TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ

Üç ayda bir yayımlanır • Üyelere ücretsiz olarak gönderilir

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“2016'nın Genç Araştırmacısı”

Söyleşi:

1. Bu ödülün sizin için anlamı nedir?

Bu ödüle uzun asistanlık süresince yaptığımız öz verili çalışmaların bir mükafatı olarak, Türk Endokrin camiasının değerli hocaları tarafından layık görülmenin hakli gururunu yaşamaktayım. Öz geçmişimde böyle bir başarı ödülünün olması, akademik kariyerimde her zaman değerli bir yere sahip olacaktır. En iyi genç araştırıcı sıfatına layık görülmenin verdiği motivasyon ve sorumluluk bilinci, bundan sonraki akademik hayatımda da bilimsel çalışmalarımı arttırarak devam ettirmemi sağlayacaktır. Bilimsel çalışma yapmak sadece bireysel gayret değil, iyi bir ekip çalışması gerektirmektedir. Bu nedenle bu ödülü almama katkısı bulunan değerli ekip arkadaşlarıma ve bilimsel çalışma altyapısı, ortamı ve olanakları sağlayan tüm hocalarıma ve idarecilere de ayrıca teşekkür ederim.

2. (Genç Araştırıcılar için) Bu ödülü almak için yaptığınız çalışmalarınızda yaşadığınız zorluklar nelerdir? Bunları nasıl aştınız?

Ben iç hastalıkları ve endokrinoloji ihtisaslarımı Ankara'nın en yoğun eğitim ve araştırma hastanelerinde tamamladım. Bu süre zarfında karşılaştığım en önemli problem zaman sorunu oldu. İş ve hasta yoğunluğu nedeniyle bilimsel çalışmalara ayırabildiğimiz süre ancak mesai saatleri dışındaki süreler olmak durumunda kaldı. Türkiye'deki bir çok kurumda da benzer sorunun yaşandığını düşünmekteyim. Asistanlık eğitimi programlarının, asistanın bilimsel araştırma-çalışma yapmaya ayırabileceği zaman kalacak şekilde planlanması gerektiğini düşünüyorum. Bilimsel çalışma zaman, sevgi, emek ve fedakarlık istiyor. Ailelerimiz, çocuklarımız ve sevdiklerimiz de bu fedakarlığa katkıda bulunuyor.

Bilimsel çalışma yapmakta karşılaşılan bir diğer önemli sorun da bütçe. Çalışmalara ayrılan bütçelerin kısıtlılığı, başvuru prosedürlerinin uzun sürmesi karşılaştığımız en önemli sıkıntılardan. Çalışmalar için gerekli malzemelerin temini yanı sıra, çalışmaların dergilere-kongrelere gönderilmesi, değerlendirme ve basım ücretlerini çoğu zaman kendimiz karşılamaktayız. Ancak son 5 yılda bu kaynaklara ulaşımın, önceki yıllara nazaran daha kolaylaştığını ve giderek iyileştiğini söyleyebilirim. Bu da umut verici bir gelişmedir.

Bilimsel envanterelere (dergiler, makale full-textleri, kitaplar) ulaşım da önceki yıllara göre nispeten daha kolay olmakla birlikte, bilimsel çalışmaları hazırlamada karşılaştığımız önemli kısıtlamalardan birisiydi. Ancak artık devlet hastanelerinde de internet üzerinden erişim olanakları artmaya başlamıştır.

3. Endokrinoloji alanında yeni çalışmaya başlayan sizden genç meslektaşlarımıza önerileriz nelerdir?

Her başarının altında sevgi, emek ve özveri yatar. Benim önerim öncelikle yaptığımız işi sevmek ve severek yapmak. Sevgi olduğu zaman emek ve özveri de peşinden geliyor. Kendini geliştirmenin en önemli yöntemi ise okumak, çok okumak ve hep okumak. Mümkün olan her türlü değişik kaynaktan okumak yeni yaratıcı fikirler geliştirmede çok yardımcı oluyor. Diğer taraftan tıp eğitimi de bir nevi usta-çırak ilişkisidir. Arkadaşlarıma danışmaktan, bulundukları ortamı ve eğiticilerini zorlamaktan çekinmemelerini öneririm. Sabırla, yılmadan, usanmadan ve usulünce soru sormak, danışmak, istemekten çekinmemek gerektiğini düşünüyorum. Son olarak, mümkün olduğunca yurt dışı deneyimi edinmelerini öneririm. Yurt dışında bir araştırma projesine katılmak, çalışmak, orada deneyim edinmek, nosyonunu genişletmenin oldukça önemli olduğunu düşünüyorum. Bir çok organizasyon bunun için burslar vermekte. Bu bursları araştırıp, başvurmak için proje üretmek, yazmak ileride bilimsel çalışmalarda da başarılı olmaya katkıda bulunuyor.

