This study investigated data of 1,063 adolescents aged 12-18 years from the fifth and sixth Korea National Health and Nutritional Examination Survey (2009-2011). The association of various factors (vitamin D level, calcium intake, body mass index (BMI), lean mass, fat mass, and physical activity) with BMD Z-scores in whole body, lumbar spine, total femur, and femur neck were analyzed. We defined vitamin D deficiency (≤ 12 ng/mL), vitamin D insufficiency (12-20 ng/mL), and sufficiency (> 20ng/mL) according to the 25-hydroxyvitamin D (25-OHD) level. We analyzed association between BMD and vitamin D levels after adjusting for other factors.
Results
The mean 25-OHD level of subjects was low (16.28 ng/ml). Of all subjects, 21.9% were vitamin D deficient, and 58.5% were vitamin D insufficient. Among the vitamin D groups, the vitamin D sufficient group had significantly higher BMD Z-scores than the vitamin D deficient group in whole body, lumbar spine, and femur neck. The sufficient vitamin D group had higher BMD Z-score than the vitamin D insufficient group in femur neck, and the vitamin D insufficient group had higher BMD Z-score than the vitamin D deficient group in whole body. Among various factors, vitamin D status, calcium intake, BMI, lean mass, fat mass, and physical activity were positively associated with BMD Z-scores. In particular, lean mass was the strongest independent factor. Vitamin D levels were positively associated with the BMD Z-scores even after adjusting for other factors.
Conclusions
Vitamin D deficiency and insufficiency were common among adolescents. This study suggested that vitamin D level was positively associated with BMD, and that sufficient vitamin D level was needed to prevent low BMD. Vitamin D status is an important factor of BMD in adolescents.

Thyroid

HPT-AXIS AND THYROID HORMONE ACTION

Phenotype and Genotype Analysis of Patients with Resistance to Thyroid Hormone β: A Single-Center Experience

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SAT-434

Introduction Resistance to thyroid hormone β (RTHβ) is caused by mutations in *THRB*, the gene that encodes thyroid hormone receptor β. The clinical phenotype is variable and may include goiter, tachycardia, and learning disability with or without hyperactive behavior. The biochemical hallmark of RTHβ is elevated T4 and T3 with non-suppressed TSH concentrations. We here describe the phenotype and genotype of three Thai patients diagnosed with RTHβ in a pediatric referral center. Patients had previously been misdiagnosed and inappropriately treated with antithyroid drugs (ATDs). **Methods** Clinical features and thyroid function tests (TFTs) of three unrelated RTHβ patients were retrospectively reviewed. Genomic DNA of the RTHβ patients and affected family members was amplified for exon 7-10 of the *THRB* gene and sequenced to identify mutation by Sanger sequencing. The impact of the p.L341V novel mutation on the affinity for T3 and T3-induced transcriptional activity was previously determined *in vitro*. **Results** Three female patients were diagnosed with RTHβ. All of them had been misdiagnosed with hyperthyroidism and treated with ATDs prior to referral. The mean age at diagnosis was 8 years. The main presenting symptoms were diffuse goiter and tachycardia. The mean duration of ATD treatment was 3 years. During the treatment, patients had fluctuating thyroid hormone and increased TSH levels. An older sister and mother of one patient also had similar TFTs abnormalities, for which the mother had undergone a subtotal thyroidectomy. RTHβ was diagnosed based on the high FT3 and FT4 with normal (non-suppressed) TSH concentrations and confirmed by mutation analysis. Anti-thyroid peroxidase, anti-thyroglobulin, and TSH receptor antibody (TRAb) were negative, excluding autoimmune thyroid disease. Heterozygous missense mutations of the *THRB* gene were identified in all patients and affected family members. Two mutations had been previously reported (p.R243W and p.L456F), and one mutation was novel (p.L341V). *In vitro* studies confirmed an important role of Leu341 in T3 binding of the TRβ and functional impairment of the p.L341V novel mutation and were reported separately. According to available literature, only nine Thai RTHβ patients (in three families) carrying three different mutations (p.G251V, p.M313T, and p.A317T) had been previously reported. Goiter was the most common clinical finding, and almost all patients had a history of receiving unnecessary treatment with ATDs. **Conclusion** We report a series of RTHβ patients carrying *THRB* gene mutations, including one novel mutation (p.L341V). Clinicians should be alert that RTHβ can be found in patients with goiter and tachycardia. Elevated T4 and T3 with non-suppressed TSH concentration is the main diagnostic clue for this disease. Mutation analysis allows definitive diagnosis of RTHβ and may help to avoid potential misdiagnosis and improper treatment.

Reproductive Endocrinology

MALE REPRODUCTIVE CASE REPORTS

Digenic Inheritance of PCSK1 and CHD7 Mutations in PAX4 Homozygous Diabetic Male with Normosmic Hypogonadotropic Hypogonadism

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SUN-032

Background: Normosmic congenital hypogonadotropic hypogonadism denotes Kallmann syndrome not associated with anosmia or hyposmia. Over the past few years, the availability of next-generation sequencing has started to unravel the complex molecular basis of congenital hypogonadotrophic hypogonadism including digenic or oligogenic pathogenecity in addition to classic monogenic causality (1).

