89 (59 boys/30 girls) on SGADs. 25(OH)D3 and iPTH levels were determined by (ARCHITECT-I1000/ABBOTT) whereas calcium (Ca), phosphate (P) and alkaline phosphatase ALP by DxC600/BECKMAN-COULTER. Vitamin D deficiency was defined as 25(OH)D3 levels <20 ng/mL insufficiency 21-29 ng/mL and normal >30 ng/mL. Statistical analysis used was independent t-test and statistically significant was considered p-value <0.05. Results: Of the 154 paediatric patients studied, only 14.3% had VitD>30 ng/mL (10,8% (7/65) on FGADs and 16,9% (15/89) on SGADs). On FGADs group 63,8% had vitamin D levels <20 ng/ml (VPA:85,36%, CBZ:12,20%, PHT:2,44%) and 9,8% (6/65) increased levels of iPTH. On SGADs group 44,94% had vitamin D levels <20 ng/m and 22.5% (20/89) increased levels of iPTH. Ca, P and ALP were in a normal range. There were no statistically significant differences of VitD and iPTH levels between the tow groups of AEDs, neither between the sexes. Conclusions: Vitamin D deficiency (54.4%; 83 out of the 154 patients) was highly prevalent among our study subjects, and only 14.3% typically considered normal. Analysis of patients on old versus new AEDs in this study showed no difference in their vitamin D levels and children on either type of AED treatment are at equal risk. Increased attention on the part of both pediatric neurologists and primary care physicians to vitamin D status and bone health among children with epilepsy is needed.

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Bone metabolism - Osteoporosis

Cod: M292

IMPACT OF THE RENAL FUNCTION ON SCLEROSTIN DETERMINATION

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Introduction
Sclerostin (SCL) is a promising biomarker for bone research. It has also been associated, in some studies, with mortality in hemodialyzed (HD) patients. However, literature is conflicting on that point and some authors have pointed out that assays used for SCL might explain these discrepancies. It remains unclear whether these discrepancies come from a lack of clearance or a lack of specificity of the antibodies used in the assays.
Patients and methods
We have measured SCL concentrations in 150 healthy and CKD patients who had undergone GFR determination with the iohexol method. We have also measured SCL before and after a single dialysis session in 44 patients. Each sample has been measured with 4 different ELISA: Biomedica (B), MSD (M), R&D (R) and Teco (T).
Results
Median [IQR] SCL concentration in the non-HD patients were very different according to the method: B : 1017 [546], M : 36 [21], R : 160 [101] and T : 629 [325] pg/mL. We did not observe any systematic differences between the methods. In univariate analysis, we observed a significant and inverse relation between GFR and SCL when measured by B, R and T but not with M. The different assays also showed a wide variation in HD patients. With B and R methods, HD patients presented median values higher than those whose GFR was >45 mL/min, but were similar with those presenting GFR >45 mL/min. With T method, the median observed in HD patients was higher than in non-HD patients, whatever the GFR. On the contrary, median SCL was lower in HD than in non-HD patients with the M method. After a dialysis session, a significant decrease was observed in HDF, but not in HD mode and was always more important if SCL was measured with T, B and R methods, compared to the M one.
Discussion
SCL determination in CKD patients is challenging and any conclusion is method-depending. Previously described relations between GFR and SCL levels may be an analytical artifact with inactive SCL fragments that would accumulate when GFR decreases and would be recognized by T, B and R, but not M method.
Conclusion
SCL determination clearly impacts finding previously observed in CKD and HD patients.