Kişisel Bilgiler

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KONUŞMA ÖZETİ

Öncelikle bana meslek hayatım boyunca gururla anacağım bir sıfatı layık gördüğünüz için en içten dileklerimle teşekkür ederim. Endokrinoloji camiasının yılın en iyi genç araştırıcısı seçtiği bir hekim olarak bundan sonraki hedefim; layık görülen bu sıfatı hakkıyla taşımak, çalışmalarıma devam etmek ve daha sonra gelecek genç araştırmacılara örnek olabilmektir. Tıp fakültesinden başlayan, iç hastalıkları ihtisasına ve nihayetinde endokrinoloji doçentliğine kadar geçen yirmi yıllık öğrenim hayatım boyunca bilgi ve tecrübelerini bana aktaran, araştırma bilinci aşılayan, araştırma yapmaya teşvik eden, desteklerini esirgemeyen ve bu ödülü almamda emeği geçen tüm değerli hocalarımı saygıyla ve sevgiyle anıyor ve teşekkürü borç biliyorum.

Ben 2002 senesinde Hacettepe Üniversitesinden mezun olduktan sonra Ankara Numune EA Hastanesinde iç hastalıkları ihtisasıma başladım. Buradaki 5 yıllık asistanlık sürecinde karşılaştığımız çok sayıda ilginç vakalardan vaka takdimi hazırlama, daha sonra klinik verileri düzenleme ve ulusal ve uluslararası kongrelere poster hazırlama ve orjinal makale yazma deneyimleri edindim. 2009 senesinde, iyi bir dereceyle yandal uzmanlık sınavını kazanarak Ankara Dışkapı EAH'nde Endokrinoloji Kliniğine başladım. Yandal eğitimim süresince çok sayıda geniş serili klinik çalışmalar yapma ve yürütme olanağı buldum. Bunlar arasında ozellikle otoımmun tıroıdıt ile vıtamnı d ılıskısını gosteren 540 vakalı makalemiz ve obstruktif uyku apnelı 350 hastalık vaka serısındekı endokrınolıjk ve metabolık degerlendırmlerle ilgi yayınlarımız lıteraturde ılgı çekmiş ve yüksek atıf sayılarına ulaşmıştır. Diğer taraftan kliniğimiz bünyesindeki hücre araştırma merkezinde adacık hücre izolasyonu, adacık hücre fizyolojisi ve ratlarda adacık hücre nakli konularında çalışmalara katıldım. 2011 senesinde ABD Miami unv bunyesındekı dıyabet arastırma enstıtusune burslu arastırma gorevlısı olarak gittim. Burada 1 seneye yakın bir sure adacık hucre naklı yapılmıs tıp 1 dıyabet hastalarının klınık takıbı ve adacık hucre naklının klınık sonucları uzerınde calısmalara katıldım. Buradakı calışmalarımla ustun basarı odulune layık goruldukten sonra donerek 2012de endokrınolıjı ihtisasımı tamamladım. 2014 te mecburı hızmetime basladıgım ankara egıtım ve arastımra hastanesınde Ekım 2015ten berı docent olarak halen gorev yapmaktayım.

Amerika Miami Universitesi Diyabet Arastirma Enstitütüsünde, diyabetik hayvan modellerinde adacık hücre nakli çalışmaları yanı sıra insan kadaverik donör pankreasından adacık hücre izolasyonu prosedürlerini ve seçilmiş Tip 1 Diyabetli hastalara adacık hücre nakli işlemi ve nakil sonrası takip protokollerini çalıştım. Bu merkezde 1980 lerden beri adacık hücre nakli klinik olarak uygulanmakta ve merkez başarısı (nakil sonrası ilk 1 sene insulin bağımsızlığı) ortalama %80 olarak sağlanmaktadır. Burslu araştırma görevlisi olarak çalıştığım süreçte oradaki ekiple birlikte ilk isim ve ikinci isim olmak üzere 2 klinik araştırma yayınladım. Bu makalelerin birisi, merkezde takip altında olan adacık hücre nakli yapılmış 52 hastada işlemle ilişkili komplikasyonlarının derlemesi ve bu komplikasyonların diğer adacık nakli yaplan merkezlerdekiyle karşılaştırması ile ilgiliydi. Ayrıca nadir bir komplikasyon olan masif karaciğer hematomunun yönetimi ve 6 aylık süreçte nasıl takip edilip yönetildiği anlatıldı. Diğer makalede ise, adacık hücre nakli yapılmış vakalarda kısa dönem kan şekeri takibi göstergesi olarak HbA1c yerine kullanılabilecek bir biyomarkerın (1,5 Anhidroglusitol) etkinliği araştırıldı. Çalışmada HbA1c değerleri hedef aralıktaki 21 adacık hücre nakilli hastanın değişik zamanlardaki 1.5 AHD değerlerine bakılarak gün içi kan şekeri dalgalanmalarını yansıtmadaki etkinliğinin HbA1c den daha iyi olduğu gösterildi. Bu makaleler impakt faktörü 4.42 ve 3.8 olan Transplantation ve Cell Transplant dergilerinde yayınlandı.

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Üyelerimizden Literatür Seçmeleri

EFFECTS OF MESENCHYMAL STEM CELLS AND VEGF ON LIVER REGENERATION FOLLOWING MAJOR RESECTION

Adas G[1], Koc B[2], Adas M[3], Duruksu G[4], Subasi C[4], Kemik O[1], Kemik A[5], Sakiz D[6], Kalayci M[1], Purisa S[7], Unal S[4], Karaoz E[8].

Langenbecks Arch Surg. 2016 Aug;401(5):725-40. doi: 10.1007/s00423-016-1380-9. Epub 2016 Apr 19.

Purpose: The study aims to determine the effects of mesenchymal stem cell (MSC) therapy and a combination therapy of MSCs transfected with vascular endothelial growth factor (VEGF) for liver regeneration after major resection.