Clinical Case: A 22-year-old male patient was referred to the endocrine clinic in 2018 with recent -onset hyperglycemia. His weight was 82.2 kg with a height of 180 cm (BMI of 25.3 kg/m^2). Physical examination revealed small testes, micropenis, and no axillary and pubic terminal hair. His smell sense was intact. His hormonal test reveals low testosterone (0.10 ng/mL) and low free testosterone (0.65 pg/mL) levels with inappropriately low gonadotrophins levels. Secretion of LH and FSH increased 2-fold after GnRH stimulation. His bone age was 13-years 6-months old, and brain magnetic resonance imaging showed the presence of olfactory bulbs, and unremarkable findings except for small size of the pituitary gland. There were no signs associated with CHARGE syndrome (coloboma ocular, heart defects, atresia or stenosis of the choanae, retardation of growth and/or development, genitourinary anomalies, and ear abnormalities). Biochemical investigation demonstrated high serum glucose level and high HbA1c (13.8%). To identify variants to cause the phenotype of the proband, we adopted trio-based whole exome sequencing (WES) and candidate gene approach. Candidate genes was listed from the orphanet (*https://www.orpha.net*). WES of the proband revealed the presence of heterozygote missense mutations of the *CHD7* gene (c.6107C>T, p.Pro2036Leu, rs369543203) and *PCSK1* gene (c.239G>A, p.Arg80Gln, rs1799904). The missense variants were predicted to have a damaging effect on the encoded protein, by SIFT and PolyPhen-2 analyses. Genetic analyses of his family revealed that his father had the same heterozygote missense mutations of the *CHD7* gene, but wild type of *PCSK1*. Proband's mother had the same heterozygote missense mutations of *PCSK1*, but wild type of *CHD7*. Furthermore, the proband had homozygote missense mutation of *PAX4* (c.575G>A, p.Arg192His, rs2233580) known as maturity-onset diabetes of the young (MODY) 9 gene. Both parents have the same but heterozygous mutation of *PAX4* p.Arg192His, and pre-diabetic range of hyperglycemia.

Conclusion: This is the first case demonstrating digenic inheritance of mutations in *PCSK1* and *CHD7* as a potential cause of normosmic hypogonadotrophic hypogonadism, interestingly in *PAX4* homozygous diabetic male.

Reference: (1) Maione L, et al. Genetic counseling for congenital hypogonadotropic hypogonadism and Kallmann syndrome: new challenges in the era of oligogenism and next-generation sequencing. Eur J Endocrinol. 2018;178(3):R55-R80.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Hypoglycemic Effect of Oral Administered Superoxide Dismutase

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SUN-656

Hypoglycemic Effect of Oral Administered Superoxide Dismutase on Type 2 Diabetes via reduction of glucogan and insulin resistance

Background & Objective: Superoxide dismutase (SOD) is carefully used in food industry for the concern of its easy degradation and difficult adsorption in digestive tract, although it plays central role in antioxidant system. It is previous reported that orally administered SOD was effective in alleviating hyperglycemia, cerebral ischemia-reperfusion and chronic hepatitis. This work aimed to investigate in-depth the hypoglycaemic effect and possible mechanism of orally administered SOD in the model of type 2 diabetic rats.

Methods: The model of type 2 diabetic rats were divided into 6 groups and orally administered with different Cu/Zn-SOD (abbreviated as SOD) samples and negative or positive controls. The 6 groups included SOD, SOD hydrolysate (pepsin-treated SOD), L-SOD (liposome-embedded SOD), model group and metformin positive groups, as well as normal group. Results of the body weight, serum indexes (including blood glucose, glycated albumin, insulin, glucagon, AMPK, MDA), SOD enzymatic activity in organs (liver, heart, kidney, skeletal muscle, spleen, and pancreas) as well as intestinal density and HE staining were measured to evaluate the hypoglycemic effect and possible mechanism.

Results: SOD showed substantial hypoglycemic effect and improved serum indicators. Moreover, L-SOD group exhibited better effect than SOD group, though the effect of SOD hydrolysate was not obvious. Colon density and HE staining showed obvious intestinal injury in the model group, and SOD was beneficial to repair intestinal structural integrity. Furthermore, the reparative effect of SOD was much better than that of the SOD hydrolysate, but not as good as that of the L-SOD. The SOD enzymatic activity of tissues was positively correlated with the curative effect of three kinds of SOD samples. The contents of serum MDA were negatively correlated with the curative effect. Compared with the model group, the insulin resistance index of SOD group, L-SOD group and positive group were significantly reduced; and glucagon significantly decreased by 68.38, 77.50 and 65.01%, respectively.

Conclusion: Oral SOD showed obvious hypoglycemic effect on type 2 diabetic rats, and liposome could improve this effect. The mechanism may be that SOD effectively reduces intestinal injury, so as to reduce glucongen and insulin resistance index.

Steroid Hormones and Receptors

STEROID AND NUCLEAR RECEPTORS

Phosphorylation Site S122 in Estrogen Receptor α Has a Tissue-Dependent Role in Female Mice

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SUN-744

Estrogen treatment increases bone mass and reduces fat mass but is associated with adverse effects in postmenopausal women. Knowledge regarding tissue-specific estrogen