TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ

Üç ayda bir yayımlanır • Üyelere ücretsiz olarak gönderilir

Sayı 47 • Temmuz - Ağustos - Eylül 2014

ENDOBRIDGE 2014 TOPLANTISI GERÇEKLEŞTİ

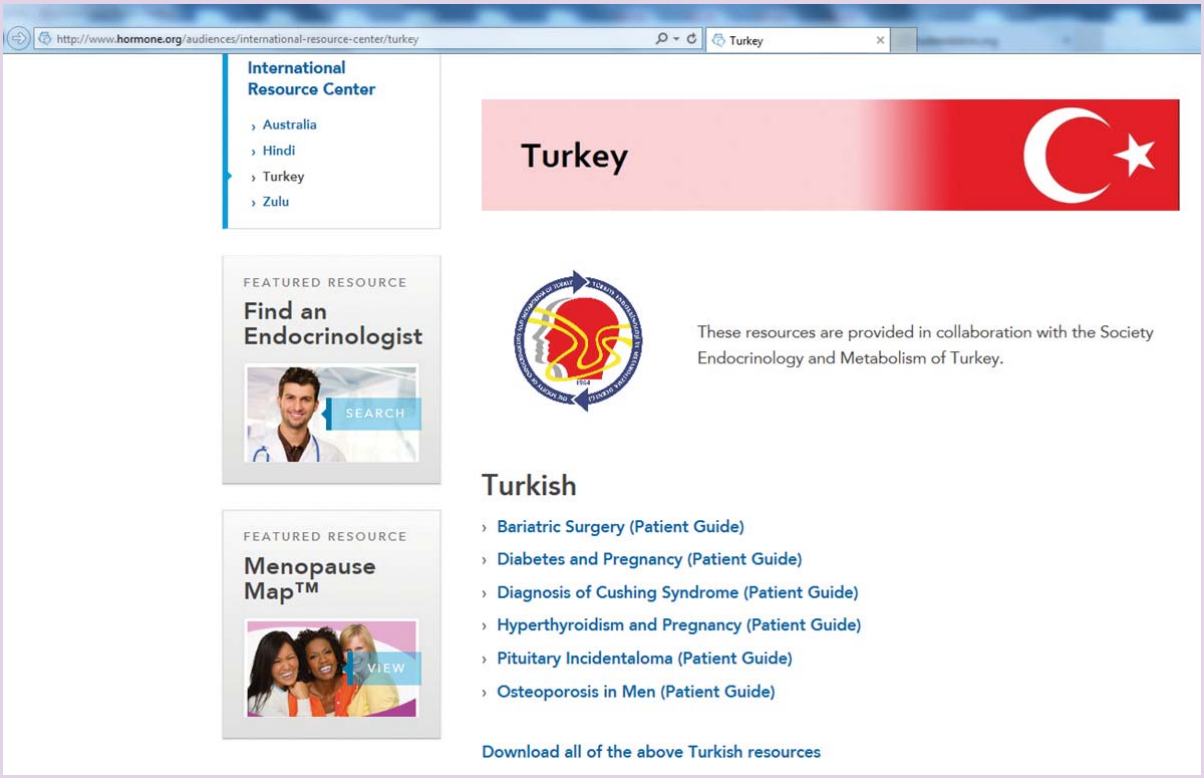
Derneğimizin endokrin dünyaları arasında köprü kurma vizyonu ile iki yıllık bir hazırlık süreci sonrasında 2013 yılında başlattığı EndoBridge toplantılarının ikincisi 35 ülkeden 410 katılımcı ile 23-26 Ekim 2014 tarihlerinde Antalya'da gerçekleşti. Geçtiğimiz yıl Amerikan Endokrin Derneği ile ortak düzenlenen toplantıya bu yıl Avrupa Endokrinoloji Derneği de katıldı. Böylece EndoBridge ikinci yılında dünyanın endokrinoloji alanında en önde gelen iki derneğini bir araya getiren ilk bilimsel toplantı olma özelliğini kazandı.

Bilimsel programında 23 konferans ve 16 interaktif vaka tartışma oturumunun yer aldığı EndoBridge 2014'de sunum dili İngilizce iken geçtiğimiz yıl olduğu gibi Türkçe, Rusça ve Arapça eşzamanlı tercüme yapıldı.

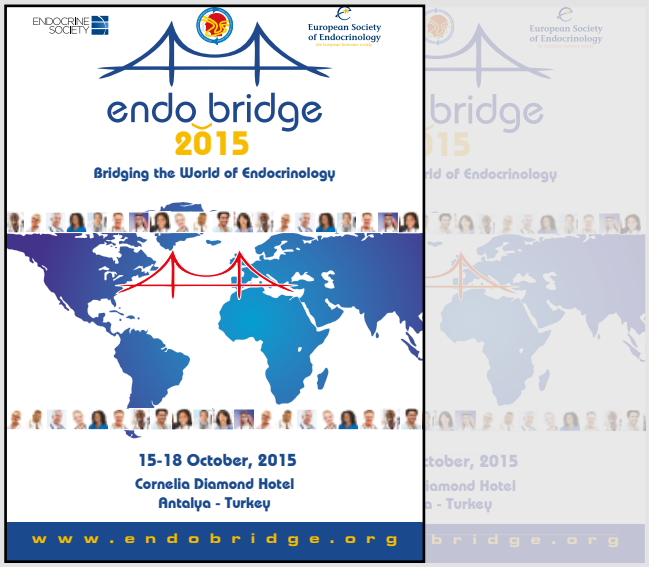
EndoBridge toplantılarının üçüncüsü Derneğimiz, Amerikan Endokrin Derneği ve Avrupa Endokrinoloji Derneği işbirliği ile 15-18 Ekim 2015 tarihlerinde Antalya'da düzenlenecek.

Hormone Health Network

Yıllık 1.5 milyonun üzerindeki ziyaret sayısı ile dünyada en çok okunan topluma ve hastalara yönelik endokrinoloji websitesi "Hormone Health Network" Derneğimizin Amerikan Endokrin Derneği ile işbirliği çerçevesinde hasta eğitim materyallerini Türkçe olarak da yayınlamaya başladı. Hormone Health Network sitesindeki Türkiye sayfasından Derneğimiz websitesine de direkt olarak bağlantı veriliyor.



Kongre ve Kurslarımız



Bilimsel Kongreler ve Uluslararası Sempozyumlar

Ayrıntılara ve 2015 yılına ait Bilimsel Toplantı Takvimine derneğimiz internet sayfasından (www.temd.org.tr) ulaşabilirsiniz.