Methods: Thirty-eight rats were divided into four groups: group 1: control (sham operation); group 2: control (70 % hepatic resection); group 3: 70 % hepatic resection + systemically transplanted MSCs; and group 4: 70 % hepatic resection + systemically transplanted MSCs transfected with the VEGF gene. MSCs were injected via the portal vein route in study groups 3 and 4. Expression levels of VEGF, fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor (TGF), hepatocyte growth factor (HGF), and augmenter of liver regeneration (ALR) were analyzed in the remnant liver tissue. We investigated the levels of angiogenic factors, VEGF-receptor, angiopoietin-1 (Angpt1) and Angpt2. Biochemical parameters of liver function in blood samples were measured and a histologic assessment of the livers was performed. The postoperative liver weight and volume of each rat were measured 14 days after surgery.

Results: The expression levels of all measured growth factors were significantly increased in groups 3 and 4 compared to the control groups. The levels of Angpt1 and Angpt2 correlated with levels of VEGF and thus were also significantly higher in the study groups. There were significant differences between the estimated liver weights and volumes of group 4 and the resected controls in group 2. With the exception of portal inflammation, levels of all histological parameters were observed to be higher in MSC-treated groups when compared with the resected controls in group 2.

Conclusions: Transplanted stem cells and MSCs transfected with VEGF significantly accelerated many parameters of the healing process following major hepatic resection. After the injection of MSCs and VEGF-transfected MSCs into the portal vein following liver resection, they were engrafted in the liver. They increased bile duct and liver hepatocyte proliferation, and secreted many growth factors including HGF, TGFβ, VEGF, PDGF, EGF, and FGF via paracrine effects. These effects support liver function, regeneration, and liver volume/weight.

MALIGNANCY RISK AND FALSE-NEGATIVE RATE OF FINE NEEDLE ASPIRATION CYTOLOGY IN THYROID NODULES ≥4.0 cm

Bestepe N[1], Ozdemir D[2], Tam AA[2], Dellal FD[2], Kilicarslan A[3], Parlak O[4], Ersoy R[2], Cakir B[2]. Surgery.

2016 Aug;160(2):405-12. doi: 10.1016/j.surg.2016.03.019. Epub 2016 May 5.

Background: We aimed to evaluate malignancy rate and to determine false negativity of fine needle aspiration biopsy (FNAB) in thyroid nodules ≥4.0 cm.

Methods: The medical records of patients who underwent thyroidectomy between January 2007 and December 2014 were reviewed. Demographic and clinical data as well as preoperative ultrasonography findings were analyzed. The nodules in these patients were grouped as ≥4.0 cm and <4.0 cm according to ultrasonography measurements. Nodules <4.0 cm were further divided into 1.0-3.9 cm and <1.0 cm. Histopathologically malignant nodules with preoperative benign cytology were defined as having false-negative FNAB.

Results: There were 1,008 nodules that measured ≥4.0 cm, 4,013 nodules that measured 1.0-3.9 cm, and 540 that measured nodules <1.0 cm. Based on histopathologic findings, 8.5%, 10.2%, and 25.6% of nodules ≥4.0 cm, 1.0-3.9 cm, and <1.0 cm were malignant, respectively (P < .001). There was no significant difference between 1.0-3.9-cm and ≥4.0-cm nodules with respect to malignancy (P = .108). False-negativity rates were 4.7% in nodules ≥4.0 cm, 2.2% in nodules measuring 1.0-3.9 cm, and 4.8% in <1.0-cm nodules. Nodules measuring <1.0 cm and ≥4.0 cm had similar false-negativity rates (P = .93), while 1.0-3.9-cm nodules had statistically lower false-negativity rates than those found in the other two groups (P = .03 and P < .001, respectively).

Conclusion: Of the nodules that were operatively excised, nodules ≥4.0 cm had a similar risk of malignancy as nodules 1.0-3.9 cm. The rate of false-negative FNAB in nodules ≥4.0 cm was twice as high as in nodules 1.0-3.9 cm; however, we do not think it is high enough to recommend a routine operation when cytology results are benign.

THE EFFECTS OF GONADOTROPIN REPLACEMENT THERAPY ON METABOLIC PARAMETERS AND BODY COMPOSITION IN MEN WITH IDIOPATHIC HYPOGONADOTROPIC HYPOGONADISM

Bayram F[1], Elbuken G[1], Korkmaz C[1], Aydogdu A[2], Karaca Z[1], Cakır I[1].

Horm Metab Res. 2016 Feb;48(2):112-7. doi: 10.1055/s-0035-1564252. Epub 2015 Oct 20.

