study aimed to examine the effects of ARBs on the expression and secretion of adiponectin and leptin in human white adipocytes.

[Materials and Methods]

Human white preadipocytes (Promo Cell) were differentiated into mature adipocytes in the medium containing insulin, dexamethasone, thyroxin and isobutylmethylxanthine. Pioglitazone and ARBs including telmisartan, irbesartan, azilsartan, candesartan, losartan, olmesartan and valsartan (1μM) were administered in the culture medium on day 4 and 8. The medium was collected on day 12 and the concentrations of adiponectin and leptin were measured by enzyme immunoassay. Real time PCR was performed to quantitate the mRNA expression of adiponectin and leptin in adipocytes. The experiments were performed in quadruplicate.

[Results]

Pioglitazone significantly increased adiponectin secretion (386.7 ± 133.7 vs. 7.3 ± 1.9 ng/ml in control) from human adipocytes. Among ARBs, adiponectin secretion significantly increased by telmisartan (136.7 ± 16.3 ng/ml) and irbesartan (69.7 ± 23.1 ng/ml), while the other 5 ARBs did not have any influence on adiponectin secretion. Real-time PCR also showed that mRNA expression increased 5.1-fold, 3.8-fold and 1.5-fold by pioglitazone, telmisartan and irbesartan, respectively. Leptin secretion significantly decreased by pioglitazone (27.7 ± 5.0 vs. 82.5 ± 3.8 ng/ml in control). Among ARBs, only telmisartan (38.7 ± 4.2 ng/ml) decreased leptin secretion. Real-time PCR also showed that mRNA expression decreased to be 0.5-fold and 0.7-fold by pioglitazone and telmisartan, respectively. GW9662, a selective antagonist of PPARγ, potently blocked pioglitazone-induced changes of adiponectin and leptin expression and secretion. On the other hand, GW9662 did not reverse telmisartan and irbesartan induced changes.

[Conclusion]

The changes in adiponectin and leptin secretion by pioglitazone are via PPARγ activation, while those by telmisartan and irbesartan may occur in PPARγ-independent manner.

Bone and Mineral Metabolism
OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Craniopharyngioma Patients Are at Risk of Impaired Bone Health

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SUN-382

Introduction

Craniopharyngioma (CP) are benign tumors originating from the sellar/hypothalamic region that are associated with neurological damage, epilepsy and endocrinopathies, which all could negatively affect bone health. Our objective was to determine fracture risk, bone mineral density (BMD) and final height in CP and evaluate independent determinants for fractures.

Methods

In this retrospective study, Dutch/Swedish patients with CP were included if data was available on fractures, bone mineral density (BMD) (T/Z-score), or final height (age >18 years). Data is presented as mean±SD unless stated otherwise. Logistic regression models were developed to evaluate determinants for fractures and osteoporosis. Low BMD was defined as T- or Z-score ≤-1 and osteoporosis as ≤-2.5 or ≤-2.0, respectively.

Results

We included 177 patients (48% female, 48% childhood-onset disease), with a median age at last follow-up of 45 years (range 15-92 years). Fractures occurred in 31 patients (18%); a fracture rate of 5.8 per 1000 person years. Eight patients suffered from multiple fractures (26%). In a multivariable logistic regression model for fractures, significant protective factors were female sex (OR 0.3 P=0.004) and surgery (OR 0.1, P=0.009), whereas a risk factor was use of anti-epileptics (OR 3.0, P=0.07). A significant risk factor for osteoporosis was age (OR 1.03, P=0.03); growth hormone replacement therapy tended to be protective (OR 0.2, P=0.10). Osteoporosis was not an explanatory variable for fractures (OR 2.1, P=0.21). Mean BMD T- and Z-scores were normal: Z-scores for L2-L4, femur neck and total body were 0.0±2.0 (range -3.5 - 6.8), -0.1±1.3 (range -2.7 - 4.7) and 0.1±1.5 (range -4.1 - 3.5), respectively. Osteoporosis occurred in 22 patients (24%); mean age of patients with osteoporosis was 53 ± 20 years. Low BMD occurred in 47 patients (50%). Medication to improve BMD was less often used in men than in women(7% vs. 18%, P=0.02). Mean final height was normal and did not differ between males/females, or adulthood/childhood-onset patients.

Conclusions

Patients with CP have a high fracture rate. In this population, epilepsy treatment was a risk factor, female sex a protective factor whereas osteoporosis did not affect the risk for fractures. Mean BMD Z-score was normal, but with a very wide range, resulting in low BMD in 50% and osteoporosis in 24% of the patients. Male CP patients are potentially undertreated with medication to improve bone health.

Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORTS II

A Sporadic Case of Camurati-Engelmann Disease: A Rare Sclerosing Bone Disorder

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MON-375

Background: Camurati-Engelmann disease (CED)is a rare sclerosing bone disorder. The skull and the diaphyses of the long tubular bones are mainly affected. The symptom developed in childhood and patients suffer from bone pain, easy fatigability, and decreased muscle mass and weakness. CED is caused by mutations in the transforming growth

factorβ1 (TGFβ1)gene on chromosome 19q13.113.3. This condition is inherited in an autosomal dominant pattern. Case: A 20- year-old male. He has a so-called marfanoid habitus with long and narrow limbs. At the age of 19,he presented pain in lower limb, then walking became difficult. None of his relatives had similar symptoms. In biochemical tests,calcium, Phosphorus and bone-related hormones levels were all in the normal range. 25(OH)vitamin D levels were low probably due to his eating habits. On radiological evaluation, X-ray showed thickening of the bone cortex of the bilateral tibia. Bone scintigraphy revealed markedly increased tracer uptake in the bilateral temporal bone, femur, and tibia. Based on clinical and radiological features CED was suspected. Sequence analysis of the transforming growth factor β1 (TGFB1)gene revealed a previously reported pathological variant (p.R218H). Discussion: CED is a rare pan-ethnic condition with more than 300 published cases worldwide. Although this case was difficult to diagnose because there was no family history and the onset of adulthood not childhood, this disease was suspected due to the typical localization of affected bone lesions by bone scintigraphy and was diagnosed by genetic testing. The majority of CED are missense variants in exon 4 leading to single amino acid substitutions in the encoded protein. Exon 4 encodes a latency-associated peptide (LAP) that suppresses the activity of TGF-β1 protein. No consensus management guidelines have been developed to date. Treatment with corticosteroids may relieve the pain, improve the muscle weakness and fatigue. Recently, the efficacy of losartan has been reported in some patients. Conclusion: Here we report a de novo case of CED diagnosed by genetic testing. Osteosclerotic diseases are very rare and are often difficult to diagnose. Genetic testing plays an important role in confirming the diagnosis.

Neuroendocrinology and Pituitary
PITUITARY TUMORS II

Risk Factors of Re-Growth of Non-Functional Pituitary Adenomas

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MON-299
" Risk factors of re-growth of non-functional pituitary adenomas." Khalimova Z.Yu., Urmanova Yu.M. Tashkent Pediatric Medical Institute, Department of Endocrinology child endocrinology, Republican Specialized Scientific Practical Medical Center of Endocrinology of Republic of Uzbekistan named by Ya.Kh.Turakulov Uzbekistan, 100125, Tashkent-city, Mirzo Ulugbek str 56 The aim of investigation to determine clinical aggressiveness diagnostic markers in patients with non-functional pituitary adenomas (NFPA) in the formation of gravity neuroendocrine disease symptoms. Material and Methods: We observed in 87 patients (including man - 44 women -43) of which have a verified diagnosis of NFPA after surgery - 31 which were subjected transnasal adenomectomy of the pituitary (TAG). Further analysis was performed on these patients, who were followed from 1 to 3 years. Results. After the analysis of the frequency of remission and relapse NFPA data selectively in patients we studied the correlation between various parameters and the frequency of relapses. NFPA developed the scale of aggressiveness allowed to identify the risk factors of markers on the 3rd degrees, allowing to create a set of measures of tumor growth relapse prevention. According to MRI data of the brain and pituitary gland, in 15 patients an endosellar tumor was found, in 16 - an endo-extrasellar tumor. In an MRI study, the structure of the NFPA had a predominantly soft tissue (n = 16) and cystic (n = 11) structure. In 4 cases (13%), the structure of the NFPA was represented by a hemorrhagic component, and in 2 (6.4%) of them, both cystic and hemorrhagic components were present. In 18 patients, microadenoma was revealed, in 12 - pituitary macroadenoma and in 1 - a giant pituitary adenoma. The developed scale of aggression markers of NFPA allowed identifying factors by 3 degrees, which allows developing a complex of measures for the prevention of tumor growth recurrence. Conclusions. 1) According to our data, the number of patients with large-cell chromophobic pituitary adenoma predominated - 24 (77.5%). In 2nd place were patients with small cell NFPA - 6 cases (19.3%). And only in 1 case was observed (3.2%) a giant malignant pituitary macroadenoma with recurrence of growth and metastasis in the brain of a teenage girl, in which dark-cell pituitary adenoma was histologically determined, 2) According to our preliminary data, the markers of aggressiveness of the course of NFPA are: young patient age, first symptoms of the disease manifest, large tumor size, asymmetry and deformation of the pituitary gland, signs of tumor invasion into adjacent tissues / arteries / cavernous sinus, presence of small cell and / or dark extracellular chromophobic adenomas, STH hypopituitarism, panhypopituitarism.

Thyroid
BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Macro-Thyroid Stimulating Hormone (TSH) in Children

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SAT-426
Macro-TSH is mainly a complex of TSH with anti-TSH autoantibodies. Due to its large molecular size (>150 kDa), it accumulates in the circulation resulting in elevated serum TSH concentrations. Because the bioactivity of macro-TSH is low, treatment with thyroxine is not necessary. The prevalence of macro-TSH is no more than 1% in adult patients with subclinical hypothyroidism. However, the prevalence of macro-TSH in children is not known. We report here two cases of macro-TSH in pediatric setting.