12-15 Şubat 2015
16th ESE Postgraduate Training Course on Endocrinology, Diabetes and Metabolism
Athens, Greece
www.ese-hormones.org

05-08 Mart 2015
ENDO 2015
San Diego, CA,USA
www.endocrinology.org

12 -14 Mart 2015
The 5th World Congress on Controversies to Consensus in Diabetes, Hypertension and Obesity
Istanbul, Turkey
www.codhy.com/2015

16 -18 Mart 2015
BES Clinical Update 2015
Birmingham, UK
www.endocrinology.org

26 – 29 Mart 2015
World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases
Milan, Italy
www.wco-iof-esceo.org

06-10 Mayıs 2015
37. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi, Antalya
www.temd.org.tr

06 -09 Mayıs 2015
22nd European Congress on Obesity
Prague, Czech Republic
www.eco2015.easo.org

13 – 17 Mayıs 2015
AACE 24th Annual Scientific and Clinical Congress
Nashville, USA
www.am.aace.com

16 - 20 Mayıs 2015
17th European Congress of Endocrinology
Dublin, Ireland
www.ece2015.org

20 – 22 Mayıs 2015
10th European Congress on Menopause and Andropause
Madrid, Spain
www.asrm.org

Üyelerimizden Literatür Seçmeleri

INVESTIGATION OF INSULIN RESISTANCE GENE POLYMORPHISMS IN PATIENTS WITH DIFFERENTIATED THYROID CANCER

Akker M, Güldiken S, Sipahi T, Palabıyık O, Tosunoğlu A, Çelik Ö, Tunçbilek N, Sezer A, Süt N.
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Mol Biol Rep. 2014 May;41(5):3541-7. doi: 10.1007/s11033-014-3218-2. Epub 2014 Feb 7.

We aimed to investigate insulin receptor substrate-1 (IRS-1), insulin receptor substrate-2 (IRS-2), insulin-like growth factor binding protein-3 (IGFBP-3) genotypes, which are thought to be involved in the pathogenesis of many solid tumors and have thus far not been studied in patients with differentiated thyroid cancer (DTC). The study consisted of 93 patients diagnosed with DTC (79 females, 14 males) and 111 healthy control subjects (63 females, 48 males). The anthropometric measurements, lipid profiles, thyroid function tests and homeostatic model assessment (HOMA) as an indicator of insulin resistance (IR) of all patients were recorded. In addition IRS-1, IRS-2 and IGFBP-3 gene polymorphisms were determined by using polymerase chain reaction and restriction fragment length polymorphism. Hardy-Weinberg equilibrium was tested for each gene polymorphisms, and genetic effects were evaluated by the Chi Square test and multiple logistic regression. Homeostasis model assessment of insulin resistance (HOMA-IR), body mass index, waist circumference and serum total cholesterol levels were significantly higher in patients with DTC than in the control group. There was no difference between the two groups with respect to IRS-1, IRS-2 and IGFBP-3 gene polymorphisms. In addition, these gene polymorphisms were found to have no effect on lymph node metastases or tumor staging. While, obesity and increased HOMA-IR may be risk factors in DTC development, we suggest that IRS-1, IRS-2 and IGFBP-3 gene polymorphisms do not play an important role in pathogenesis of DTC.

DAY-NIGHT VARIATIONS IN THYROID STIMULATING HORMONE AND ITS RELATION WITH CLINICAL STATUS AND METABOLIC PARAMETERS IN PATIENTS WITH CIRRHOSIS OF THE LIVER

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Endocrine. 2014 Jul 26. [Epub ahead of print]

To investigate day-night variations in thyroid stimulating hormone (TSH) and its relation with clinical status and metabolic parameters in patients with cirrhosis. Forty-one patients with negative thyroid antibodies and normal thyroid function tests who were diagnosed with cirrhosis were included. Thirty-five age- and gender-matched healthy subjects were included in control group.TSH, fT3, and fT4 levels, which were measured both in the morning and late evening. The difference between nocturnal TSH and morning TSH (ΔTSH) were compared between groups. Relation between Child-Turcotte-Pugh, model for End-Stage Liver Disease (MELD) and MELD-Na scores and levels of thyroid hormones, ΔTSH and serum sodium (Na) levels was investigated. Relation between ΔTSH and clinical status and metabolic parameters was also evaluated. The mean morning fT3, nocturnal fT3, nocturnal TSH, and ΔTSH levels were significantly lower, morning and nocturnal fT4 levels were higher in patients with cirrhosis ($p < 0.001$, $p < 0.001$, $p = 0.004$, $p < 0.001$, and $p < 0.001$).As the ROC analysis, day-night variation was detected to be impaired in the event that difference between nocturnal TSH level and morning TSH level was lower than 1 uIU/mL in patients with cirrhosis with a sensitivity of 92.7 % and specificity of 71.4 % ($p < 0.001$).A significant positive correlation was found between serum Na levels and fT3 in patients with cirrhosis ($r = 0.479$, $p = 0.001$), and a significant negative correlation was found between the severity of clinical status and low levels of fT3 in patients with cirrhosis ($p < 0.001$).Nocturnal TSH increase does not occur in cases of cirrhosis without known thyroid disease and with normal thyroid function tests, which may be an early finding of impaired thyroid functions in patients with cirrhosis.

FASTING AND POST-PRANDIAL GLUCAGON LIKE PEPTIDE 1 AND ORAL CONTRACEPTION IN POLYCYSTIC OVARY SYNDROME.

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Clin Endocrinol (Oxf). 2014 Oct;81(4):588-92. doi: 10.1111/cen.12468. Epub 2014 May 19.

Objective: We aimed to investigate whether fasting and meal regulated glucagon like peptide 1 (GLP-1) secretion are altered in patients with polycystic ovary syndrome (PCOS) compared to healty women and whether oral contraceptive use influence GLP-1 secretion dynamics in the syndrome.
Design: Prospective observational study.
Patients: Fourteen lean normal glucose tolerant patients with PCOS and 11 age- and body mass index (BMI)-matched healthy women.
Measurements: Glucagon like peptide 1, glucose and insulin levels were measured during a standardized meal tolerance test and area under the curves (AUCs) were calculated. Whereas healthy controls were assessed at baseline, all tests were repeated in women with PCOS after treatment with ethinyl estradiol 30 μg/drospirenone 3 mg (EE/DRSP) for 3 months.
Results: Both fasting and post-meal levels of GLP-1 were significantly reduced in women with PCOS compared to controls ($P = 0{\cdot}022$ and $P = 0{\cdot}028$, respectively). AUC for GLP-1 was also lower in PCOS ($P = 0{\cdot}012$). Glucose and insulin measurements did not show a significant change between the groups. In the PCOS group, GLP-1, glucose and insulin levels did not show any change after 3 months of EE/DRSP use.
Conclusion:: GLP-1 levels both at fasting and in response to a meal are blunted in lean women with PCOS compared to healthy women. Short term oral contraception do not alter GLP-1 secretion in PCOS. Disturbance in incretin secretion dynamics might contribute to the risk of impaired glucose tolerance and type 2 diabetes in PCOS.