Testosterone replacement therapy (TRT) in idiopathic hypogonadotrophic hypogonadism (IHH) slows the process of metabolic syndrome (MetS), diabetes mellitus, and cardiovascular diseases by its inversing effects on insulin resistance, dyslipidemia, and blood pressure. Since there are not enough data regarding the effects of gonadotropin replacement therapy (GRT), we aimed to investigate the impact of GRT on MetS parameters in IHH patients. Sixteen patients with IHH and 20 age and body mass index (BDI)-matched healthy controls were enrolled into the study. Patients were evaluated at baseline and 6 months after the GRT. Sex hormones, insulin like growth factor-1, prolactin, insulin, C-reactive protein (CRP), homocysteine, and lipid levels were measured at baseline and after the treatment. Anthropometric measurements, including BMI, body fat ratio (BFR), fat free mass (FFM), waist circumference, and waist-to-hip ratio (WHR), were also performed. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index was calculated. Body fat ratio, triglyceride, HOMA-IR, and CRP levels were higher, whereas bone age, fat free mass, and creatinine levels were lower in the patients with hypogonadism. HOMA-IR indices and basal insulin levels decreased significantly after 6 months of GRT compared with baseline levels. Triglyceride levels, and BFRs diminished significantly by an accompanying decline in WHR. FFM of the patients increased following the GRT. No significant changes were detected in CRP, homocysteine, total and LDL-cholesterol levels. Similar to TRT, hCG treatment decreases HOMA-IR, triglyceride levels, BFR and WHRs, and increases FFM in patients with IHH.

HIGHER TSH CAN BE USED AS AN ADDITIONAL RISK FACTOR IN PREDICTION OF MALIGNANCY IN EUTHYROID THYROID NODULES EVALUATED BY CYTOLOGY BASED ON BETHESDA SYSTEM

Baser H[1], Topaloglu O[2], Tam AA[2], Evranos B[3], Alkan A[4], Sungu N[5], Dumlu EG[6], Ersoy R[2], Cakir B[2]. Endocrine.

2016 Aug;53(2):520-9. doi: 10.1007/s12020-016-0919-4. Epub 2016 Mar 14.

Recently, it has been suggested that thyrotropin (TSH) concentration can be used as a marker for prediction of thyroid malignancy. In this study, we aimed to investigate the association between TSH levels and prediction of malignancy in euthyroid patients with different Bethesda categories. The data of 1433 euthyroid patients with 3206 thyroid nodules who underwent thyroidectomy were screened retrospectively. The preoperative cytology results, thyroid function tests, thyroid autoantibodies, and presence of histopathological Hashimoto's thyroiditis (HT) were recorded. Of the 1433 patients, 585 (40.8 %) had malignant and 848 (59.2 %) had benign histopathology. Malignant group had smaller nodule size, elevated TSH levels, and higher rate of presence of HT compared to benign group (p < 0.001, all). Cytology results of 3206 nodules were as follows: 832 nondiagnostic (ND), 1666 benign, 392 atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), 68 follicular neoplasm/suspicious

for follicular neoplasm (FN/SFN), 133 suspicious for malignancy (SM), and 115 malignant. Both SM and malignant cytology groups had higher TSH levels than other 4 Bethesda categories ($p < 0.05$, all). Benign cytology group had significantly lower TSH levels compared to other cytology groups ($p < 0.05$, all). Patients with malignant final histopathology in ND and AUS/FLUS cytology groups had significantly higher TSH levels compared to patients with benign final histopathology ($p < 0.05$, all). Moreover, TSH levels showed to increase from Bethesda categories II to VI. In addition to cytology, higher TSH levels can be used as a supplementary marker in prediction of malignancy in certain Bethesda categories.

WITHDRAWAL OF DOPAMINE AGONIST THERAPY IN PROLACTINOMAS: IN WHICH PATIENTS AND WHEN?

Dogansen SC[1], Selcukbiricik OS[2], Tanrikulu S[2], Yarman S[2].
Pituitary. 2016 Jun;19(3):303-10. doi: 10.1007/s11102-016-0708-3.

Purpose: The aim of the study was to assess the effect of dopamine agonist (DA) withdrawal, the current recurrence rate of hyperprolactinemia, and possible factors that predict recurrence in patients with prolactinoma.

Methods: We evaluated DA withdrawal in 67 patients with prolactinoma (50 female/17 male) who received DA treatment for at least 2 years and showed normalization of prolactin (PRL) levels and tumor disappearance or ≥50 % tumor shrinkage, retrospectively. Accordingly, patients were divided into two groups as remission and recurrence groups, and factors that predict recurrence were evaluated.

Results: The overall remission rate was 46 %; the remission ratios were 65 % in microprolactinomas and 36 % in macroprolactinomas. Remission rates were 39 % in the bromocriptine withdrawal group and 55 % in the cabergoline withdrawal group. The maximum tumor diameter and baseline PRL levels were significantly higher in the recurrence group ($p = 0.001$ and $p = 0.003$, respectively). The mean duration of DA therapy was significantly longer in the remission group (88.7 ± 48.1 and 66.7 ± 30.4 months, respectively, $p = 0.026$). The mean time to recurrence was 5.3 ± 3.2 months. The mean PRL levels at recurrence time were significantly lower than baseline PRL levels ($p = 0.001$).

Conclusion: The most important predictors of recurrence were maximum tumor diameter and baseline PRL levels in this study. The remission rate in our study group was higher, which was thought to be associated with the longer duration of DA treatment and that our patients were selected according to certain criteria. Despite these positive results, close monitoring is necessary for detection of early and late recurrence, especially within the first year after DA withdrawal.

COMPARISON OF SALIVARY AND CALCULATED FREE CORTISOL LEVELS DURING LOW AND STANDARD DOSE OF ACTH STIMULATION TESTS IN HEALTHY VOLUNTEERS

Elbuken G[1], Tanriverdi F, Karaca Z, Kula M, Gokahmetoglu S, Unluhizarci K, Kelestimur F. Endocrine.
2015 Mar;48(2):439-43. doi: 10.1007/s12020-014-0378-8. Epub 2014 Aug 13.