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Cod: M293

DETERMINATION OF SERUM VITAMIN K1 AND VITAMIN K2 (MK-4, MK-7) BY HPLC IN POSTMENOPAUSAL WOMEN

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Backround: The role of vitamin K extends well beyond the regulation of blood clotting to impact bone formation, and development of heart disease, and possibly cancer. Vitamins K1 and K2 are the cofactors for the enzyme gamma-glutamylcarboxylase, which is involved in carboxylation of the vitamin K-dependent proteins. Objective of this study was to evaluate a new HPLC metod for determination of vitamin K1 and two forms of vitamin K2 (MK-4, MK-7) in patient serum, and determine the vitamin levels in postmenopausal women.
Methods: A HPLC method for the determination of vitamin K1 and vitamin K2 in human serum with fluorescence detection after post-column zinc reduction was developed. The internal standard (IS) was obtained from Immundiagnostik AG, Germany. 20 μL of IS were added to 500 μL of serum and 2 mL of ethanol were added to precipitate the proteins. The mixture was extracted with 4 mL of hexane for 10 min and then centrifuged. The organic layers were then evaporated at 50 °C under a stream of nitrogen. The dry residue was reconstituted with 2 mL of hexane and solid phase extraction was then used. The separation was accomplished at 22 °C. The detection was performed at 246 nm (excitation) and 430 nm (emission). The flow rate of mobile phase was 1.0 mL/min. We measured 245 patient samples from postmenopausal women and 30 patients before and after substitution with 45 μg/day vitamin K2 (Femoralex).
Results: The HPLC method has been successfully validated. A linear relationship between serum concentration and peak area was obtained for all three substances with correlation coefficient r2=0.9993 for vitamin K1 and r2=0.9995 for vitamin MK-7 and r2=0.9992 for MK-4. The intra and interday accuracy and precision were evaluated on two QC samples by multiple analysis and CV were less than 8%. The results in serum samples (expressed as median ± SEM) are as follows: 0.147 ± 0.209 ng/mL for vitamin K1, 0.695 ± 0.232 ng/mL for MK-4 and 0.738 ± 1.526 ng/mL for MK-7.
Conclusions: We evaluated and validated a new method for determination of vitamin K1, MK-4 and MK-7 and determined the serum levels in postmenopausal women, and also in postmenopausal women treated with 45 μg/day of MK-7. The final concentrations of MK-7 was increased five times after the treatment.

Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00064203 (University Hospital Motol, Prague, Czech Republic)

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Bone metabolism - Osteoporosis

Cod: M294

PERFORMANCE CHARACTERISTICS OF A NEW INTACT PTH ASSAY

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Background: The measurement of Parathyroid Hormone (PTH) is useful in the differential diagnosis of hyper- and hypocalcemia as well as for evaluating parathyroid function in several diseases, including renal failure and bone disorders. Our aim has been to perform an analytical verification of the novel ADVIA Centaur® Intact PTH assay using direct chemiluminometric technology, which uses constant amounts of two different monoclonal mouse antibodies directed against PTH. We also compared the obtained PTH results using this assay with the previous ADVIA Centaur® intact PTH assay based on polyclonal goat antibodies.

Methods: PTH was measured using both assays in plasma (EDTA) from 259 patients, covering the measuring range from 4 to 742 pg/mL. Limit of blank, linearity and precision were evaluated.

Results: Limit of blank defined as mean + 2SD from of a blank sample containing no PTH was 0.275 pg/mL. Within-run precision was studied using controls (mean values 45.2, 252.6 and 910.1 pg/mL) and 3 pools (mean values of 19.2, 17.6 and 309.6 pg/mL), obtaining a coefficient of variation (CV) from 2.4% to 3.6%. Between run precision was calculated using the same controls and pools, obtaining a CV from 2.43% to 6.2%. Dilution linearity was determined by serial dilutions (from 1:2 to 1:32) of five high-concentration patient samples (PTH concentration was 1165 to 1915 pg/mL). The equations obtained by linear regression showed a slope from 0.925 to 1.017, with intercepts from -8.47 to 9.47.
Method comparison between both assays using Passing-Bablok regression analysis resulted in a slope of 0.921 (0.907 to 0.939) and an intercept of 4.13 (2.8 to 5.33), with a correlation coefficient of 0.995.

Conclusions: ADVIA Centaur® Intact PTH assay showed good correlation with the previous ADVIA Centaur® iPTH assay based on polyclonal antibodies and represents an accurate and precise automated tool for the measurement of intact PTH.