ANNEXIN V EXPRESSION AND ANTI-ANNEXIN V ANTIBODIES IN TYPE 1 DIABETES.

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J Clin Endocrinol Metab. 2014 Mar;99(3):932-7. doi: 10.1210/jc.2013-2592. Epub 2014 Jan 1.

Backgraund: Annexin V (AnxV) has potent anticoagulant properties and regulatory functions for apoptosis and inflammation. Antibodies against annexin V (anti-AnxVs) may inhibit AnxV functions, leading to thrombosis during autoimmune diseases. Type 1 diabetes is an autoimmune disease and related with an ongoing autoimmune inflammation and thrombotic complications. There is no study evaluating anti-AnxVs/AnxV in a disease setting.
Objective: The aim of this study was to evaluate the status of AnxV and anti-AnxVs in patients with type 1 diabetes.
Methods: One hundred twenty-one patients with type 1 diabetes and 92 healthy controls were included in this study. Serum levels of AnxV and anti-AnxVs and expression of the AnxV gene and its common polymorphism in Kozak sequence (-1C>T) were studied. As a functional assay, the binding capacity of AnxV to platelets was evaluated.
Results: As compared with controls, type 1 diabetic patients had significantly low serum AnxV levels and AnxV gene expression. The number of anti-AnxV positivity and their serum levels were significantly higher in type 1 diabetic patients than controls. AnxV binding to platelets were significantly decreased in the type 1 diabetic patients. The frequencies of the -1C>T polymorphism of AnxV gene did not differ between groups.
Conclusion:s: This study demonstrated the significant changes in AnxV levels and its function in type 1 diabetic patients. These results support the hypothesis that the defective AnxV system may have a role in ongoing autoimmune activity and the development of thrombotic complications in type 1 diabetes. Further studies are necessary to elucidate the clinical impact of anti-AnxVs and dysregulated AnxV function in type 1 diabetes.

EVALUATION OF THE OVARIAN RESERVE FUNCTION IN PATIENTS WITH METABOLIC SYNDROME IN RELATION TO HEALTHY CONTROLS AND DIFFERENT AGE GROUPS.

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J Ovarian Res. 2014 Jun 10;7:63. doi: 10.1186/1757-2215-7-63. eCollection 2014.

Objective: To evaluate the ovarian reserve function in female patients with metabolic syndrome (MetS).
Methods: This study evaluated 136 subjects, 67 with MetS and 69 controls. Subjects were divided into three age groups. Group I included 49 subjects aged 20-29 years, 22 with MetS and 27 controls; group II included 45 subjects aged 30-39 years, 22 with MetS and 23 controls; and group III included 42 subjects aged 40-49 years, 23 with MetS and 19 controls. Demographic characteristics, anthropometrics, blood biochemistry, and gonadotrophic hormones were compared as total ovarian volume and antral follicle count on ovarian transvaginal ultrasonography.
Results: Serum levels of FSH, LH, E2 and progesterone were similar in the MetS and control groups, while testosterone levels were significantly higher in MetS patients than controls, both in the overall population ($p = 0.024$) and in those aged 20-29 years ($p = 0.018$). Total ovarian volume was significantly lower in MetS patients than controls, in both the overall population ($p = 0.003$) and those aged 20-29 years ($p = 0.018$), while antral follicle counts were similar. Ovarian volume correlated positively with antral follicle count (AFC) ($r = 0.37$; $p < 0.001$) and negatively with age ($r = 0.34$; $p < 0.001$) and FSH concentration ($r = 0.21$; $p = 0.013$). AFC was negatively correlated with age ($r = 0.36$; $p < 0.001$).
Conclusion: Ovarian reserve function is significantly lower in MetS patients than in healthy control subjects, particularly in women aged 20-29 years.

PROGRESSION TO IMPAIRED GLUCOSE TOLERANCE OR TYPE 2 DIABETES MELLITUS IN POLYCYSTIC OVARY SYNDROME: A CONTROLLED FOLLOW-UP STUDY.

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Fertil Steril. 2014 Apr;101(4):1123-8.e1. doi: 10.1016/j.fertnstert.2013.12.050. Epub 2014 Feb 4

Objective: To investigate whether retesting with the oral glucose tolerance test (OGTT) is useful and necessary for all women with polycystic ovary syndrome (PCOS).
Design: Follow-up study.
Setting: Tertiary medical center.
Patient(s): Eighty-four women with PCOS and 45 healthy controls.
Intervention(s): Peripheral venous blood sampling.
Main outcome measure(s): We performed a 75-g 2-hour OGTT in women with normal glucose tolerance (NGT) and impaired glucose tolerance (IGT) at the time of the first test with and without PCOS.
Result(s): The average follow-up period for women with PCOS was 2.6 years (range, 2-4.17 years). Seventy-eight of these women had NGT at baseline, 11.5% converted to IGT, with an annualized incidence rate of 4.5%. Of those women with IGT at baseline (n = 6), 33.3% converted to type 2 diabetes mellitus, with an annualized incidence rate of 10.4%. In the healthy subjects, the average follow-up period was 2.6 years (range, 2-4.08 years). Forty-two of these women had NGT at baseline, 2.3% converted to IGT, giving a progression of 0.9% per year. Among the three women with IGT at baseline, 33.3% reverted to NGT, and 66.6% had persistent IGT.
Conclusion(s): Conversion rates from NGT to IGT or type 2 diabetes mellitus were accelerated in women with PCOS compared with healthy subjects. Women with PCOS should be tested regularly for early detection of abnormal glucose tolerance. In addition, the interval for periodic rescreening should be determined by further studies involving more women with PCOS.

EFFICACY AND SAFETY PROFILE OF EVOLOCUMAB (AMG145), AN INJECTABLE INHIBITOR OF THE PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9: THE AVAILABLE CLINICAL EVIDENCE.

Cicero AF, Tartagni E, Ertek S.

Expert Opin Biol Ther. 2014 Jun;14(6):863-8. doi: 10.1517/14712598.2014.902929. Epub 2014 Mar 24.

INTRODUCTION: Despite the proven efficacy of statins, they are often reported to be inadequate to achieve low-density lipoprotein cholesterol (LDL-C) goals (especially in high-risk patients). Moreover, a large number of subjects cannot tolerate statins or full doses of these drugs. Thus, there is a need for additional effective LDL-C reducing agents.