Salivary cortisol (SC) has been increasingly used as a surrogate biomarker of free cortisol (FC) for the assessment of hypothalamo-pituitary-adrenal (HPA) axis, but there are not enough data regarding its use during ACTH stimulation tests. Therefore, we aimed to determine the responses of SC, calculated free cortisol (cFC) and free cortisol index (FCI) to ACTH stimulation tests in healthy adults. Forty-four healthy volunteers (24 men and 20 women) were included in the study. Low-dose (1 μg) and standard-dose (250 μg) ACTH stimulation tests were performed on two consecutive days. Basal and stimulated total cortisol (TC) and cortisol-binding globulin (CBG) levels and SC levels were measured during both doses of ACTH stimulation tests. cFC (by Coolens' equation) and FCI levels were calculated from simultaneously measured TC and CBG levels. The minimum SC, cFC, FCI levels after low-dose ACTH stimulation test were 0.21, 0.33, 16.06 μg/dL, and after standard-dose ACTH were 0.85, 0.46, 26.11 μg/dL, respectively, in healthy individuals who all had TC responses higher than 20 μg/dL. Peak CBG levels after both doses of ACTH stimulation tests were found to be higher in women than in men. So, by its effect, peak cFC and FCI levels were found to be lower in female than in male group. Neither TC nor SC levels were affected by gender. cFC and FCI levels depend on CBG levels and they are affected by gender. Cut-off levels for SC, cFC, FCI levels after both low- and standard-dose ACTH stimulation are presented. Studies including patients with adrenal insufficiency would be helpful to see the diagnostic value of these suggested cut-off levels.

SERUM LEVELS OF SRAGE ARE ASSOCIATED WITH BODY MEASUREMENTS, BUT NOT GLYCEMIC PARAMETERS IN PATIENTS WITH PREDIABETES

Guclu M[1], Ali A[2], Eroglu DU[3], Büyükuysal SO[4], Cander S[1], Ocak N[4].
Metab Syndr Relat Disord. 2016 Feb;14(1):33-9. doi: 10.1089/met.2015.0078. Epub 2015 Nov 16.

Background: Our aim was to assess serum levels of the soluble receptor for advanced glycation end products (sRAGE) and to examine their association with anthropometric and metabolic parameters in patients with prediabetes and obese controls.

Methods: The two study groups were composed of 42 patients with prediabetes and diabetic neuropathy and 42 age-, gender-, body weight (BW)-, and body mass index (BMI)-matched obese adults as the control group. Prediabetes was diagnosed by the following criteria issued by the American Diabetes Association: impaired fasting glucose [fasting plasma glucose (FPG) level of 100-125 mg/dL], impaired glucose tolerance (2 hr plasma glucose level of 140-199 mg/dL after a 75 grams oral glucose challenge), or a glycated hemoglobin (HbA1C) level of 5.7%-6.4%.

Results: There were no differences between the groups in terms of age, gender distribution, BW, or BMI. Despite these similarities, patients with prediabetes had higher FPG, HbA1c, and 2-hr postchallenge glucose levels, higher systolic and diastolic blood pressure, and larger waist and hip circumferences compared with the obese controls. Lipid measurements, complete blood counts, kidney and liver function tests, high-sensitivity C-reactive protein, and sRAGE levels were similar between the two groups. We found significant negative correlations between sRAGE levels and BW, BMI, waist and hip circumferences, waist-to-hip ratios, and low-density lipoprotein (LDL) cholesterol levels. There were no significant correlations with other parameters, including demographic, metabolic, and blood pressure measurements.

Conclusions: In contrast to glycemic parameters, serum levels of sRAGE were negatively correlated with body measurements indicative of obesity in the prediabetic state. In addition, the negative correlation with LDL cholesterol levels suggests that sRAGE has a more robust association with metabolic syndrome than with prediabetes.

GH AND PITUITARY HORMONE ALTERATIONS AFTER TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) is a crucially important public health problem around the world, which gives rise to increased mortality and is the leading cause of physical and psychological disability in young adults, in particular. Pituitary dysfunction due to TBI was first described 95 years ago. However, until recently, only a few papers have been published in the literature and for this reason, TBI-induced hypopituitarism has been neglected for a long time. Recent studies have revealed that TBI is one of the leading causes of hypopituitarism. TBI which causes hypopituitarism may be characterized by a single head injury such as from a traffic accident or by chronic repetitive head trauma as seen in combative sports including boxing, kickboxing, and football. Vascular damage, hypoxic insult, direct trauma, genetic predisposition, autoimmunity, and neuroinflammatory changes may have a role in the development of hypopituitarism after TBI. Because of the exceptional structure of the hypothalamo-pituitary vasculature and the special anatomic location of anterior pituitary cells, GH is the most commonly lost hormone after TBI, and the frequency of isolated GHD is considerably high. TBI-induced pituitary dysfunction remains undiagnosed and therefore untreated

in most patients because of the nonspecific and subtle clinical manifestations of hypopituitarism. Treatment of TBI-induced hypopituitarism depends on the deficient anterior pituitary hormones. GH replacement therapy has some beneficial effects on metabolic parameters and neurocognitive dysfunction. Patients with TBI without neuroendocrine changes and those with TBI-induced hypopituitarism share the same clinical manifestations, such as attention deficits, impulsion impairment, depression, sleep abnormalities, and cognitive disorders. For this reason, TBI-induced hypopituitarism may be neglected in TBI victims and it would be expected that underlying hypopituitarism would aggravate the clinical picture of TBI itself. Therefore, the diagnosis and treatment of unrecognized hypopituitarism due to TBI are very important not only to decrease morbidity and mortality due to hypopituitarism but also to alleviate the chronic sequelae caused by TBI.