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Cod: M295

CALCIUM INTAKE IN POST-MENOPAUSAL WOMEN IN TUNISIA AND ITS RELATIONSHIP WITH PARATHYROID HORMONE, VITAMIN D AND BONE STATUS

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Background:
Our study aims to assess dietary calcium intake and its relationship with serum 25-hydroxyvitamin D and serum intact parathyroid hormone (PTH), both known for playing a significant role in the pathogenesis of age-related bone loss, and to compare the intake according the osteoporosis diagnosis among post-menopausal women in Tunisia.
Methods:
Our survey analysed the dietary intake and supplementation of calcium in 207 Tunisian postmenopausal women. Based on a food frequency questionnaire, patients reported their daily food intake and frequency as well as their use of prescribed medications and nutritional supplements. Morning fasting blood was collected for the measurement of PTH and 25-OH vitamin D. Osteoporosis diagnosis was established based on a dual energy X-ray absorptiometry, measuring the bone mineral density (BMD) of lumbar-spine and femoral sites.
Results:
Mean daily dietary calcium intake was 374,98 ± 151,1 mg. Only 5,5% received more than 600 mg of calcium from dietary sources daily. The recommended doses of 1200 mg per day were only reached by the 32% of the post-menopausal women who were taking calcium supplementation. A low calcium intake was significantly associated with higher serum PTH ($r= -0.146$; $p = 0.04$). An ANOVA test revealed a significant difference in the PTH concentration according to the number of years of calcium supplementation ($p=0,002$). Calcium intake was positively correlated with the vitamin D concentration ($r= 0,178$; $p = 0.01$). A significant relationship was detected between total dietary calcium intake and lumbar bone mineral density in osteopenic women ($r=-0.278$, $p= 0.003$) but not with the femoral bone mineral density.
Conclusions:
Daily calcium intake among postmenopausal osteoporotic women in Tunisia was significantly lower than the recommended dosages. A low calcium intake is associated in our study with lower vitamin D and higher PTH concentrations and lower lumber bone density. High calcium intake may have a better vitamin D effect and concentration. The Tunisian diet lacks calcium-rich foods and does not seem sufficient to reach the recommended dose without supplementation.

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Cod: M296

INCIDENCE OF HYPOCALCEMIA DUE TO DENOSUMAB IN METASTATIC BREAST CANCER.

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Introduction:
Denosumab is fully human monoclonal antibody to the receptor activator of nuclear factor κ B ligand (Rank L). By blocking the binding of Rank L to Rank, Denosumab decreases the number and activity of osteoclasts, decreases bone resorption and increases bone mineral density, so, a major part of calcium metabolism is blocked.
The use of Denosumab in bone metastasis has been shown to be efficacious in the prevention of skeletal related events, but is associated with significantly increased risk of developing hypocalcemia.
The aim of our study is to determine the incidence of hypocalcemia in patients receiving Denosumab in bone metastasis breast cancer and evaluate risk factors for developing hypocalcemia.
Methods:
30 patients with metastatic breast cancer are included in our study. The average age was 68 years old (mean 68±12 years).
They received Denosumab for prevention of skeletal related events.
Prior to starting treatments, all patients were supplemented on vitamine D and calcium.
Serum albumin adjusted calcium, albumin, phosphate, creatinine, urea, creatinine clearance, and Urine calcium and phosphate were measured before and every month after administration of Denosumab.
The monitoring was performed from October2015 to august 2016.
Results
The renal function of all patients receiving Denosumab during the monitoring was normal: creatinine clearance was always $^{>}$ 65 ml/min
1 patient in our study has hypocalcemia = 80 mg/l (Grade 1)
4 patients have low urinary calcium, the value are respectively 25, 32, 35 and 43 mg/24 h
Serum calcemia of these patients are normal for 3 patients and the lower value 25 mg/ 24 h is present in the patient with Grade 1 hypocalcemia, suggesting that hypocalciuria may be a risk factor for later occurring hypocalcemia.
This study is ongoing including 100 bone metastatic cancer patients.
Conclusion
Our results emphasize the importance of checking and supplementing vitamine D and calcium prior to administration of Denosumab as well as checking creatinine clearance, serum and urine calcium levels periodically after drug administration.

