ALN. The treatment effect of Romo continued after patients transitioned to an antiresorptive agent. These data will help to foster treatment decisions in postmenopausal women at high risk for VFx.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

The Content of Serum Clusterin in Patients with Diabetic Macular Edema Depending on the Kind of Glucose Lowering Therapy

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MON-668

Relevance. Insight into the pathophysiology of diabetic macular edema (DME) has led to novel treatments, including anti-VEGF, corticosteroid-based treatment strategies and novel therapies, such as a clusterin blood retina barrier (BRB) cytoprotection. It has been shown the protective effect of clusterin on oxidative stress-induced cell death and its emerging roles in reduction of both BRB breakdown and neural retina damage. **Goal.** To assess the content of serum clusterin in patients with type 2 diabetes (T2D) and diabetic macular edema depending on the type of glucose lowering therapy. **Material and methods.** This study was conducted in 82 patients with T2D and DME. The average age of patients was 65.25 ± 10.85 years (±SD) [25; 84], the average duration of diabetes was 14.0 ± 7.05 years (±SD) [1; 35], the average level of HbA1c was 8.40 ± 1.58% (±SD). The criteria for inclusion in the open study was voluntary informed consent, age 18 years and more, the presence of T2DM. Non-inclusion criteria were the presence of endocrine diseases, which can lead to type 2 diabetes, T1D, acute infectious diseases, cancer, decompensation of comorbid pathology, mental disorders, antipsychotics, antidepressants, neurodegenerative diseases of the central nervous system, proteinuria, damage to the optic nerve, glaucoma and mature cataracts. 43 patients received oral glucose lowering drugs (OGLD: sulfonylureas, biguanides), 39 patients received insulin therapy. All patients had instrumental ophthalmological examinations. The concentration of serum clusterin was measured by «Human Clusterin ELISA» kits. Statistical analysis was performed by one-way ANOVA analysis. **Results.** A study of level variability of blood clusterin in patients with DME showed its dependence from the type of glucose lowering therapy. Comparison of mean values of strum clusterin in patients with DME and T2DM revealed the following statistically significant differences: OGLD 87,08 ± 3,15 mcg/ml [95% CI 82,63 - 91,54 mcg/ml]; insulin therapy 74,79±2,98 mcg/ml [95% CI 70,58 - 78,99 mcg/ml] (p=0,006). Apparently, clusterin is involved in the pathogenesis of DME and may have a potential in reducing of the pathogenic effect of diabetes on the neurovascular unit. The data obtained make it possible to discuss the neuroprotective role of clusterin in DME with the use of voiced oral hypoglycemic drugs, which usually prescribe for patients with mild form of T2D or for the patients with moderate severity T2D (i. e. at the initial stages of development of diabetes). **Conclusion.** Against the background of glucose lowering drugs in patients with type 2 diabetes and diabetic macular edema statistically significant (p=0,006) increases the content of serum clusterin compared to insulin therapy.

Bone and Mineral Metabolism

CLINICAL ASPECTS OF OSTEOPOROSIS AND VITAMIN D ACTION

Efficacy and Safety of Romosozumab vs Alendronate Is Similar Across Different Levels of Renal Function Among Postmenopausal Women with Osteoporosis

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MON-378

Postmenopausal women with osteoporosis may also have renal insufficiency. We conducted a post hoc analysis of the ARCH study to determine the efficacy and safety of romosozumab (Romo) vs alendronate (ALN) among patients with different levels of baseline renal function.

In ARCH, 4,093 postmenopausal women, 55–90 years old, were randomized 1:1 to receive monthly subcutaneous Romo 210 mg or weekly oral ALN 70 mg for 12 months (double-blind phase [DBP]). Eligible patients had a bone mineral density (BMD) T score of ≤ –2.5 at the total hip (TH) or femoral neck (FN) and either ≥ 1 moderate/severe vertebral fracture (VFx) or ≥ 2 mild VFx; or a T score of ≤ –2.0 at the TH or FN and either ≥ 2 moderate/severe VFx or an Fx of the proximal femur sustained 3–24 months before randomization. Pts were excluded for significantly impaired renal function (eGFR < 35 mL/min/1.73 m^2, calculated using the MDRD equation). For the current analysis, patients were categorized by baseline eGFR: normal renal function (eGFR ≥ 90), mild renal insufficiency (eGFR 60–89), or moderate renal insufficiency (eGFR 30–59). The least squares mean (LSM) % change from baseline in BMD at the lumbar spine (LS), TH, and FN; incidence of new VFx; incidence of adverse events (AEs); and changes in renal function were assessed for each eGFR category at month 12 of the DBP.

At baseline, 15% of patients had eGFR ≥ 90, 60% had eGFR 60–89, 24% had eGFR 30–59, and 0.3% had eGFR 15–29. In the overall patient population, LSM % change (95% CI) from baseline in BMD (Romo vs ALN) was 13.7% (13.4–14.0) vs 5.0% (4.7–5.2) for LS, 6.2% (5.9–6.4) vs 2.8% (2.7–3.0) for TH, and 4.9% (4.7–5.2) vs 1.7% (1.5–2.0) for FN ($P < 0.001$ at each site). Changes in BMD were similar irrespective of baseline eGFR. Among patients with eGFR ≥ 90, eGFR 60–89, and eGFR 30–59, the incidence of new

