TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ

Üç ayda bir yayımlanır • Üyelere ücretsiz olarak gönderilir

Sayı 56 • Ekim - Kasım - Aralık - 2016



ndoBridge[®] yıllık toplantılarının dördüncüsü, Türkiye Endokrinoloji ve Metabolizma Derneği, Amerikan Endokrin Derneği ve Avrupa Endokrinoloji Derneklerinin (European Society of Endocrinology) işbirliği ile 20-23 Ekim 2016 tarihlerinde Antalya'da gerçekleşti. EndoBridge[®] kurucu başkanı Prof. Dr. Okan Bülent Yıldız, endokrinoloji alanında dünyada birçok ilke imza atan projenin 2016 yıllık toplantısının 29 ülkeden 420 katılımcıyı buluşturduğunu ve son dört yılın en yüksek yabancı delege sayısına ulaştığını belirtti. Prof. Yıldız, Türkiye'de daha önceden planlanmış uluslararası toplantıların hemen tamamının iptal edildiği ya da başka bir ülkeye alındığı olağanüstü koşullar altında, 2016 toplantısını başarılı bir şekilde ve yine Antalya evsahipliğinde tamamlamış olmaktan dolayı EndoBridge[®] Uluslararası Yürütme Kurulu olarak memnuniyet duyduklarını, ve toplantı ile ilgili katılımcı ve konuşmacılardan çok sayıda pozitif geri bildirim aldıklarını söyledi. 20 Ekim Dünya Osteoporoz Günü nedeniyle bu yıl açılış oturumunda kemik hastalıklarına yer verilirken toplantı her yıl olduğu gibi Türkçe, Rusça ve Arapça eşzamanlı çeviri ile İngilizce olarak yapıldı ve Avrupa Akreditasyon Konseyi tarafından kredilendirildi. EndoBridge[®] 2016 bilimsel programında 24 konferans ve 16 interaktif vaka tartışması oturumu ile birlikte 60'ın üzerinde sözlü ve poster vaka sunumuna yer verildi.

Beşinci EndoBridge[®] yıllık toplantısı 19-22 Ekim 2017 tarihleri arasında Antalya'da düzenlenecek.



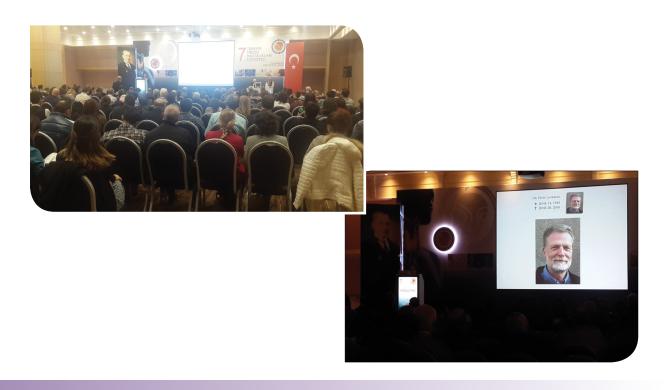


12. HİPOFİZ SEMPOZYUMU GERÇEKLEŞTİRİLDİ

12. Hipofiz Sempozyumu bu yıl 4-5 Kasım 2016 tarihlerinde Hacettepe Üniversitesi Tıp Fakültesi ev sahipliğinde ve derneğimiz çatısı altında Ankara/Sheraton Otel'de yaklaşık 200 meslektaşımızın katılımı ile başarı ile gerçekleştirildi. 2 gün süren sempozyumda hipofizin tüm konuları ele alınmış ve katılan meslektaşlarımıza verimli bir program sunulmaya çalışılmıştır.

7. TÜRKİYE TİROİD HASTALIKLARI KONGRESİ TAMAMLANDI

7. Türkiye Tiroid Hastalıkları Kongresi 25-26 Kasım tarihlerinde başarı ile gerçekleştirilen kongremize yaklaşık 250 meslektaşımız katılmıştır. Kongrenin ilk gününde yapılan Endokrinologlar için Tiroid Kanseri, İleri Klinik, Sonografik Tanı ve takip Kursuna meslektaşlarımızın ilgili oldukça yoğun olmuş, 50 kişi ile belirlenen kontenjan sayısı 75 ile kapatılmıştır.



Kongre, Kurslar ve Sempozyumlar





Bilimsel Kongreler, Ulusal ve Uluslararası Sempozyumlar

03-07 Mayıs 2017

39. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi Belek/Antalya www.temd.org.tr www.temhk2017.org

23-26 Mart 2017 WCO-IOF-ESCEO 2017 Fortezza da Basso, Florrence, Italy http://www.wco-iof-esceo.org/

01-04 Nisan 2017 ENDO2017 Orange Country Convention Center Orlando, FL https://www.endocrine.org/endo-2017

15-16 Nisan 2017

6. Lipid Metabolizması ve Bozuklukları Eğitim Kursu Trakya Üniversitesi BALKAN KONGRE MERKEZİ Konferans Salonu, Edirne

20 - 23 Mayıs 2017 19th European Congress of Endocrinology (ECE 2017) Lisbon, Portugal http://www.ece2017.org/

09-13 Haziran 2017

70th Scientific Sessions (ADA 2017) San Diego, CA http://ada-2017.org/?gclid=CJb_os-WO6tlCFciRGwodWJ8AAg **19-22 Ekim 2017** EndoBridge 2017 Regnum Carya Hotel, Antalya http://www.endobridge.org/

Üyelerimizden Literatür Seçmeleri

NATURAL HISTORY OF CONGENITAL GENERALIZED LIPODYSTROPHY: A NATIONWIDE STUDY FROM TURKEY.