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Bone metabolism - Osteoporosis

Cod: M297

EFFECT OF ETHNICITY OF OBSERVED 25-OH VITAMIN D STATUS

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Background: Reference interval studies of 25-OH vitamin D status in Singapore have previously demonstrated ethnic differences between Chinese, Indian and Malay individuals. Whether this translates into observed differences in clinical specimens has not known. This study examines the pattern and categorisation of 25-OH vitamin D concentrations measured on clinical requests during 2015 with respect to ethnicity.

Methods: Anonymised details of all 25-OH vitamin requests for 2015 were extracted from the laboratory database. 25-OH vitamin D was measured on serum samples using the Roche e601 immunoassay analyser (using manufacturer supplied reagents, controls and calibrators). Results were categorised against the 2010 US Institute of Health categories of vitamin D status: at risk of deficiency: <12 ug/L ; at risk of inadequacy; 12-19 ug/L; sufficient 20-50 ug/L; possibly harmful >50ug/L.

Results: In 2015, 15331 25-OH vitamin D measurements were performed and the ethnicity classification was Chinese: 12095 ; Indian: 1456; Malay: 1075; Other: 705. Following the order of Chinese, Indian, Malay and Other, the classification rates (%) were <12 ug/L: 8.0, 14.7, 19.5, 12.5; 12-19 ug/L: 15.8; 24.5; 27.4; 19.4; 20-50 ug/L: 73.2; 59.0; 52.4; 65.1; >50 ug/L: 3.0; 1.9; 0.7; 3.0. Combining the bottom two categories to defined insufficiency (<20 ug/L), the rates were Chinese 23.8%, Indian 39.1%, Malay 47.0% and Other 31.9%.

Discussion: As expected, the Chinese had the lowest rate 25-OH vitamin D insufficiency (approx. 20%). Both the Indian (approx. 40%) and Malay (almost 50%) groups had significantly higher rates. The difference between Indians and Malays was unexpected as previous work has suggested higher rates of insufficiency in Indians vs Malays. Further work is needed to establish whether indeed observed 25-OH vitamin D concentrations in Malays are lower than published reference interval studies suggest.

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LUMIPULSE® G WHOLE PTH: KEY PERFORMANCE CHARACTERISTICS

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Background:
Parathyroid hormone (PTH) influences calcium and phosphorous homeostasis directly through bones and kidneys. PTH concentrations are measured to diagnose hyper- an hypocalcaemia in patients with renal disorders, and to assess parathyroid function in mineral and bone disorders. It is known that the PTH (1-84) fragment is the bioactive compound in blood. The new Lumipulse G whole PTH, specifically measuring this PTH (1-84) form was standardized against NIBSC 95/646. Key features of the assay are highlighted in this summary.
Methods:
The Lumipulse G whole PTH assays are delivered as single and ready-to-use immunoreaction cartridges which can be run on the LUMIPULSE G600II and the G1200 instruments. The levels of PTH (1-84) are determined using 50 µL of serum or plasma. Each cartridge generates quantitative results within approximately 30 minutes. The analytical assay performance was characterized according to the CLSI guidelines. Paired serum and EDTA plasma samples were used to define the reference range. A method comparison was conducted towards the Liaison 1-84 PTH (Diasorin) using samples in the range of 7.2 – 1520.9 pg/mL.
Results:
The obtained total variation (serum and plasma samples) ranged from 1.4% to 4.1%, which demonstrates a high level of precision. Analytical sensitivity was investigated on PTH (1-84) depleted samples and in our study the LoD and LoQ for the Lumipulse G whole PTH assay were shown to be 0.6 pg/mL and 4.0 pg/mL, respectively. Dilutional linearity was found on serially diluted samples up to a 1: 200 dilution (recovery spec. = 100 ± 10%). Using Passing-Bablok regression analysis, comparing the Lumipulse G with the Diasorin assay showed a slope of 0.94, an intercept of 7.4, and a correlation coefficient of 0.98. The 95% reference interval was calculated using samples of 133 apparently healthy individuals (robust statistical method) and ranged from 5.5 to 31.9 pg/mL in serum, and from 4.8 to 36.3 pg/mL in EDTA plasma samples.
Conclusions:
The performance parameters of the Lumipulse G whole PTH assay described above demonstrate acceptable within-lab variation, good sensitivity, and excellent dilutional linearity. More importantly, a good agreement with the Diasorin assay and a comparable reference range was observed.