ASSOCIATION OF MULTIFOCALITY, TUMOR NUMBER, AND TOTAL TUMOR DIAMETER WITH CLINICOPATHOLOGICAL FEATURES IN PAPILLARY THYROID CANCER

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Endocrine. 2016 Sep;53(3):774-83. doi: 10.1007/s12020-016-0955-0. Epub 2016 Apr 18.

Tumor multifocality is not an unusual finding in papillary thyroid carcinoma (PTC), but its clinical significance is controversial. In this study, we aimed to evaluate impact of multifocality, tumor number, and total tumor diameter on clinicopathological features of PTC. Medical records of 912 patients who underwent thyroidectomy and diagnosed with PTC were reviewed retrospectively. Patients were grouped into four according to number of tumoral foci: N1 (1 focus), N2 (2 foci), N3 (3 foci), and N4 (≥4 foci). The diameter of the largest tumor was considered the primary tumor diameter (PTD), and total tumor diameter (TTD) was calculated as the sum of the maximal diameter of each lesion in multicentric tumors. Patients were further classified into subgroups according to PTD and TTD. Multifocal PTC was found in 308 (33.8 %) patients. Capsular invasion, extrathyroidal extension, and lymph node metastasis were significantly higher in patients with multifocal tumors compared to patients with unifocal PTC. As the number of tumor increased, extrathyroidal extension and lymph node metastasis also increased ($p = 0.034$ and $p = 0.004$, respectively). The risk of lymph node metastasis was 2.287 (OR = 2.287, $p = 0.036$) times higher in N3 and 3.449 (OR = 3.449, $p = 0.001$) times higher in N4 compared to N1. Capsular invasion, extrathyroidal extension, and lymph node metastasis were significantly higher in multifocal patients with PTD ≤10 mm and TTD >10 mm than unifocal patients with tumor diameter ≤10 mm ($p < 0.001$, $p < 0.001$ and $p = 0.001$, respectively). There was no significant difference in terms of these parameters in multifocal patients with PTD ≤10 mm and TTD >10 mm and unifocal patients with tumor diameter >10 mm. In this study, increased tumor number was associated with higher rates of capsular invasion, extrathyroidal extension, and lymph node metastasis. In a patient with multifocal papillary microcarcinoma, TTD >10 mm confers a similar risk of aggressive histopathological behavior with unifocal PTC greater than 10 mm.

MALIGNANCY IS ASSOCIATED WITH MICROCALCIFICATION AND HIGHER AP/T RATIO IN ULTRASONOGRAPHY, BUT NOT WITH HASHIMOTO'S THYROIDITIS IN HISTOPATHOLOGY IN PATIENTS WITH THYROID NODULES EVALUATED AS BETHESDA CATEGORY III (AUS/FLUS) IN CYTOLOGY

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Endocrine. 2016 Oct;54(1):156-168. Epub 2016 May 12.

The predictors of malignancy are important for the decision of appropriate management in nodules with atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS). Our aim was to determine the ultrasonographical, clinical, and biochemical predictors of malignancy in these patients. A total of 427 patients with cytologically Bethesda Category III (AUS/FLUS) thyroid nodules were included in this retrospective study. We divided the nodules into two subgroups according to the histopathology as benign and malignant, and compared the preoperative ultrasonographical, clinical, and biochemical findings. In overall, 427 patients with 449 AUS/FLUS nodules who had undergone surgery, the rate of malignancy was 23.4 % (105/449). When evaluated separately, the rate of malignancy was 25.8 % in nodules with AUS (82/318) and 17.6 % in nodules with FLUS (23/131) ($p = 0.061$). The vast majority of malignant specimens in histopathology consisted of papillary thyroid carcinoma (PTC) (n = 91, 86.7 %). Preoperative ultrasonographic features of 105 malignant nodules in histopathology were compared with the 344 benign nodules in histopathology. Anteroposterior/Transverse (AP/T) ratio was significantly higher in malignant group compared to benign group ($p = 0.013$). In multiple logistic analysis, we found that higher AP/T ratio and microcalcification were independently associated with malignancy ($p < 0.05$). The malignancy-associated cut-off value of AP/T ratio at maximum sensitivity and specificity was ≥0.81. We did not find any correlation between malignancy and Hashimoto's thyroiditis in histopathology in multivariate analysis ($p > 0.05$). In Bethesda Category III nodules with higher AP/T ratio and microcalcification, surgery might be considered as a first therapeutic option instead of repeat fine-needle aspiration biopsy or observation.

POLYCYSTIC OVARY SYNDROME IS ASSOCIATED WITH INCREASED OSTEOPONTIN LEVELS

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Eur J Endocrinol. 2016 Apr;174(4):415-23. doi: 10.1530/EJE-15-1074. Epub 2015 Dec 23.