Akinci B¹, Onay H¹, Demir T¹, Ozen S¹, Kayserili H¹, Akinci G¹, Nur B¹, Tuysuz B¹, Nuri Ozbek M¹, Gungor A¹, Yildirim Simsir I¹, Altay C¹, Demir L¹, Simsek E¹, Atmaca M¹, Topaloglu H¹, Bilen H¹, Atmaca H¹, Atik T¹, Cavdar U¹, Altunoglu U¹, Aslanger A¹, Mihci E¹, Secil M¹, Saygili F¹, Comlekci A¹, Garg A¹. *J Clin Endocrinol Metab. 2016 Jul; 101(7):2759-67. doi: 10.1210/jc.2016-1005. Epub 2016 May 4.*

Context: Congenital generalized lipodystrophy (CGL) is a rare autosomal recessive disorder characterized by near-total lack of body fat.

Objective: We aimed to study natural history and disease burden of various subtypes of CGL.

Design: We attempted to ascertain nearly all patients with CGL in Turkey.

Setting: This was a nationwide study.

Patients or other participants: Participants included 33 patients (22 families) with CGL and 30 healthy controls.

Main outcome measure(s): We wanted to ascertain genotypes by sequencing of the known genes. Whole-body magnetic resonance imaging was used to investigate the extent of fat loss. Metabolic abnormalities and end-organ complications were measured on prospective follow-up. Results: Analysis of the AGPAT2 gene revealed four previously reported and four novel mutations (CGL1; c.144C>A, c.667_705delinsCTGCG, c.268delC, and c.316+1G>T). Analysis of the BSCL2 gene revealed four different homozygous and one compound heterozygous possible disease-causing mutations (CGL2), including four novel mutations (c.280C>T, c.631delG, c.62A>T, and c.465-468delGACT). Two homozygous PTRF mutations (c.481-482insGTGA and c.259C>T) were identified (CGL4). Patients with CGL1 had preservation of adipose tissue in the palms, soles, scalp, and orbital region, and had relatively lower serum adiponectin levels as compared to CGL2 patients. CGL4 patients had myopathy and other distinct clinical features. All patients developed various metabolic abnormalities associated with insulin resistance. Hepatic involvement was more severe in CGL2. End-organ complications were observed at young ages. Two patients died at age 62 years from cardiovascular events.

Conclusions: CGL patients from Turkey had both previously reported and novel mutations of the AGPAT2, BSCL2, and PTRF genes. Our study highlights the early onset of severe metabolic abnormalities and increased risk of end-organ complications in patients with CGL.

DOES EDUCATION EFFECT THE RATES OF PROPHYLACTIC VACCINATION IN ELDERLY DIABETICS?

Altay M¹, Ateş i², Altay FA³, Kaplan M², Akça Ö⁴, Özkara A⁴. Diabetes Res Clin Pract. 2016 Oct; 120:117–23. doi: 10.1016/j.diabres.2016.08.002. Epub 2016 Aug 9.

Aims: This study is performed for inspecting vaccination rates in geriatric patients, negatory effects leading to unvaccination and changes occurring in vaccination rates by patient education.

Methods: This study is planned in a combination of two formats: retrospectively for determining last 5years' vaccination rates of patients and prospectively for determining the change in vaccination rates after patient education. Totally 579 diabetic patients, 206 patients of 65years and over (group 1) and 373 patients under 65years (group 2) were admitted to the study.

Results: Among preeducational reasons of avoiding vaccination, not to need vaccination was more frequently seen in group 2 when compared to group 1 (98.1% vs 91.7%, p<0.001). Pneumococ, influenzae and hepatitis vaccination rates all increased after education in the whole study population. (1.4% vs 12.4%, 12.1% vs 36.6%, 0.5% vs 3.8%, respectively; p<0.001).

Conclusions :It is seen that giving detailed information to geriatric patients about necessary vaccines and removing suspicions and anxiety about vaccination (about adverse events, for example) makes the vaccination rates raise. Primarily health professionals should be educated for this aim and they shouldn't withhold the effort to give sufficient education to patients on time.

THE IMPACT OF LEVOTHYROXINE SODIUM TREATMENT ON OXIDATIVE STRESS IN HASHIMOTO'S THYROIDITIS.

Ates I¹, Altay M², Yilmaz FM³, Topcuoglu C³, Yilmaz N⁴, Berker D⁵, Guler S⁶. *Eur J Endocrinol. 2016 Jun;174(6):727-34. doi: 10.1530/EJE-15-1061. Epub 2016 Mar 7.*

Objective: Although several studies reported increased oxidative stress in Hashimoto's thyroiditis (HT), the effect of levothyroxine treatment on oxidative status is not studied extensively. Therefore, we conducted this study to investigate the effects of levothyroxine replacement on oxidative stress in HT.

Design and methods: Thirty-six patients recently diagnosed with HT-related hypothyroidism and 36 healthy controls were included in the study. Levothyroxine replacement was started to patients with hypothyroidism, and had been followed-up for 6 months.