Areas covered: Evolocumab (AMG145) is a monoclonal antibody inhibiting the proprotein convertase subtilisin/kexin type 9 that binds to the liver LDL receptor and prevents it from normal recycling by targeting it for degradation. Phase I and II trials revealed that its subcutaneous injection, either alone or in combination with statins, is able to reduce LDL-C from 40 to 80%, apolipoprotein B100 from 30 to 59% and lipoprotein(a) from 18 to 36% in a dose-dependent manner. The incidence of side effects seems to be low and mainly limited to nasopharyngitis, injection site pain, arthralgia and back pain.

Expert opinion: Evolocumab is an innovative powerful lipid-lowering drug, additive to statins and with an apparently large therapeutic range associated to a low rate of mild adverse events. If available data will be confirmed in long-term trials with strong outcomes, Evolocumab will provide an essential tool to treat high-risk patients who need to reach ambitious LDL-C target

SAFETY AND TOLERABILITY OF INJECTABLE LIPID-LOWERING DRUGS: A REVIEW OF AVAILABLE CLINICAL DATA.

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Expert Opin Drug Saf. 2014 Aug;13(8):1023-30. doi: 10.1517/14740338.2014.932348. Epub 2014 Jun 24.

Introduction: To answer the need of a better low-density lipoprotein (LDL) cholesterol control in statin-treated patients at high risk for cardiovascular disease, new injectable lipid-lowering drugs with innovative mechanisms of action are in advanced phase of development or have just been approved.

Areas covered: Evolocumab and alirocumab are fully human monoclonal antibodies inhibiting the proprotein convertase subtilisin/kexin type 9 (PCSK9) that binds to hepatic LDL receptor and prevents it from normal recycling by targeting it for degradation. Mipomersen specifically binds to a segment of the human apolipoprotein B100 messenger RNA, blocking the translation of the gene product. Phase II (for evolocumab and alirocumab) and III (for evolocumab) trials show that PCSK9 inhibitors are equally well tolerated, with adverse events mainly limited to mild-to-moderate nasopharyngitis, injection-site pain, arthralgia and back pain. Mipomersen use is mainly associated to hepatosteatosis, increased transaminases (> 3 times the upper limit of normal), mild-to-moderate injection-site reactions and flu-like symptoms.

Expert opinion: PCSK9 inhibitors have demonstrated their good safety and tolerability in a large number of subjects with different clinical conditions, including statin-intolerance, enlarging their potential use in a broader range of patients. Further data on long-term mipomersen safety are required.

POSTLOAD HYPERGLYCEMIA IS ASSOCIATED WITH INCREASED SUBCLINICAL INFLAMMATION IN PATIENTS WITH PREDIABETES.

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Scand J Clin Lab Invest. 2013 Aug;73(5):422-7. doi: 10.3109/00365513.2013.798870. Epub 2013 Jun 14.

Background/Aims: In this present study, we aimed: (i) To clarify if prediabetes is associated with subclinical inflammation independent of underlying obesity, and (ii) to evaluate the effect of postload glucose concentration on subclinical inflammation markers in a group of patients with elevated fasting glucose.

Material and Methods: In a cohort of 165 patients with newly detected fasting hyperglycemia, according to 75 g oral glucose tolerance test (OGTT), subjects were classified either as newly diagnosed type 2 diabetes (diabetes group, n = 40), impaired fasting glucose (IFG) plus impaired glucose tolerance (IGT) (IFG/IGT group, n = 42) or IFG only (IFG group, n = 83). A control group (n = 47) consisted of age- and body mass index (BMI)-matched healthy subjects with a normal OGTT. Circulating concentrations of lipids, insulin, interleukin-6 (IL-6), interleukin-8 (IL-8) and high sensitive C-reactive protein (hsCRP) were measured. HOMA index was calculated.

Results: Subclinical inflammation markers were elevated in patients with diabetes and IFG/IGT compared to healthy controls and also IFG patients (diabetes vs. control: $p < 0.05$ for hsCRP, IL-8, and IL-6; IFG/IGT vs. control: $p < 0.05$ for hsCRP, and IL-6; diabetes vs. IFG: $p < 0.05$ for hsCRP, and IL-6; IFG/IGT vs. IFG: $p < 0.05$ for hsCRP, and IL-6). In multiple regression analysis, postload glucose concentration was independently associated with circulating hsCRP and IL-6 concentrations when the data was controlled for age, gender, BMI and lipid concentrations ($p < 0.05$ for hsCRP, and IL-6).

Conclusion:: Our results suggest that patients with prediabetes, independent of underlying obesity, have increased concentrations of subclinical inflammation which is mostly driven by postload glucose concentrations.

ETIOPATHOGENESIS OF SHEEHAN'S SYNDROME: ROLES OF COAGULATION FACTORS AND TNF-ALPHA.

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Int J Endocrinol. 2014;2014:514891. doi: 10.1155/2014/514891. Epub 2014 Apr 10.

Sheehan's Syndrome (SS) is defined as pituitary hormone deficiency due to ischemic infarction of the pituitary gland as a result of massive postpartum uterine hemorrhage. Herein, we aimed to investigate the roles of Factor II (G20210A), Factor V (G1691A), MTHFR (C677T and A1298C), PAI-1 4G/5G, and TNF- α (-308 G > A) gene polymorphisms in the etiopathogenesis of SS. Venous blood samples were obtained from 53 cases with SS and 43 healthy women. Standard methods were used to extract the genomic DNAs. Factor II (G20210A), Factor V (G1691A), and MTHFR (C677T and A1298C) polymorphisms were identified by real-time PCR. PAI-1 4G/5G and TNF- α (-308 G > A) gene polymorphisms were detected with polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) methods. According to statistical analysis, none of the polymorphisms were found to be

significantly higher in the SS group compared to the control group. Hence, we suggest that genetic factors other than Factor II, Factor V, MTHFR, PAI-1, and TNF- α gene polymorphisms should be researched in the etiopathogenesis of SS.

OXIDATIVE STRESS IN PATIENTS WITH THYROIDECTOMY AND THYROPARATHYROIDECTOMY UNDER REPLACEMENT THERAPY.

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Endocrine. 2014 Apr 24. [Epub ahead of print]

Several studies have demonstrated an imbalance between free radicals and the antioxidative system in individuals with thyroid dysfunction. However, oxidative stress has not been evaluated in patients with thyroidectomy and thyroparathyroidectomy, who are under replacement therapy. The objective of this study was to evaluate the oxidative stress using malondialdehyde, nitric oxide, and catalase levels in patients with thyroidectomy and thyroparathyroidectomy. Nineteen patients with thyroidectomy, 20 patients with thyroparathyroidectomy, and 20 controls with no history of thyroid or parathyroid disease or surgery were included in the study. Serum malondialdehyde, nitric oxide, and catalase levels were examined. Levels of nitric oxide and malondialdehyde were elevated, and catalase levels decreased in patients with thyroidectomy and thyroparathyroidectomy compared with controls (p value for all the parameters: $p < 0.001$). Free tetraiodothyronine was a potential predictor of malondialdehyde in the patient groups (p: 0.002). Catalase was negatively correlated with nitric oxide ($p < 0.01$) and malondialdehyde ($p < 0.01$). The results of the current study demonstrated that oxidative stress increased in patients with thyroidectomy and thyroparathyroidectomy despite the application of replacement therapies.