VFx (Romo/ALN) was 3.3%/7.3% (relative risk reduction [RRR] = 57%; 95% CI: 1–81), 3.2%/3.9% (RRR = 19%; 95% CI: -28–49), and 3.4%/6.2% (RRR = 51%; 95% CI: 5–75), respectively. The incidences of AEs, serious AEs, and fatal AEs were similar in both treatment groups within each eGFR category as well as across eGFR categories; there was a higher incidence of positively adjudicated cardiovascular events in the Romo vs ALN group overall and across eGFR categories. One patient in the Romo group with eGFR 60–89 at baseline and 1 in the ALN group with eGFR ≥ 90 at baseline had an AE of mild hypocalcemia. Similar percentages of patients in the Romo and ALN groups had changes in renal function over 12 months of treatment.
In conclusion, the efficacy and safety of Romo vs ALN was similar across different levels of renal function.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Severe Hypocalcemia Secondary to Pseudohypoparathyroidism

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SAT-371

Introduction: Pseudohypoparathyroidism (PHP) is a rare disorder characterized by PTH resistance due to a mutation in the *GNAS* gene causing decreased cyclic AMP generation. The 5 subtypes of PHP include type 1a, 1b, 1c, 2, and pseudo-PHP with type 1a being the most common. Patients with PHP present with hypocalcemia, hyperphosphatemia, appropriately elevated PTH, and suppressed calcitriol levels. PHP type 1a patients have characteristic features including obesity, short stature, round facies, and shortened metacarpals. PHP patients should be evaluated for other endocrinopathies as mutations in the *GNAS* gene may result in resistance to other hormones like TSH, GHRH, and gonadotropins.
Case Report: This patient is a 25 year old male who presented to clinic for evaluation of hypocalcemia. He denied any personal or family history of calcium disorders, thyroid disease, or parathyroid disease. He admitted to severe fatigue and muscle cramps for over one year leading to a car accident. He was sent to the emergency room and diagnosed with hypocalcemia requiring IV calcium gluconate. He was then seen by his family physician and was found to have elevated intact PTH and low 25-hydroxy vitamin D levels. He was placed on cholecalciferol 5000 international units (IU) daily, ergocalciferol 50,000 IU once weekly, calcium carbonate 500 mg (6 tablets daily), and referred to endocrinology. The physical exam was unremarkable. The laboratory values tested were an intact PTH of 645 pg/mL (10–65 pg/mL), ionized calcium of 4.2 mg/dL (4.6–5.08 mg/dL), magnesium of 2.1 mg/dL (1.5–2.3 mg/dL), 25-OH vitamin D of 31.7 ng/mL (20–100 ng/mL), and creatinine of 0.81 mg/dL (0.7–1.3 mg/dL) four months after starting the above mentioned calcium and vitamin D supplementation. Further testing revealed a phosphorus level of 4.8 mg/dL (2.3–4.7 mg/dL), calcitriol level of 55.8 pg/mL(19.9–79.3 pg/mL), TSH of 10.46 uIU/mL (0.4–4.2 uIU/mL) and free T4 of 1.5 ng/dL (0.8–1.7 ng/dL). His labs were consistent with PHP. Although unknown which PHP subtype, it is likely not type 1a as he lacks its characteristic phenotype. His abnormal thyroid function tests may be secondary to TSH resistance associated with the *GNAS* gene mutation. He was told to continue the current dose of calcium carbonate but to discontinue ergocalciferol and cholecalciferol. He was placed on calcitriol 0.5 mcg daily. He will have repeat levels of his ionized calcium, calcitriol, TSH, and free T4 in two weeks. If TSH is still above 10 uIU/mL, we will start levothyroxine replacement.
Conclusion: Although a rare disorder, clinicians should have a high index of suspicion for PHP to prevent complications of hypocalcemia (tetany, arrhythmias, seizures) and metabolic bone disease from PTH resistance.
References: Mantovani, G. Pseudohypoparathyroidism: Diagnosis and Treatment, *The Journal of Clinical Endocrinology & Metabolism*, Volume 96, Issue 10, 1 October 2011, Pages 3020–3030.

Adrenal

ADRENAL CASE REPORTS II

The Creatinine, the Crib and the Manometer - Navigating the Labyrinth of Primary Aldosteronism

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SUN-191

A 21-year-old Ethiopian female with a five-year history of hypertension presented to medicine clinic with headaches and fatigue for two weeks. She was hypertensive to 163/113 mmHg. She had recently moved to the US and no prior medical records were available. She had been taking an unknown antihypertensive until three weeks prior. She was found to have a creatinine of 3.49 mg/dL. Renal ultrasound revealed bilateral, small echogenic kidneys without any evidence of renal artery stenosis. An intrauterine pregnancy was also incidentally discovered. Her aldosterone level was elevated to 486 ng/dL and her renin activity was 1.3 ng/ml/hr, with a ratio of 373, diagnostic of primary aldosteronism. Due to the markedly high ratio, a saline suppression test was deemed unnecessary for confirmation. Her serum potassium was normal at 3.6 mEq, likely due to poor renal clearance. Given renal failure, a CT non-contrast of the adrenal glands was performed with normal findings. She elected to terminate the high-risk pregnancy.
Based upon her young age at presentation, family history of early onset hypertension, grossly elevated aldosterone: renin ratio and unrevealing workup for a primary tumor or hyperplastic adrenals, a diagnosis of familial hyperaldosteronism was considered. She failed a month-long trial of dexamethasone therapy, therefore glucocorticoid remediable aldosteronism was excluded. She was subsequently started on spironolactone with good response. Adrenal vein sampling was considered to find a surgical target for adrenalectomy but could not be performed given worsening kidney function. After discussion with Nephrology she opted for a pre-emptive renal transplant evaluation, rather than pursuing dialysis. Genetic testing for subclassification has been negative for mutations in KCNJ5 and CACNA1H with ongoing testing for novel mutations.