Results: Mean basal serum total antioxidant status (TAS), total thiol, arylesterase, and paraoxonase 1 (PON1) levels were significantly lower, and serum total oxidant status (TOS) and oxidative stress index (OSI) were significantly higher in the patients with hypothyroid than the controls. In the hypothyroid group serum TAS, total thiol, arylesterase, and PON1 levels increased and serum TOS and OSI levels decreased significantly after levothyroxine treatment. Pretreatment serum TAS, total thiol, PON1, and arylesterase levels were positively correlated with free levothyroxine (fT4) and

negatively correlated with thyroid-stimulating hormone (TSH), antithyroid peroxidase (anti-TPO), and antithyroglobulin (anti-TG) levels. Also, pretreatment serum TOS and OSI levels were negatively correlated with TT4 levels and positively correlated with TSH, anti-TPO, and anti-TG. We have also found that the fT4 and anti-TPO levels are independent predictors of the oxidative stress parameters in stepwise multivariable linear regression analysis.

Conclusion: This study suggests that levothyroxine replacement decreases oxidant status and increases antioxidant status following the 6 months of levothyroxine replacement in hypothyroidism that develops in accordance with the HT.

EVALUATION OF MEIBOMIAN GLAND DYSFUNCTION IN POLYCYSTIC OVARY SYNDROME AND OBESITY.

Baser G¹, Yildiz N², Calan M³. *Curr Eye Res. 2016 Oct 28:1-5. [Epub ahead of print]*

Purpose/Aim of the study: The purpose of this study was to evaluate the interaction between Polycystic ovary syndrome (PCOS) and Meibomian gland dysfunction (MGD) and obesity, to reveal whether there is a correlation between the testosterone levels and body-mass index (BMI) levels and the dry-eye complaints of these patients.

Material and methods: The study included 92 patients with PCOS and 52 healthy patients from March 2013 to March 2014. All patients underwent a physical examination, pelvic ultrasound, and clinical and biochemical tests, including free testosterone levels to confirm the diagnosis of PCOS. The BMIs of all subjects were recorded. In addition, the presence of posterior blepharitis, as an indicator of MGD, was recorded. All patients underwent the dryeye tests including Schirmer 1 and tear film break-up time (BUT). Complaints of dry-eye of the patients were evaluated with the ocular surface disease index (OSDI) questionnaire. The scores of both groups were compared.

Results: The presence of MGD was 72.82% in the PCOS group and 61.53% in the control group. There was no correlation between the testosterone levels and study parameters in both groups. BUT levels negatively correlated with BMI in subjects without PCOS (r = -0.520, p = 0.001), whereas positively correlated with MGD and OSDI scores (r = 0.610, p = 0.632; p = 0.001, p = 0.001; respectively).

Conclusion: Tear film instability due to MGD is common in PCOS and in subjects with high BMI. The MGD in PCOS patients is independent of the BMI.

Keywords: Body-mass index; dry-eye syndrome; meibomian gland dysfunction; obesity; polycystic ovary syndrome

THE PREVALENCE AND PHENOTYPIC FEATURES OF POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Bozdag G¹, Mumusoglu S¹, Zengin D¹, Karabulut E², Yildiz BO³. Hum Reprod. 2016 Dec;31(12):2841-2855. Epub 2016 Sep 22.

Study question: What is the reported overall prevalence of polycystic ovary syndrome (PCOS) according to the criteria of the National Institutes of Health (NIH), Rotterdam or the Androgen Excess and PCOS Society (AE-PCOS Society)?

Summary answer: The reported overall prevalence of PCOS (95% CI) according to diagnostic criteria of the NIH, Rotterdam and the AE-PCOS Society is 6% (5-8%, n = 18 trials), 10% (8-13%, n = 15 trials) and 10% (7-13%, n = 10 trials), respectively.

What is already known: PCOS is the most common endocrine disorder among women of reproductive age. Although many studies have investigated the prevalence of PCOS, there are discrepancies in their results, in part due to the use of various definitions of the syndrome and its subphenotypes, differences between study cohorts, ethnicities, and types of recruitment and sampling.

Study design, size, duration: A systematic review and meta-analysis were performed on all published studies that have reported the prevalence of PCOS according to at least one subset of diagnostic criteria.

Participants/materials, setting, methods: To identify relevant studies based on the PRISMA statement, PubMed and Ovid databases were searched up to September 2015 by two blind investigators using the terms 'PCOS', 'polycystic ovarian disease', 'Stein Leventhal syndrome', 'Androgen Excess Society', 'National Institute of Health', 'Rotterdam', 'ESHRE/ASRM', 'criteria' and 'prevalence'. Articles that represented the prevalence of PCOS according to at least one subset of diagnostic criteria were included. Exclusion criteria were a focus on adolescent subjects, an absence of data on prevalence, inappropriate design or non-English reporting. An appraisal tool to evaluate the methodological quality of the available studies was generated by the authors.

Main results and the role of chance: A total of 55 reports remained following screening of the abstracts and text for the subject of the study. Of these, 24 articles were eligible and evaluated for qualitative and quantitative synthesis. Since heterogeneity was observed among studies, a random-effects model was used to estimate the prevalence and its 95% CI. The proportions of PCOS prevalence (95% CI) according to the diagnostic criteria of NIH, Rotterdam and AE-PCOS Society were 6% (5-8%, n = 18 trials), 10% (8-13%, n = 15 trials) and 10% (7-13%, n = 10 trials), respectively. When only unselected population studies were included, the given rates were 6% (5-8%, n = 3 trials), 9% (7-12%, n= 6 trials) and 10% (7-14%, n = 3 trials). The respective proportions for hirsutism, hyperandrogenaemia, polycystic ovaries (PCO) and oligo-anovulation were 13% (8-20%, n = 14 trials), 11% (8-15%, n = 9 trials), 28% (22-35%, n = 12 trials) and 15% (12-18%, n = 19 trials), respectively.