COPEPTIN, A SURROGATE MARKER FOR ARGININE VASOPRESSIN, IS ASSOCIATED WITH CARDIOVASCULAR RISK IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME.

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J Ovarian Res. 2014 Mar 14;7:31. doi: 10.1186/1757-2215-7-31.

Backgraund: Women with polycystic ovary syndrome (PCOS) have higher risk for cardiovascular disease (CVD). Copeptin has been found to be predictive for myocardial ischemia. We tested whether copeptin is the predictor for CVD in PCOS patients, who have an increased risk of cardiovascular disease.
Methods: This was a cross sectional controlled study conducted in a training and research hospital. The study population consisted of 40 reproductive-age PCOS women and 43 control subjects. We evaluated anthropometric and metabolic parameters, carotid intima media thickness and copeptin levels in both PCOS patients and control group.
Results: Mean fasting insulin, homeostasis model assessment insulin resistance index (HOMA-IR), triglyceride, total cholesterol, low density lipoprotein cholesterol (LDL-C), free testosterone, 17-OH progesterone, Dehydroepiandrosterone sulfate (DHEAS), carotid intima media thickness (CIMT) levels were significantly higher in PCOS patients. Mean copeptin level was in 12.61 ± 3.05 pmol/L in PCOS patients while mean copeptin level was 9.60 ± 2.80 pmol/L in healthy control women ($p < 0.001$). After adjustment for age and BMI, copeptin level was positive correlated with fasting insulin, free testosterone levels, CIMT, and HOM A-IR.
Conclusion:s: Copeptin appeared to have an important role in metabolic response and subsequent development of atherosclerosis in insulin resistant, hyperandrogenemic PCOS patients.

IMPACT OF TREATMENT SATISFACTION ON QUALITY OF LIFE OF PATIENTS WITH ACROMEGALY.

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Pituitary. 2014 Dec;17(6):557-63. doi: 10.1007/s11102-013-0544-7.

Purpose: To evaluate satisfaction of acromegalic subjects with their medical treatment and its contribution to their quality of life.
Methods: This cross-sectional study included a total of 159 medications used in 133 subjects with acromegaly (controlled n = 84 and uncontrolled n = 49, female/male: 81/52). Subjects were asked to complete questionnaires on symptoms of depression (BDI) and satisfaction with the medical therapy they received for acromegaly (TSQM). Acromegaly cases also completed Acromegaly Quality of Life Questionnaire (AcroQoL).
Results: Subjects on pegvisomant therapy scored lower on convenience ($p = 0.007$). Cases on combination therapy had lower domain scores for effectiveness, convenience and global satisfaction in comparison to the cases on monotherapy ($p = 0.01$, $p = 0.01$ and $p = 0.01$, respectively). The time elapsed since diagnosis and the duration of medical therapy were positively correlated with effectiveness score ($r = 0.2$, $p = 0.007$ and $r = 0.2$, $p = 0.04$, respectively). The AcroQoL score was positively correlated with all domains of TSQM (for effectiveness $r = 0.2$, $p = 0.01$; for side effects $r = 0.3$, $p = 0.001$; for convenience $r = 0.3$, $p = 0.004$ and for global satisfaction $r = 0.2$, $p = 0.01$). In contrast, the BDI score was inversely correlated with all domains of TSQM (for effectiveness $r = -0.3$, $p = 0.001$; for side effects $r = -0.2$, $p = 0.006$; for convenience $r = -0.3$, $p < 0.001$ and for global satisfaction $r = -0.3$, $p = 0.001$).
Conclusion:: In acromegaly, quality of life, status of depression and satisfaction of the subjects with their treatment are intercorrelated.

POLYMORPHISM OF THE NFKB1 AFFECTS THE SERUM INFLAMMATORY LEVELS OF IL-6 IN HASHIMOTO THYROIDITIS IN A TURKISH POPULATION.

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Immunobiology. 2014 Jul;219(7):531-6. doi: 10.1016/j.imbio.2014.03.009. Epub 2014 Mar 20.

Hashimoto thyroiditis (HT) is a chronic inflammatory autoimmune disease of thyroid gland affected by interaction of multiple genes and various cytokines. Variants in the genes coding for the NFKB and IKB proteins can be potentially involved in the development of the inflammatory diseases. NFKB, a key transcription factor of the regulation of immune responses, is interesting candidate for association

studies about autoimmune disorder. The aim of the present study was to investigate the relationship between NFKB1 and NFKBIA (NFKB1 inhibitor gene) polymorphisms, and the risk of HT in a Turkish Population in the context of IL-6 serum levels which may contribute to susceptibility to the disease. We analyzed the distribution of NFKB1-94ins/del ATTG and NFKBIA 3'UTR A→G polymorphisms using PCR-RFLP method and IL-6 serum levels using ELISA method in 120 HT patients and 190 healthy controls in Turkish population. Although, there was no statistical significant difference in distribution of the genotypes and alleles of NFKB1-94ins/del ATTG or NFKBIA 3'UTR A→G polymorphisms in patients and control subjects as single, ins/ins/GG combined genotype had protective effect on the disease when compared to ins/ins/AG combined genotype as combined genotypes of both polymorphisms. In addition to this finding, IL-6 serum levels in HT patients with del/del genotype were significantly higher than in patients with del/ins genotype ($p<0.001$). According to the combined genotype analysis of NFKB1-94ins/del ATTG and NFKBIA 3'UTR A→G polymorphisms, IL-6 levels were also higher in patients with del/del genotype when at least one G allele existing ($p=0.007$). Therefore, our findings suggest that the functional promoter NFKB1-94ins/del ATTG polymorphism was significantly associated with population HT disease through acting by directly modulating IL-6 serum levels.

INCREASED PULSE WAVE VELOCITY AND RELATIONSHIP WITH INFLAMMATION, INSULIN, AND INSULIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE.

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2014 Jul;26(7):725-32. doi: 10.1097/MEG.0000000000000104.