Objective: Osteopontin (OPN) is a multi-functional secreted glycoprotein that plays a crucial role in glucose metabolism and inflammatory process. Growing evidence suggests that there is a link between OPN and ovarian function. However, no such link has yet been found for OPN in polycystic ovary syndrome (PCOS). Our aim was to ascertain whether circulating OPN levels are altered in women with PCOS and to determine whether OPN levels differ between the follicular phase and mid-cycle of the menstrual cycle in eumenorrheic women.

Design and methods: In total, 150 women with PCOS and 150 age- and BMI-matched controls without PCOS were recruited for this prospective observational study. OPN levels were measured using ELISA. Metabolic parameters were also determined.

Results: Circulating OPN levels were significantly elevated in PCOS women compared with controls (69.12±31.59 ng/ml vs 42.66±21.28 ng/ml; P<0.001). OPN levels were significantly higher at mid-cycle than in the follicular phase in eumenorrheic women. OPN was positively correlated with BMI, homeostasis model assessment of insulin resistance (HOMA-IR), free testosterone, and high sensitivity C-reactive protein (hs-CRP). Multivariate logistic regression analyses revealed that the odds ratio (OR) for PCOS was 3.64 for patients in the highest quartile of OPN compared with those in the lowest quartile (OR=3.64; 95% CI=2.42-5.57; P=0.011). Our findings indicate that BMI, HOMA-IR, hs-CRP, and free testosterone are independent factors influencing serum OPN levels and that OPN is an independent predictor for HOMA-IR.

Conclusion: PCOS is associated with increased OPN levels.

RELATIONSHIP BETWEEN PARATHORMONE AND OBESITY-LINKED DISORDERS

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Metab Syndr Relat Disord. 2015 Dec;13(10):470-6. doi: 10.1089/met.2015.0062. Epub 2015 Oct 9.

Background: In this study, we aimed to investigate whether high parathormone (PTH) levels in obese patients contribute to the metabolic complications of obesity.

Methods: A total of 400 obese subjects aged 18-65 years were included. Anthropometric bioelectrical bioimpedance measures, blood tests, and 75 gram oral glucose tolerance test results were evaluated.

Results: Of the 400 obese subjects, 335 were female. The mean age was 39 ± 10 years. The median body mass index was 36 (interquartile range 34-41). Subjects were divided into quartiles according to blood PTH levels.

Groups included quartile 1 [n = 100, median PTH; 42 (range 36-45)], quartile 2 [n = 100, median PTH; 55 (51-59)], quartile 3 [n = 100, median PTH; 73 (68-78)], and quartile 4 [n = 100, median PTH; 99 (89-125)]. Quartiles were evaluated with a generalized linear model adjusted for age, sex, and season of recruitment. Systolic and diastolic blood pressure, fasting glucose, homeostatic model assessment-estimated insulin resistance, insulin sensitivity index, triglyceride level, and high-density lipoprotein cholesterol (HDL-C) were not different among quartiles. PTH and 25 hydroxyvitamin D (25(OH)D) were not associated with higher odds of prevalent metabolic syndrome in obese subjects (odds ratio, OR, 0.99 [95% confidence interval, CI, 0.981.00], P = 0.38 and 0.99 95% CI 0.96-1.01], P = 0.46, respectively). Decreased 25(OH)D levels were significantly correlated with higher odds of low HDL-C (OR 0.96 [95% CI 0.93-0.99], P = 0.04).

Conclusions: PTH does not contribute to the occurrence of metabolic components of obesity, but there is a positive correlation between 25(OH) D and HDL-C.

EFFECTS OF THYROTROPHIN, THYROID HORMONES AND THYROID ANTIBODIES ON METABOLIC PARAMETERS IN A EUTHYROID POPULATION WITH OBESITY

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Clin Endocrinol (Oxf). 2016 Oct;85(4):616-23. doi: 10.1111/cen.13095. Epub 2016 May 26.

Objective: To investigate whether thyroid function in the euthyroid range and thyroid autoimmunity status would affect metabolic measures in individuals with obesity.

Design: Cross-sectional.

Patients: We retrospectively evaluated 5300 consecutive obese (BMI ≥30 kg/m(2)) subjects attending the Obesity Outpatient Clinic. Subjects with overt or subclinical thyroid disease, diabetes mellitus, chronic disease or using any medication were excluded. After exclusion, 1275 euthyroid [TSH values >0·4 and <4·5 μIU/ml, free triiodothyronine (FT3), free thyroxine (FT4) in the normal reference range] obese subjects (aged 18-65 years) were eligible for the study.

Measurements: The physical and biochemical records of the subjects at first admission to the obesity outpatient clinic were examined.

Results: Eighty-three per cent (n = 1063) of the study population were women. Antithyroid peroxidase (anti-TPO) positivity was 14%, and antithyroglobulin (anti-TG) positivity was 15%. TSH was 1·8 μIU/ml (1·3-2·4) in antibody-negative subjects and 2·1 μIU/ml (1·4-2·9) in antibody-positive subjects. Neither TSH nor thyroid antibody positivity was associated with insulin resistance (IR) and atherogenic dyslipidaemia after adjustment for confounders. FT3 was positively associated with IR (P < 0·001) and atherogenic dyslipidaemia (P = 0·03); however, this association lost its significance after adjustment for age, gender and BMI. FT4 was negatively associated with IR and this association remained even after adjustment for confounders (P < 0·001).