Limitations, reasons for caution: The effects of ethnic differences, particularly, on the presence or severity of hirsutism cannot be ruled out in any way. In addition, there was a lack of standardization in defining phenotypes of the syndrome and selection bias was evident in most of the studies regarding recruitment of the cohorts.

Wider implications of the findings: Geographical differences in frequencies of the components of the syndrome, such as oligoanovulation and clinical/biochemical androgen excess, must be taken into account in the development and implementation of regional diagnostic and precision treatment strategies. Further efforts and resources are required to increase standardization of the methods and comparability of the study results on prevalence and phenotypic characterization of PCOS around the globe.

Study funding/competing interests: No funding to declare. The authors have no conflicts of interest to declare.

PARATHYROIDECTOMY IN ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM REDUCES CAROTID INTIMA-MEDIA THICKNESS AND ARTERIAL STIFFNESS.

Cansu GB¹, Yılmaz N², Özdem S³, Balcı MK⁴, Süleymanlar G⁵, Arıcı C⁶, Boz A⁷, Sarı R⁴, Altunbaş HA⁴. *Clin Endocrinol (0xf). 2016 Jan;84(1):39-47. doi: 10.1111/cen.12952. Epub 2015 Oct 12.*

Objective: Although an International Workshop has suggested that cardiovascular assessment in asymptomatic primary hyperparathyroidism (PHPT) patients is not necessary, improvements in risk factors of subclinical atherosclerosis have been shown following parathyroidectomy. The objectives of this study were to determine whether parathyroidectomy in asymptomatic PHPT patients causes any change in carotid intima-media thickness (CIMT), arterial stiffness [pulse wave velocity (PWV)] and soluble CD40 ligand (sCD40L) levels.

Design: Prospective study evaluating female patients diagnosed with asymptomatic PHPT in a single centre over a 6-month period.

Patients: A total of 48 subjects were included: 17 hypercalcaemic (HC, mean age: 51 ± 8 years, Ca: 2.73 ± 0.17 mmol/l) and 16 normocalcaemic (NC, mean age: 58 ± 7 years, Ca: 2.30 ± 0.10 mmol/l) PHPT patients, and 15 healthy controls (mean age: 52 ± 4 years, Ca: 2.27 ± 0.07 mmol/l).

Measurements: Biochemical tests, CIMT, PWV and sCD40L levels were compared at baseline and 6 months after parathyroidectomy (PTx).

Results: At baseline, CIMT and PWV values in the HC and NC patients were higher than in the control group. While there was a significant reduction in CIMT ($601 \pm 91 \ \mu m vs 541 \pm 65 \ \mu m$, P = 0.006) and PWV ($9.6 \pm 1.8 \ vs 8.4 \pm 1.5 \ m/s$, P = 0.000) in the hypercalcaemic group at the end of the 6th month after PTx, no change was observed in normocalcaemic group (P = 0.686 and P = 0.196 respectively). No differences were observed in sCD40L levels between patient and control groups or between baseline and 6 months in patients undergoing parathyroidectomy.

Conclusion: Parathyroidectomy leads to an improvement in the structural and functional impairment associated with atherosclerosis in the vascular wall in asymptomatic hypercalcaemic PHPT patients.

HISTOPATHOLOGIC EVALUATION OF NONALCOHOLIC FATTY LIVER DISEASE IN HYPOTHYROIDISM-INDUCED RATS.

Demir \S^1 , Ünübol M², Aypak SÜ³, İpek E⁴, Aktaş S⁵, Ekren GS³, Yılmaz M⁶, Tunca R⁴, Güney E².

Int J Endocrinol. 2016;2016:5083746. doi: 10.1155/2016/5083746. Epub 2016 Apr 7.

It is speculated that thyroid hormones may be involved in nonalcoholic fatty liver disease (NAFLD) pathogenesis. A literature scan, however, demonstrated conflicting results from studies investigating the relationship between hypothyroidism and NAFLD. Therefore, our study aims to evaluate NAFLD, from the histopathologic perspective, in hypothyroidism-induced rats. Wistar rats were divided into 2 groups: the experimental group consumed water containing methimazole 0.025% (MMI, Sigma, USA) for 12 weeks and the control group consumed tap water. At the end of week 12, serum glucose, ALT, AST, triglyceride, HDL, LDL, TSH, fT4, fT3, visfatin, and insulin assays were performed. Sections were stained with hematoxylin-eosin and "Oil Red-O" for histopathologic examination of the livers. In our study, we detected mild hepatosteatosis in all hypothyroidisminduced rats. There was statistically significant difference with respect to obesity between the two groups (p < 0.001). The mean fasting blood glucose was $126.25 \pm 23.4 \text{ mg/dL}$ in hypothyroidisminduced group and $102.63 \pm 15.51 \text{ mg/dL}$ in the control group, with a statistically significant difference between the groups (p = 0.032). The two groups did not differ statistically significantly with respect to visfatin levels (p > 0.05). In conclusion, we found that hypothyroidism-induced rats had mild hepatosteatosis as opposed to the control group histopathologically. Our study indicates that hypothyroidism can cause NAFLD.