Objective: Both ulcerative colitis and Crohn's disease are forms of inflammatory bowel disease (IBD), which is characterized by chronic, progressive inflammation of the gastrointestinal tract. Recent studies have shed new light on the importance of inflammation in the pathogenesis of arterial stiffness.
Aim: This study aimed to evaluate the relationship between pulse wave velocity (PWV) measurement and biochemical parameters in inactive and active IBD patients without cardiovascular risk factors and perform a comparison with the control group.
Materials and Methods: We enrolled 102 IBD patients without cardiovascular risk factors and 74 matched controls, and evaluated each patient in active and inactive disease periods. All patients completed a standard questionnaire form and we assessed various laboratory parameters. We carried out vascular measurements using a Mobil-O-Graph 24-h pulse wave analysis monitor, an automatic oscillometric device.
Results: Although cardiovascular risk factors, such as total cholesterol and low-density lipoprotein cholesterol, were significantly lower ($P<0.05$) in IBD patients than the controls, 24 h, day and night PWV values, erythrocyte sedimentation rate, C-reactive protein, insulin, homeostasis model assessment of insulin resistance, and homocysteine were higher in patients with active and inactive IBD than the controls ($P<0.05$). Multiple linear regression analysis showed that PWV was correlated positively with age and duration of IBD.
Conclusion:: This study showed increased PWV, homocysteine, erythrocyte sedimentation rate, C-reactive protein, insulin, and homeostasis model assessment of insulin resistance in patients with active and inactive IBD and provides evidence of the potential contribution of inflammation and inflammation-related factors toward arterial stiffening independent from conventional cardiovascular risk factors.

MECHANISMS IN ENDOCRINOLOGY: VITAMIN D AS A POTENTIAL CONTRIBUTOR IN ENDOCRINE HEALTH AND DISEASE.

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Eur J Endocrinol. 2014 Sep;171(3):R101-10. doi: 10.1530/EJE-14-0158. Epub 2014 May 28.

Objective: It has been suggested that vitamin D may play a role in the pathogenesis of several endocrine diseases, such as hyperparathyroidism, type 1 diabetes (T1DM), type 2 diabetes (T2DM), autoimmune thyroid diseases, Addison's disease and polycystic ovary syndrome (PCOS). In this review, we debate the role of vitamin D in the pathogenesis of endocrine diseases.
Methods: Narrative overview of the literature synthesizing the current evidence retrieved from searches of computerized databases, hand searches and authoritative texts.
Results: Evidence from basic science supports a role for vitamin D in many endocrine conditions. In humans, inverse relationships have been reported not only between blood 25-hydroxyvitamin D and parathyroid hormone concentrations but also with risk of T1DM, T2DM, and PCOS. There is less evidence for an association with Addison's disease or autoimmune thyroid disease. Vitamin D supplementation may have a role for prevention of T2DM, but the available evidence is not consistent.
Conclusion:s: Although observational studies support a potential role of vitamin D in endocrine disease, high quality evidence from clinical trials does not exist to establish a place for vitamin D supplementation in optimizing endocrine health. Ongoing randomized controlled trials are expected to provide insights into the efficacy and safety of vitamin D in the management of endocrine disease.

ASSOCIATION OF PARP-1, NF-KB, NF-KBIA AND IL-6, IL-1B AND TNF-A WITH GRAVES DISEASE AND GRAVES OPHTHALMOPATHY.

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Gene. 2014 Sep 1;547(2):226-32. doi: 10.1016/j.gene.2014.06.038. Epub 2014 Jun 21.

Backgraund: Graves Disease (GD) is an autoimmune disorder affected by an interaction of multiple genes such as Nuclear Factor-κB (NF-κB), Nuclear Factor-κB Inhibitor (NF-κBIA), Poly (ADP-

ribose) polymerase-1 (PARP-1) and cytokines like Interleukin-1β (IL-1β), Interleukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α) and mostly accompanied by an ocular disorder, Graves Ophthalmopathy (GO). We hypothesize that there is a relationship between GD, GO, polymorphisms of inflammatory related genes and their association with cytokines, which may play important roles in autoimmune and inflammatory processes.

Subjects and Methods: To confirm our hypothesis, we studied the polymorphisms and cytokine levels of 120 patients with GD and GO using PCR-RFLP and ELISA methods, respectively.

Results: We found that patients with GG genotype and carriers of G allele of PARP-1 G1672A polymorphism are at risk in the group having GD (p=0.0007) while having GA genotype may be protective against the disease. PARP-1 C410T polymorphism was found to be associated with GO by increasing the risk by 1.7 times (p=0.004). Another risk factor for development of GO was the polymorphism of del/ins of NFkB1 gene (p=0.032) that increases the risk by 39%. Levels of cytokines were also elevated in patients with GD, but no association was found between levels of cytokines and the development of GO as there was no change in levels of cytokines.

Conclusions: We suggest that, PARP-1 and NFkB1 gene polymorphisms may be risk factors for developing Graves Disease and Ophthalmopathy.

ACYLATED AND DESACYLATED GHRELIN, PREPTIN, LEPTIN, AND NESFATIN-1 PEPTIDE CHANGES RELATED TO THE BODY MASS INDEX.

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Int J Endocrinol. 2013;2013:236085. doi: 10.1155/2013/236085. Epub 2013 Nov 25.

This study examines the levels of acylated and desacylated ghrelin, preptin, leptin, and nesfatin-1 peptide changes related to the body mass index (BMI). The subjects were allocated to 5 groups depending on their BMIs as follows: Group I (BMI <18.5 kg/m(2)); Group II (BMI 18.5-24.9 kg/m(2)); Group III (BMI 25-29.9 kg/m(2)); Group IV (BMI 30-39.9 kg/m(2)); Group V (BMI >40 kg/m(2)). Serum acylated and desacylated ghrelin, preptin, and leptin levels were measured by the enzyme-linked immunosorbent assay (ELISA) and nesfatin-1 was measured by the enzyme immunoassay (EIA). Desacylated ghrelin levels showed a gradual and statistically significant drop from Group I to Group V, while preptin and leptin levels exhibited a gradual and significant increase from Group I to Group IV. Serum nesfatin-1 levels gradually, but not significantly, increased from Group I to Group III and showed a significant decrease in Groups IV and V. In **Conclusion:**, leptin, preptin, and acylated ghrelin (AG) levels increased with higher BMI, whereas desacylated ghrelin (DAG) decreased and nesfatin-1 showed no clear relationship to BMI.

CORNEAL BIOMECHANICAL PROPERTIES OF PATIENTS WITH ACROMEGALY.

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Br J Ophthalmol. 2014 May;98(5):651-7. doi: 10.1136/bjophthalmol-2013-304277. Epub 2014 Jan 31.

Purpose: Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) excess in acromegaly have various effects on many organs. The ophthalmologic effects of GH and IGF-1 excess have not yet been investigated in detail. The aim of the current study is to compare the corneal biomechanical properties of patients with acromegaly and those of healthy subjects.

Methods: 45 patients with acromegaly (F/M=27/18) and 42 age-matched and gender-matched healthy individuals (F/M=24/18) were enrolled in this cross-sectional study. Central corneal thickness (CCT), corneal resistance factor (CRF), corneal hysteresis (CH), corneal compensated intraocular pressure (IOPcc) and Goldmann correlated IOPG were measured in patients with acromegaly and in healthy individuals using the Ocular Response Analyser (ORA). GH and IGF1 values were also determined in the study group.