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Cod: M299

VITAMIN D IN OSTEOPOROTIC PATIENTS

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Background: Current data demonstrate that an adequate vitamin D status protects bone health by improving bone mineral density and reducing the risk of fracture. The aim of this study was to investigate and compare vitamin D concentrations in patients with osteoporosis divided according to positive history of bone fractures.

Methods: Retrospectively, clinical records of 66 adult females with osteoporosis were retrieved from the hospital information system. The study group was divided according to the presence of bone fracture and the concentrations of vitamin D were extracted from our laboratory records. Vitamin D concentrations were determined by electrochemiluminiscent method (ECLIA) on the Elecsys 2010 analyzer (Roche Diagnostics GmbH, Mannheim, Germany).

Results: In the whole osteoporosis group aged 71 (26-87) investigated vitamin D concentrations were 50 ± 25 nmol/L and showed no correlation with age (P = 0.503). Recommended vitamin D concentrations (≥ 75 nmol/L) were found in 13% of patients, while insufficient (50-74 nmol/L) and deficient concentrations (< 50 nmol/L) were observed in 29% and 58% of patients, respectively. Osteoporosis patients with fractures (N = 41) had lower concentrations of vitamin D compared to patients without fractures (N = 25), 43 ± 21 nmol/L vs. 61 ± 28 nmol/L, respectively (P = 0.005). Only 27% of patients with osteoporosis and 15% of patients with osteoporotic fractures were receiving vitamin D supplementation therapy.

Conclusions: The majority of the osteoporosis patients investigated showed lower vitamin D concentrations than recommended. Deficient vitamin D concentrations were observed in patients with osteoporotic fractures. Adequate vitamin D supplementation is important in the regulation of calcium and phosphorus metabolism, essential for bone health.

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Bone metabolism - Osteoporosis

Cod: M300

SERUM VITAMIN D STATUS: HEALTHY ADULT POPULATION VS. ICU PATIENTS AND IMPACT ON THEIR OUTCOME

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Background: 25-hydroxyvitamin D (25OH-D, vitamin D) is an important immunomodulator and its deficiency may exacerbate the incidence and outcome of infectious complications in critically-ill patients. We hypothesized that lower levels of 25-hydroxyvitamin D (25OH-D) upon admission to the intensive care unit (ICU) would be associated with sepsis development, longer ICU stay and higher in-hospital mortality among critically-ill patients.
Methods: 25-hydroxyvitamin D status was categorized as: deficiency (≤ 15 ng/mL), insufficiency (15–30 ng/mL), and sufficiency (≥ 30 ng/mL). The primary outcome was sepsis, as defined by systemic inflammatory response syndrome (SIRS) following a documented infection. 25-hydroxyvitamin D levels were measured at ICU admission was measured in 227 initially non-septic, critically-ill patients, 18 years old or older. An additional group of 191 healthy subjects (blood donors at the Evangelismos hospital) was also used for comparison of 25-hydroxyvitamin D levels with those of the patient cohort.
Results: ICU admission median 25-hydroxyvitamin D levels of critically-ill patients were much lower than those of healthy subjects {7.97 ng/ml (interquartile range [IQR] 4.17-13.97 vs. 16.77 ng/ml (10.85-21.81), $p< 0.0001$)}. Among the patient cohort, ICU admission 25-hydroxyvitamin D levels did not differ between patients who subsequently developed sepsis (N= 145) and those who did not (N= 82), nor did they differ between survivors (N= 201) and non-survivors (N= 26). ICU admission 25-hydroxyvitamin D levels and length of stay (days) in the ICU were not statistically significantly correlated ($p= 0.31$). The same analyses were also applied only on the fraction of patients who subsequently developed sepsis and again there was no correlation between vitamin D levels and sepsis outcomes.
Conclusions: Critically-ill patients appear to have lower 25-hydroxyvitamin D levels compared to healthy subjects. Among critically-ill patients, 25-hydroxyvitamin D deficiency at ICU admission does not predict sepsis development. Moreover, critically-ill patients who are not vitamin D sufficient do not have an increased risk of in-hospital mortality or longer stay in the ICU. This also applies only on the fraction of patients who subsequently developed sepsis.