INCREASED ADIPSIN IS ASSOCIATED WITH CAROTID INTIMA MEDIA THICKNESS AND METABOLIC DISTURBANCES IN POLYCYSTIC OVARY SYNDROME.

Gursoy Calan O¹, Calan M², Yesil Senses P³, Unal Kocabas G², Ozden E⁴, Sari KR⁴, Kocar M⁴, Imamoglu C⁵, Senses YM³, Bozkaya G⁶, Bilgir O⁴. *Clin Endocrinol (Oxf). 2016 Dec;85(6):910–917. doi: 10.1111/cen.13157. Epub 2016 Aug 15.*

Context: Adipsin, a protein secreted mainly from the adipose tissue, is a structural homologous of complement factor D, a rate-limiting enzyme of the alternative complement system. Growing evidence suggests that the alternative complement system plays a role both in the regulation of energy homoeostasis and in the atherosclerosis. Polycystic ovary syndrome (PCOS) is a reproductive and metabolic disease.

Objective: To ascertain whether circulating adipsin levels are altered in women with PCOS, and whether there is an association between adipsin and metabolic parameters or carotid intima media thickness (CIMT).

Participants: A total of 144 women with PCOS and 144 age- and BMI-matched controls without PCOS were recruited for this cross-sectional study.

Main outcome measures: Circulating adipsin levels were measured using ELISA. Metabolic, hormonal parameters and CIMT were also determined.

Results: Adipsin levels were significantly elevated in women with PCOS compared with controls (91.52 \pm 14.11 vs 60.31 \pm 9.71 ng/ml, P < 0.001). Adipsin positively correlated with BMI, homoeostasis model assessment of insulin resistance (HOMA-IR), free testosterone, high-sensitivity C-reactive protein (hs-CRP) and CIMT in both groups. Multivariate logistic regression analyses revealed that the odds ratio for PCOS was 3.25 for patients in the highest quartile of adipsin compared with those in the lowest quartile (OR=3.25, 95% CI=2.64.4.00, P = 0.016). Our findings further indicate that BMI, HOMA-IR, hs-CRP and free testosterone are independent factors influencing serum adipsin levels and that adipsin is an independent predictor for CIMT.

Conclusion: Circulating adipsin levels are significantly higher in women with PCOS, and the peptide is closely related to increased cardiovascular risk and metabolic disturbances.

IS THERE A ROLE OF ACTH IN INCREASED CHOROIDAL THICKNESS IN CUSHING SYNDROME?

Karaca C¹, Karaca Z, Kahraman N, Sirakaya E, Oner A, Mirza GE. *Retina*. 2017 Mar;37(3):536-543. doi: 10.1097/IAE.000000000001198.

Purpose: To evaluate choroidal thickness (CT) in patients with Cushing syndrome (CS) with enhanced depth imaging optical coherence tomography.

Methods: Twenty-eight patients with CS and 38 healthy volunteers were enrolled in this observational cross-sectional study. Patients with newly diagnosed CS who have been admitted to Erciyes University Department of Endocrinology in 3 years time interval were compared with age- and sex-matched healthy volunteers. Choroidal thickness was measured at the fovea and 2 points nasal and 2 points temporal to the fovea with 500-µm intervals each.

Results: Choroidal thickness measurements were higher in patients with CS than in the control group at all examination points; however, the difference was found to be significant at the center of the fovea $(367.8 \pm 94.4 \ \mu m \ vs. \ 329 \pm 90.5 \ \mu m)$ and 1,000 $\ \mu m$ temporal to the fovea. Choroidal thickness measurements were significantly higher in adrenocorticotrophic hormone (ACTH)-dependent CS group than in the control group at all measurement points (CT at fovea 388.2 \pm 92.4 $\ \mu m \ vs. \ 329.1 \pm 90.5 \ \mu m)$. All CT measurements were found to be correlated with ACTH levels.

Conclusion: Cushing syndrome is associated with increased CT. The ACTH-dependent CS may increase CT more than ACTH-independent CS. This effect may be directly related to ACTH itself or increased plasma cortisol levels or both.

F2A AS POTENTIAL BIOMARKERS OF OXIDATIVE STRESS IN PATIENTS WITH PREDIABETES.

Kant M¹, Akış M², Çalan M³, Arkan T⁴, Bayraktar F⁵, Dizdaroglu M⁶, İşlekel H⁷. DNA Repair (Amst). 2016 Dec;48:1–7. doi: 10.1016/j.dnarep.2016.09.004. Epub 2016 Sep 26.