Results: The mean CH and CRF values were higher in acromegalic patients (12.1±2.2 and 12.3±2.4, respectively) than in healthy subjects (11.0±1.6 and 10.8±1.5, respectively; for CH, p=0.014; for CRF, p=0.001). Mean IOPG measurement was higher in the acromegaly group than in the control group (p=0.017). There was no statistically significant difference in measured CCT (p=0.117) and IOPcc (p=0.594) values between acromegalic patients and healthy subjects.

Conclusion:s: These findings indicate that acromegaly has target organ effects on the eye. Consequently, it can change corneal biomechanical properties such as corneal hysteresis and the CRF. Corneal biomechanical properties are known to affect the accuracy of IOP measurements. These findings should be taken into account when measuring IOP values in acromegaly patients, as IOP readings may be overestimated.

IODINE STATUS IN TURKISH POPULATIONS AND EXPOSURE TO IODIDE UPTAKE INHIBITORS.

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Perchlorate, nitrate, and thiocyanate are competitive inhibitors of the sodium iodide symporter of the thyroid membrane. These inhibitors can decrease iodine uptake by the symporter into the thyroid gland and may disrupt thyroid function. This study assesses iodine status and exposure to iodide uptake inhibitors of non-pregnant and non-lactating adult women living in three different cities in Turkey (Istanbul, Isparta and Kayseri). We measured iodine

and iodide uptake inhibitors in 24-hr urines collected from study participants (N=255). All three study populations were mildly iodine deficient, with median urinary iodine (UI) levels of 77.5 µg/L in Istanbul, 58.8 µg/L in Isparta, and 69.8 µg/L in Kayseri. Perchlorate doses were higher in the study population (median 0.13 µg/kg/day), compared with a reference population (median 0.059 µg/kg/day), but lower than the U.S. EPA reference dose (0.7 µg/kg/day). Urinary thiocyanate levels increased with increasing exposure to tobacco smoke, with non-smokers (268 µg/L) significantly lower than light smokers (1110 µg/L), who were significantly lower than heavy smokers (2410 µg/L). This pilot study provides novel data indicating that study participants were moderately iodine deficient and had higher intakes of the iodide uptake inhibitor perchlorate compared with a reference population. Further investigation is needed to characterize the thyroid impact resulting from iodine deficiency coupled with exposure to iodide uptake inhibitors such as perchlorate, thiocyanate and nitrate.

THE USE OF 1.5-ANHYDROGLUCITOL FOR MONITORING GLYCEMIC CONTROL IN ISLET TRANSPLANT RECIPIENTS.

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Cell Transplant2014;23(10):1213-9. doi: 10.3727/096368913X669734. Epub 2013 Jun 25.

We evaluated whether 1,5-anhydroglucitol (1,5-AG) (GlycoMark(®)), a test for measuring postprandial glucose and glucose variability, could be a tool for assessing short-term glycemic control in islet cell transplant (ICT) subjects. Data of 21 subjects, with type 1 DM and allogenic islet transplantation, who had concomitant fructosamine, HbA1c, 1,5-AG (n = 85 samples), and capillary glucose self-monitoring measurements (n = 2,979) were analyzed retrospectively at different time points after ICT. A significant negative association was observed between 1,5-AG and HbA1c (p = 0.02), but not with fructosamine. When HbA1c was divided in quartiles as <5.6, 5.6-5.9, 5.9-6.2, and >6.2, a decrease of an estimated 0.70 ± 0.30 µg/ml in 1,5-AG was associated with each quartile of increase in HbA1c (p < 0.0001). There was a significant decline of 1.64 ± 0.3mg/dl in postprandial glucose values for each 1 unit increase in 1,5-AG (p < 0.0001). For those with HbA1c ≥ 6.0% when 1,5-AG was ≥8.15 µg/ml, the mean estimated glucose level was 103.71 ± 3.66 mg/dl, whereas it was 132.12 ± 3.71 mg/dl when 1,5-AG was <8.15 µg/ml. The glucose variability (Glumax - Glumin) in subjects with 1,5-AG <8.15 µg/ml was 46.23 mg/dl greater than the subjects with 1,5-AG ≥8.15 µg/ml (HbA1c ≥ 6.0%). There was no significant association between GlycoMark and glucose variability where HbA1c < 6%. 1,5-AG significantly associated with postprandial glucose levels and glucose variability in ICT recipients with near-normal HbA1c (6.0-6.5%) levels. These findings suggest that 1,5-AG can be used to differentiate those ICT subjects with higher glucose variability despite having near-normal HbA1c. However, prospective studies are needed to evaluate the association between GlycoMark levels and the parameters of graft dysfunction/failure.

EVALUATION OF SERUM FIBRINOGEN, PLASMINOGEN, A2-ANTI-PLASMIN, AND PLASMINOGEN ACTIVATOR INHIBITOR LEVELS (PAI) AND THEIR CORRELATION WITH PRESENCE OF RETINOPATHY IN PATIENTS WITH TYPE 1 DM

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J Diabetes Res. 2014;2014:317292. doi: 10.1155/2014/317292. Epub 2014 Apr 10.

Backgraund: Diabetic retinopathy (DR) is the leading cause of blindness in the world. Retinopathy can still progress despite optimal metabolic control. The aim of the study was to determine whether different degrees of DR (proliferative or nonproliferative) were associated with abnormally modulated hemostatic parameters in patients with T1DM.
Method: 52 T1DM patients and 40 healthy controls were enrolled in the study. Patients were subdivided into three categories. Group I was defined as those without retinopathy, group II with NPRP, and group III with PRP. We compared these subgroups with each other and the control group (Group IV) according to the serum fibrinogen, plasminogen, alpha2-anti-plasmin (α2-anti-plasmin), and PAI.
Results: We detected that PAI-1, serum fibrinogen, and plasminogen levels were similar between the diabetic and control groups (P = 0.209, P = 0.224, and P = 0.244, resp.), whereas α2-anti-plasmin was higher in Groups I, II, and III compared to the control group (P < 0.01, P < 0.05, and P < 0.001, resp.). There was a positive correlation between serum α2-anti-plasmin and HbA1c levels (r = 0,268, P = 0.031).
Conclusion:: To our knowledge there is scarce data in the literature about α2-anti-plasmin levels in type 1 diabetes. A positive correlation between α2-anti-plasmin with HbA1c suggests that fibrinolytic markers may improve with disease regulation and better glycemic control.

CHARACTERISATION OF THREE NOVEL CYP11B1 MUTATIONS IN CLASSIC AND NON-CLASSIC 11B-HYDROXYLASE DEFICIENCY.