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Bone metabolism - Osteoporosis

Cod: M301

SELECTED BONE TURNOVER MARKERS IN EUTHYROID WOMEN WITH OSTEOPOROTIC FRACTURES

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Background: The evaluation of bone metabolism is useful for the individual monitoring of osteoporotic patients treatment. The aim of this study was to evaluate bone metabolism in women with osteoporotic fractures and to investigate the effect of TSH on biomarkers of bone cell activity.
Methods: The study group consisted of 34 postmenopausal women (53-76 yrs), admitted to the Department of Orthopaedics and Traumatology at the University Hospital due to osteoporotic fracture. Reference group consisted of 27 women without fracture (52-76 yrs). All women were characterized by a normal thyroid function. In both groups concentration of TSH, free thyroxine (fT4), 25(OH)D, carboxy-terminal telopeptide of type 1 collagen (CTX) and amino-terminal propeptide of type 1 procollagen (PINP) were measured in serum.
Results: Patients with fractures had higher CTX ($p \leq 0{,}008$) and fT4 ($p \leq 0{,}04$) concentrations as compared with women without fracture. Women from study group were characterized by lower TSH ($p<0{,}007$) and vitamin D concentration ($p \leq 0{,}0002$). In both, study and reference group median vitamin D concentration was lower (13,3 i 21,6 ng/ml respectively) than optimal value (30 ng/ml). Most of women with fractures (79%) had low-normal TSH concentration at first tertile (0.35-1.87 μIU/mL). In both, study and reference group a significant correlation between bone resorption and bone formation markers was found ($r = 0.51$; $r = 0.75$, respectively). No relationship was observed between TSH concentration and bone formation and resorption markers in all groups.
Conclusion: Women with osteoporotic fractures showed increased bone resorption however, no significant relationship between serum TSH concentration and bone turnover.

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Bone metabolism - Osteoporosis

Cod: M302

RELATIONSHIP BETWEEN PARATHORMONE, VITAMIN D3(25-OH) AND PATIENTS' AGE IN EAST-TALLINN CENTRAL HOSPITAL

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BACKGROUND
Parathormone, together with vitamin D3(25-OH) and calcitonin, brings about mobilization of calcium and phosphate from the skeletal system and increases the uptake of calcium in the intestine and the excretion of phosphate via the kidneys. The secretion of parathormone is inhibited by high calcium concentrations and promoted by low calcium concentrations.
Present study is aimed to illustrate a relationship between PTH, vitamin D3(25-OH) and patients' age in East-Tallinn Central Hospital.

METHODS
Vitamin D3(25-OH) and parathormone levels were quantified by electrochemiluminescence immunoassay (Roche Diagnostics, Cobas 6000). Patients' information was collected using LIS program. 5568 patient samples with determined parathormone values and 36350 patient samples with determined vitamin D3(25-OH) values were detected during the periood of 1.10.2014-30.09.2016 and used to select samples, where both of these tests were made. As a result, 492 sample results were obtained and used for further statistical analysis.

RESULTS
Vitamin D3(25-OH) and parathormone were negatively correlated. Vitamin D3(25-OH) distribution was almost symmetrical (mean 59,7 nmol/L, median 56 nmol/L, which was lower than optimal value and considered as moderate deficiency) and had a slight tendency to decrease with age. Parathormone distribution was asymmetrical (mean 6,8 pmol/L; median 5,4 pmol/L, which was within reference range) and had a tendency to increase with age. Grouping patients by their age into four groups (<40; 40-59; 60-79; >80 years old) also showed an inverse correlation between Vitamin D3(25-OH) and parathormone in every group.
CONCLUSIONS
Present study has shown a negative correlation between Vitamin D3(25-OH) and parathormone, positive correlation between parathormone and patients' age and weak negative correlation between vitamin D3(25-OH) and patients' age.