Prediabetes is the preclinical stage of type 2 diabetes mellitus (T2DM) with intermediate state of hyperglycemia. Hyperglycemia results in a state of oxidative stress, which may contribute to the production of insulin resistance, β-cell dysfunction and long-term complications of diabetes. Novel approaches are required for prevention and treatment of diabetes. New biomarkers that can be used in risk stratification and therapy control as supplementary to current parameters are needed. These biomarkers may facilitate a more individualized and sufficient treatment of diabetes. Therefore, the aim of this study was to investigate the levels of oxidatively induced DNA damage products, 8-oxo-2'deoxyguanosine (8-oxo-dG) (also known as 8-OH-dG), (5'R)- and (5'S)-8,5'-cyclo-2'-deoxyadenosines (R-cdA and S-cdA), and the lipid peroxidation product 8-iso-prostaglandin $F_{2\alpha}$ (8-iso-PGF_{2\alpha}) as reliable oxidative stress markers in patients with prediabetes or T2DM in comparison with healthy volunteers. Urine samples were collected from these subjects. Absolute quantification of 8-oxo-dG, R-cdA, S-cdA and 8-iso-PGF₂ α was achieved by liquid chromatographyisotope dilution tandem mass spectrometry. The levels of 8-oxo-dG, S-cdA and 8-iso-PGF₂ α were significantly greater in prediabetes patients than those in healthy volunteers. T2DM patients also had higher levels of 8-oxo-dG than healthy volunteers. No statistically significant difference was observed for R-cdA levels. 8-Oxo-dG levels positively correlated with R-cdA and S-cdA levels for prediabetes and newly diagnosed T2DM. S-cdA levels and HbA1c were found negatively correlated in prediabetes patients. Also 8-iso-PGF2a levels and HbA1c were found negatively correlated in prediabetes patients. These results indicate that oxidatively induced macromolecular damage appears before the establishment of T2DM. Thus, our data suggest that oxidatively induced DNA damage and lipid peroxidation products that were found to be elevated in prediabetic stage may be used as early disease markers in patients at risk for T2DM.

T2-WEIGHTED MRI SIGNAL PREDICTS HORMONE AND TUMOR RESPONSES TO SOMATOSTATIN ANALOGS IN ACROMEGALY.

Potorac I¹, Petrossians P¹, Daly AF¹, Alexopoulou O², Borot S³, Sahnoun-Fathallah M⁴, Castinetti F⁴, Devuyst F⁵, Jaffrain-Rea ML⁶, Briet C⁷, Luca F⁸, Lapoirie M⁹, Zoicas F¹⁰, Simoneau I¹¹, Diallo AM¹², Muhammad A¹³, Kelestimur F¹⁴, Nazzari E¹⁵, Centeno RG¹⁶, Webb SM¹⁷, Nunes ML¹⁸, Hana V¹⁹, Pascal-Vigneron V²⁰, Ilovayskaya I²¹, Nasybullina F²², Achir S²³, Ferone D¹⁵, Neggers SJ¹³, Delemer B¹², Petit JM¹¹, Schöfl C²⁴, Raverot G⁹, Goichot B⁸, Rodien P⁷, Corvilain B⁵, Brue T⁴, Schillo F³, Tshibanda L¹, Maiter D², Bonneville JF¹, Beckers A²⁵.

Endocr Relat Cancer. 2016 Nov;23(11):871-881. Epub 2016 Sep 20.

GH-secreting pituitary adenomas can be hypo-, iso- or hyper-intense on T2-weighted MRI sequences. We conducted the current multicenter study in a large population of patients with acromegaly to analyze the relationship between T2-weighted signal intensity on diagnostic MRI and hormonal and tumoral responses to somatostatin analogs (SSA) as primary monotherapy. Acromegaly patients receiving primary SSA for at least 3 months were included in the study. Hormonal, clinical and general MRI assessments were performed and assessed centrally. We included 120 patients with acromegaly. At diagnosis, 84, 17 and 19 tumors were T2-hypo-, iso- and hyper-intense, respectively. SSA treatment duration, cumulative and mean monthly doses were similar in the three groups. Patients with T2-hypo-intense adenomas had median SSA-induced decreases in GH and IGF-1 of 88% and 59% respectively, which were significantly greater than the decreases observed in the T2-iso- and hyper-intense groups (P<0.001). Tumor shrinkage on SSA was also significantly greater in the T2-hypo-intense group (38%) compared with the T2-iso- and hyper-intense groups (8% and 3%, respectively; P<0.0001). The response to SSA correlated with the calculated T2 intensity: the lower the T2-weighted intensity, the greater the decrease in random GH (P<0.0001, r=0.22), IGF-1 (P < 0.0001, r = 0.14) and adenoma volume (P < 0.0001, r = 0.33). The T2-weighted signal intensity of GH-secreting adenomas at diagnosis correlates with hormone reduction and tumor shrinkage in response to primary SSA treatment in acromegaly. This study supports its use as a generally available predictive tool at diagnosis that could help to guide subsequent treatment choices in acromegaly.

PREGO (PRESENTATION OF GRAVES' ORBITOPATHY) STUDY: CHANGES IN REFERRAL PATTERNS TO EUROPEAN GROUP ON GRAVES' ORBITOPATHY (EUGOGO) CENTRES OVER THE PERIOD FROM 2000 TO 2012.

Perros P¹, Žarković M², Azzolini C³, Ayvaz G⁴, Baldeschi L⁵, Bartalena L⁶, Boschi A⁵, Bournaud C⁷, Brix TH⁸, Covelli D⁹, Ćirić S², Daumerie C¹⁰, Eckstein A¹¹, Fichter N¹², Führer D¹³, Hegedüs L⁸, Kahaly GJ¹⁴, Konuk O¹⁵, Lareida J¹², Lazarus J¹⁶, Leo M¹⁷, Mathiopoulou L¹⁸, Menconi F¹⁷, Morris D¹⁹, Okosieme O¹⁶, Orgiazzi J²⁰, Pitz S²¹, Salvi M⁹, Vardanian-Vartin C²², Wiersinga W²³, Bernard M²⁴, Clarke L²⁵, Currò N²⁶, Dayan C¹⁶, Dickinson J²⁵, Knežević M²⁷, Lane C¹⁹, Marcocci C¹⁷, Marinò M¹⁷, Möller L¹³, Nardi M²⁸, Neoh C²⁵, Pearce S¹, von Arx G¹², Törüner FB⁴

Br J Ophthalmol. 2015 Nov;99(11):1531–5. doi: 10.1136/bjophthalmol–2015–306733. Epub 2015 May 7.