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Eur J Endocrinol. 2014 Apr 10;170(5):697-706. doi: 10.1530/EJE-13-0737. Print 2014 May.

Backgraund: Congenital adrenal hyperplasia (CAH) is one of the most common autosomal recessive inherited endocrine diseases. Steroid 11β-hydroxylase (P450c11) deficiency (11OHD) is the second most common form of CAH.
Aim: The aim of the study was to study the functional consequences of three novel CYP11B1 gene mutations (p.His125Thrfs*8, p.Leu463_Leu464dup and p.Ser150Leu) detected in patients suffering from 11OHD and to correlate this data with the clinical phenotype.
Methods: Functional analyses were done by using a HEK293 cell in vitro expression system comparing WT with mutant P450c11 activity. Mutant proteins were examined in silico to study their effect on the three-dimensional structure of the protein.

Results: Two mutations (p.His125Thrfs*8 and p.Leu463_Leu464dup) detected in patients with classic 11OHD showed a complete loss of P450c11 activity. The mutation (p.Ser150Leu) detected in a patient with non-classic 11OHD showed partial functional impairment with 19% of WT activity.
Conclusion:: Functional mutation analysis enables the correlation of novel CYP11B1 mutations to the classic and non-classic 11OHD phenotype respectively. Mutations causing a non-classic phenotype show typically partial impairment due to reduced maximum reaction velocity comparable with non-classic mutations in 21-hydroxylase deficiency. The increasing number of mutations associated with non-classic 11OHD illustrate that this disease should be considered as diagnosis in patients with otherwise unexplained hyperandrogenism.

LOW SERUM LEVELS OF VITAMIN D IN METASTATIC CANCER PATIENTS: A CASE-CONTROL STUDY.

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Med Oncol. 2014 Mar;31(3):861. doi: 10.1007/s12032-014-0861-3. Epub 2014 Feb 4.

Accompanying comorbidities observed during the cancer treatment usually affect the course and outcome of the therapy. Hypovitaminosis D, which is one of these conditions, is a resolvable problem, if recognized. In this study, we investigated whether the serum 25(OH)D levels of the patients who were presented to our outpatient clinic were different from the serum levels of the healthy population living in the same area. Our study included 90 patients who were presented to the Medical Oncology outpatient clinic and 90 age, gender, body mass index and ethnic origin matched controls without a known disease, who were presented to the outpatient clinics of the Departments of Internal Diseases and Family Medicine for routine controls. Blood count tests, detailed biochemistry tests (including serum levels of Cr, Ca and P), measurement of serum 25(OH)D levels and C-reactive protein were performed in serum samples of all of the patients and controls. Mean serum levels of 25(OH)D were 13.5 ng/ml (SD 5.1) in all cancer patients, 13.1 ng/ml (SD 4.2) in the patients who were presented for adjuvant therapy, 13.8 ng/ml (SD 5.5) in the patients who were presented at metastatic stage and 18.4 ng/ml (SD 12.5) in the controls. Mean serum CRP levels were 5.4 mg/dl (SD 1.2) in the control group, 8.4 mg/dl (SD 4.3) in the adjuvant therapy group and 20.3 (SD 16.8) in the patients with metastatic disease. Generally, all cancer patients (p 0.003) and the patients with metastatic cancer (p 0.004) had lower serum 25(OH)D levels compared to controls, and there was an inverse correlation between serum 25(OH)D and CRP levels in patients with metastatic cancer (p 0.036). In metastatic cancer patients, hypovitaminosis D may be a comorbidity and it is recommended to consider during initial evaluation and follow-up. Because it might improve these patients quality of life and chemotherapy adherence.

UNUSUAL EFFECTS OF GH DEFICIENCY IN ADULTS: A REVIEW ABOUT THE EFFECTS OF GH ON SKIN, SLEEP, AND COAGULATION.

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Based on the literature data in the last two decades, growth hormone deficiency (GHD) in adults has been accepted as a clinical entity. Due to the presence of GH and IGF-I receptors throughout the body, the physiological effects of the GH-IGF-I axis are still under investigation. The effects of GH on skin, sleep, and coagulation parameters in adults have only been investigated in detail only in the recent years. In this review, our aim was to summarize the literature regarding the effects of GHD and GH replacement treatment on the skin, sleep, and coagulation parameters in adults.

INCRETINS: THEIR PHYSIOLOGY AND APPLICATION IN THE TREATMENT OF DIABETES MELLITUS.

Tasyurek HM, Altunbas HA, Balci MK, Sanlioglu S.
Diabetes Metab Res Rev. 2014 Jul;30(5):354-71. doi: 10.1002/dmrr.2501.

Therapies targeting the action of incretin hormones have been under close scrutiny in recent years. The incretin effect has been defined as postprandial enhancement of insulin secretion by gut-derived factors. Likewise, incretin mimetics and incretin effect amplifiers are the two different incretin-based treatment strategies developed for the treatment of diabetes. Although, incretin mimetics produce effects very similar to those of natural incretin hormones, incretin effect amplifiers act by inhibiting dipeptidyl peptidase-4 (DPP-4) enzyme to increase plasma concentration of incretins and their biologic effects. Because glucagon-like peptide-1 (GLP-1) is an incretin hormone with various anti-diabetic actions including stimulation of glucose-induced insulin secretion, inhibition of glucagon secretion, hepatic glucose production and gastric emptying, it has been evaluated as a novel therapeutic agent for the treatment of type 2 diabetes mellitus (T2DM). GLP-1 also manifests trophic effects on pancreas such as pancreatic beta cell growth and differentiation. Because DPP-4 is the enzyme responsible for the inactivation of GLP-1, DPP-4 inhibition represents another potential strategy to increase plasma concentration of GLP-1 to enhance the incretin effect. Thus, anti-diabetic properties of these two classes of drugs have stimulated substantial clinical interest in the potential of incretin-based therapeutic agents as a means to control glucose homeostasis in T2DM patients. Despite this fact, clinical use of GLP-1 mimetics and DPP-4 inhibitors have raised substantial concerns owing to possible side effects of the treatments involving increased risk for pancreatitis, and C-cell adenoma/carcinoma. Thus, controversial issues in incretin-based therapies under development are reviewed and discussed in this manuscript.

Kitap Bölümü

- **New Horizons in Geriatric Medicine Osteoporosis**
  Muzaffer İlhan ve Ertuğrul Taşan

- **Dyslipidemias in Kidney Disease How Lipid-Lowering Agents Work: The Good, the Bad, and the Ugly**
  Faruk Turgut, İhsan Üstün ve Cumali Gökçe

Yeni Doçentlerimiz

Doç. Dr. Ece Harman

Üyemizi tebrik eder, başarılar dileriz.

Yeni Üyelerimiz

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