Conclusion: TSH and thyroid antibody positivity were not related with metabolic measures. Low-normal FT4 had an inverse association with HOMA-IR even after adjustment for confounders.

EVALUATION OF ACUTE AND CHRONIC MRI FEATURES OF SACROILIITIS IN ASYMPTOMATIC PRIMARY HYPERPARATHYROID PATIENTS

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Clin Rheumatol. 2016 Nov;35(11):2777-2782. Epub 2016 Jan 19.

Asymptomatic primary hyperparathyroidism (PHPT) is characterized with autonomous overproduction of parathyroid hormone without signs or symptoms associated with hyperparathyroidism. Before symptoms become obvious, PHPT may affect structures like sacroiliac joints, which consist of bone. So, in the asymptomatic PHPT patients, structural and inflammatory changes in sacroiliac joints may lead to confusion during diagnosis workup of axial spondyloarthropathy. In this study, we evaluated active and chronic sacroiliac magnetic resonance imaging (MRI) changes relevant to sacroiliitis in the patients with asymptomatic PHPT and interpreted bone marrow edema within the scope of Assessment of SpondyloArthritis International Society-Outcome Measures in Rheumatology Clinical Trials (ASAS-OMERACT) criteria. Forty-nine patients with asymptomatic PHPT, 26 patients with newly diagnosed axial spondyloarthropathy (SpA), and 37 healthy controls were enrolled. All subjects were evaluated by sacroiliac MRI for four active (bone marrow edema, enthesitis, capsulitis, and synovitis) and four chronic (subchondral sclerosis, subchondral/periarticular erosions, periarticular fat deposition, and bony bridges/ankylosis) lesions relevant to sacroiliitis. Bone marrow edema compatible with ASAS-OMERACT active sacroiliitis criteria in sacroiliac MRI was fulfilled by 16.3 % (8/49) of the asymptomatic PHPT patients which was similar with controls but statistically lower than axial SpA. Moreover, asymptomatic PHPT patients and controls were similar for other chronic or active MRI findings. Also, we detected lower frequency of all other MRI findings, except enthesis, in asymptomatic PHPT patients according to axial SpA. Acute inflammatory including bone marrow edema fulfilling ASAS-OMERACT active sacroiliitis criteria and chronic structural sacroiliac lesions relevant to sacroiliitis in MRI were detected in asymptomatic PHPT similar frequency with controls but as expected, lower than axial SpA. But, these findings could not be attributed to excessive secretion of parathyroid hormone.

PANCREATIC DAMAGE INDUCED BY CIGARETTE SMOKE: THE SPECIFIC PATHOLOGICAL EFFECTS OF CIGARETTE SMOKE IN THE RAT MODEL

Topsakal S, Ozmen O,* Aslankoc R, Aydemir DH
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In recent years, pancreatic pathologies have become common problems and their etiology and pathogenesis are generally unknown. Studies have shown that smoking may increase the risk of pancreatic disorders but very scant knowledge is available about the pathogenesis of cigarette induced pancreatic pathology. This study aimed to evaluate the oxidative stress status, biochemical, pathological and immunohistochemical findings of rats exposed to cigarette smoke, pathogenesis of smoking related pancreatic damage and usability of Alpha Lipoic Acid (ALA) for amelioration of cigarette smoking induced harmful effects on rat pancreas. Twenty eight female, Sprague Dawley rats were randomly distributed into three groups. The sham group (S) (n = 8), rats were given 0.1 ml of physiological serum by oral gavage for 8 weeks. The cigarette smoke exposed group (CSE) (n = 10), rats were exposed to successive periods of cigarette smoke for 2 hours per day per 8 weeks and given 0.1 ml of physiological serum orally during the study. The cigarette smoke exposed and ALA treated group (CSE + ALA) (n = 10), animals were exposed to cigarette smoke (2 hours per day per 8 weeks) and simultaneously treated with 100 mg per kg per day ALA orally during the study. At the end of the study, the serum samples were collected for insulin, glucagon, glucose and amylase analyses. Tissue samples were collected for biochemical, histopathological and immunohistochemical examinations. Total oxidant status (TOS), total antioxidant status (TAS) levels and oxidative stress index (OSI) were evaluated in the pancreas samples. Immunohistochemical analyses of insulin, glucagon, calcitonin gene related protein (CGRP), active caspase-3, hypoxia inducible factor-1 (Hif-1), Hif-2 and tumor necrosis factor (TNF-α) expressions of pancreas were examined. Cigarette smoke caused statistically significant increase in serum amylase and glucose but decreased insulin levels indicating both endocrine and exocrine cell damage. There were no statistically significant differences in serum glucagon levels between the groups. Histopathological examination of the pancreas exhibited generally normal tissue architecture but slightly degenerative and apoptotic cells were noticed both in the endocrine and exocrine part of the pancreas in the CSE group. Immunohistochemical analyses revealed marked increase in active caspase-3, Hif-1 and Hif-2, CGRP and TNF-α expressions with a slight increase in glucagon immunoreactivity in cells while a marked decrease was observed in insulin expression in some Langerhans islets in the CSE group. ALA ameliorated biochemical and pathological findings in the CSE + ALA group. These findings clearly demonstrated that cigarette smoke can cause damage in both endocrine and exocrine cells in rat pancreas and ALA has an ameliorative effect of cigarette induced lesions.

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