Background/aims: The epidemiology of Graves' orbitopathy (GO) may be changing. The aim of the study was to identify trends in presentation of GO to tertiary centres and initial management over time.

Methods: Prospective observational study of European Group On Graves' Orbitopathy (EUGOGO) centres. All new referrals with a diagnosis of GO over a 4-month period in 2012 were included. Clinical and demographic characteristics, referral timelines and initial decisions about management were recorded. The data were compared with a similar EUGOGO survey performed in 2000.

Results: The demographic characteristics of 269 patients studied in 2012 were similar to those collected in the year 2000, including smoking rates (40.0% vs 40.2%). Mild (60.5% vs 41.2%, p<0.01) and inactive GO (63.2% vs 39.9%, p<0.01) were more prevalent in 2012. The times from diagnosis of thyroid disease to being seen in EUGOGO centres (6 vs 16 months) and from first symptoms of GO (9 vs 16 months) or from diagnosis of GO (6 vs 12 months) to first consultation in EUGOGO centres were shorter in 2012 (p<0.01). The initial management plans for GO were no different except surgical treatments for patients with mild inactive disease were more frequently offered in the 2012 cohort than in 2000 (27.3% vs 17%, p<0.05), and selenium supplements were offered only in the 2012 cohort (21.2% vs 0%, p<0.01).

Conclusions: These findings suggest that the clinical manifestations of patients with GO may be changing over time in Europe.

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GUT-BRAIN AXIS AND METABOLISM IN POLYCYSTIC OVARY SYNDROME.

Saydam BO, Yildiz BO¹. Curr Pharm Des. 2016;22(36):5572-5587.

Polycystic ovary syndrome (PCOS) is a common and complex endocrine disorder, often accompanied and complicated by insulin resistance, glucose intolerance and obesity. Gut, brain and metabolism are highly related with each other in obesity and diabetes as well as in PCOS. Central nervous system regulates food intake through complex interactions of homeostatic and hedonic systems while gastrointestinal system contributes to food intake and metabolism via orexigenic and anorexigenic gastrointestinal hormones. Ghrelin is the only circulating orexigenic hormone whereas anorexigenic peptides include glucagon like peptide-1 (GLP-1), gastric inhibitory peptide (GIP), peptide YY (PYY) and cholecystokinin (CCK). Compared to healthy women, patients with PCOS show decreased or unaltered fasting ghrelin levels, along with decreased or unaltered postprandial suppression of this hormone. GLP-1, PYY and CCK show unaltered or decreased levels both in fasting and postprandial states in PCOS whereas fasting levels of another gut hormone, GIP is either unaltered or increased. Dietary interventions associated with weight loss or short term oral contraceptive use in PCOS do not alter fasting or postprandial levels of these hormones. However use of metformin is associated with an increase in ghrelin, PYY, GLP-1 and GIP in women with PCOS. GLP-1 agonists and bariatric surgery, both having a significant impact on gut-brain axis, appear to be effective therapeutic options in obese women with PCOS. Finally, alterations in gut microbiota and possible interactions with gut-brain axis in PCOS is a topic of interest. Understanding the relationship between PCOS and homeostatic and hedonic systems, gastrointestinal hormones, and gut microbiota as well as potential effects of different therapeutic interventions on these systems will provide further understanding and novel treatment opportunities for this syndrome.

CIRCULATING MICRORNAS AS POTENTIAL BIOMARKERS FOR TRAUMATIC BRAIN INJURY-INDUCED HYPOPITUITARISM.

Taheri S¹, Tanriverdi F², Zararsiz G³, Elbuken G², Ulutabanca H⁴, Karaca Z², Selcuklu A⁴, Unluhizarci K², Tanriverdi K⁵, Kelestimur F². *J Neurotrauma. 2016 Oct 15;33(20):1818-1825. Epub 2016 Mar 30.*

Traumatic brain injury (TBI), a worldwide public health problem, has recently been recognized as a common cause of pituitary dysfunction. Circulating microRNAs (miRNAs) present in the sera are characteristically altered in many pathological conditions and have been used as diagnostic markers for specific diseases. It is with this goal that we planned to study miRNA expression in patients with TBIinduced hypopituitarism. Thirty-eight patients (27 male, 11 female; mean age, 43 ± 18 years) who had been admitted to the neurosurgery intensive care unit due to TBI were included in the acute phase of the study. In the chronic phase, miRNA expression profile blood samples were drawn from 25 patients who had suffered TBI 5 years ago. In the acute phase (on Days 1, 7, and 28), a substantial amount of patients (26%, 40%, and 53%; respectively) had hypopituitarism (acute adrenocorticotropic hormone deficiency). In the chronic phase eight of 25 patients (32%) had TBI-induced-hypopituitarism. Forty-seven age-gender-similar healthy controls (25 male, 22 female, mean age: 41 ± 14 years) were included in the study. In order to identify potential candidate miRNA/miRNAs whose levels had been altered in response to TBI-induced hypopituitarism, 740 miRNA expression analyses were performed in the sera of TBI patients by high throughput real-time polymerase chain reaction. Statistical analyses showed that miRNA-126-3p (miR-126-3p) and miRNA-3610 (miR-3610) were detected in the sera of patients who developed hypopituitarism on the 1st, 7th, and 28th days, and in the 5th year following TBI. In addition, miRNA-3907 showed statistically significant and constant dynamic changes on the 1st, 7th, and 28th days, and in the 5th year in the patients with TBI. Our results indicated that altered expression of miR-126-3p and miR-3610 may play an important role in the development of TBIinduced hypopituitarism.

Elevated urinary levels of 8-oxo-2'-deoxyguanosine, (5'R)- and (5'S)-8,5'-cyclo-2'-deoxyadenosines, and 8-iso-prostaglandin

THE ASSOCIATION OF OBESITY WITH HEARING THRESHOLDS IN WOMEN AGED 18-40 YEARS.

Üçler R¹, Turan M², Garça F², Acar İ³, Atmaca M⁴, Çankaya H². Endocrine. 2016 Apr;52(1):46-53. doi: 10.1007/s12020-015-0755-y. Epub 2015 Oct 1.

An elevation in hearing thresholds and decrease in hearing sensitivity in adults, particularly due to aging, are quite common. Recent studies have shown that, apart from aging, various other factors also play a role in auditory changes. Studies on the association of hearing loss (HL) with obesity are limited in advanced age cases and present contradictions. In this study, the association between obesity and hearing thresholds in women aged 18-40 years has been assessed. Forty women diagnosed with obesity (mean age, 31.8 years) and 40 healthy non-obese female controls (mean age, 30.5 years) were included in this prospective study. Each subject was tested with low (250, 500, 1000 and 2000 Hz) and high (4000, 6000 and 8000 Hz) frequency audiometry. In the case and control groups, the average hearing thresholds at low frequencies were 16.03 ± 4.72 and 16.15 ± 2.72 (p = 0.885) for the right ear, respectively, and 16.15 ± 5.92 and 14.71 \pm 3.18 (p = 0.180) for the left ear, respectively. The average hearing threshold levels at high frequencies were 20.70 \pm 10.23 and 15.33 \pm 3.87 (p = 0.003), respectively, for the right ear, and 22.91 \pm 15.54 and 15.87 ± 4.35 (p = 0.007), respectively, for the left ear with statistical significance. This is the first report on the association of obesity with hearing threshold in women aged 18-40 years. We have demonstrated that obesity may affect hearing function, particularly that related to high frequencies. Hearing loss can be prevented by avoidance or control of obesity and its risk factors. Moreover, an auditory screening of obese cases at an early stage may provide early diagnosis of HL and may also contribute to their awareness in the fight against obesity.

EVOLUTIONARY DETERMINANTS OF POLYCYSTIC OVARY SYNDROME: PART 1.

Ünlütürk U¹, Sezgin E², Yildiz BO³.

Fertil Steril. 2016 Jul; 106(1):33-41. doi: 10.1016/j.fertnstert.2016.05.010. Epub 2016 May 26.

Polycystic ovary syndrome (PCOS) is a common and complex genetic disorder that develops under varying degrees of hyperandrogenemic and hyperinsulinemic conditions that cause phenotypic variability ranging from mild hirsutism to anovulation and infertility. In addition to increased risk of reproductive disability, PCOS is associated with metabolic diseases including type 2 diabetes, dyslipidemia, and cardiovascular disease. Similar prevalence rates and shared genetic susceptibility of PCOS among different populations suggest that genetic risk factors were already present in the ancestors of humans. Contemporary human genetic studies inform us that the origin of human ancestors is from Africa. Sharing common susceptibility loci between Chinese and European ancestry suggests that PCOS may have persisted for more than 50,000 years, before the migration of humans out of Africa. Although PCOS is the most common cause of anovulatory infertility, its high prevalence is still a paradox. From an evolutionary perspective, the pathogenic mechanisms underlying PCOS might be candidate factors for survival advantage of the human being. Former compensatory advantageous factors may become pathogenic mechanisms underlying complex metabolic disease with prolonged life expectancy and transition to sedentary lifestyle.

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EDİTÖR YAZISI

REPRODUCTIVE ENDOCRINOLOGY: CONTRACEPTIVES, EXERCISE AND DIET — ARE ALL THREE NEEDED IN PCOS?

Bulent O. Yildiz, Nature Reviews Endocrinology, 12,438–440(2016), doi:10.1038/nrendo.2016.106

Oral contraceptives are the mainstay of long-term PCOS treatment, but have potential adverse cardiometabolic effects. In a randomized controlled trial comparing oral contraceptive use and structured exercise in women with PCOS and overweight on a calorie-restricted diet, androgen excess was ameliorated with oral contraceptive use and structured exercise improved markers of cardiometabolic risk.

KITAP BÖLÜMÜ

Ovulation Induction

Evidence Based Guidelines for Daily Practise, October, 2016 by CRC Press Other Endocrine Disorders Causing Anovulartion:Congenital Adrenal Hyperplasia. *Hector F. Escobar-Morreale and Fahrettin Keleştimur*

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