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Dear Fellow Member of ESI,

Greetings from the Endocrine Society of India. It was long felt need of many members to have our own Newsletter which is going to cater to our specific needs. And to honour the demand of members the Executive Committee has decided in the last ESICON at Delhi to bring out a "Newsletter of Endocrine Society of India". The Joint Secretary of ESI will be entrusted with the responsibility of bringing out the issues. The nature and content of the Newsletter is open to discussion and we fervently seek your opinion on the same. Hope you would like this novel effort of Executive Committee of ESI and suggest ways to improve on it.

Best regards,
Prof. Krishna Seshadri,
Secretary,
Endocrine Society of India

Dear Fellow Member of ESI,

It gives me immense pleasure to see the wishes of many members of ESI to have our own newsletter bearing fruit. I congratulate the Executive Committee to have taken steps in favour of that to fulfill the needs of our members. I presume you would like the content of the Newsletter and would advise us on means of improving the same.

Long live our Endocrine Society of India,
Best wishes,
Prof. S.K. Singh,
President,
Endocrine Society of India



Dear Fellow Member of ESI,

It is indeed a moment to cherish, being the beginning of our new venture of creating a Newsletter for the members of the ESI. The Executive Committee of the ESI in the last ESICON in New Delhi has deliberated on this issue and had decided to publish this newsletter to fill the gap in the expectations of many members of the long felt need to create our own Newsletter. I have been assigned this responsibility along with my colleagues, namely Dr. Rajesh Rajput and Dr. KVS Hari Kumar to cater to the need of the members. We feel that the Newsletter should cater to our needs of circulating about news on the recently concluded meetings/conferences and also be a source of some academic insights. I feel we should also include the abstracts of some notable publications in recent past of our interest in the scientific literature of repute (which per chance might have escaped your notice) along with a very brief commentary written by someone amongst the members. Following this you may be inclined to read the complete article based on the commentary, which would really be an achievement for the basic purpose of the Newsletter.

I take this opportunity to thank all the contributors for sending their commentaries in response to my request. I also would like to request our existing members to help us in this venture by contributing commentaries which are likely to be of use to the fellow members. Needless to mention, your suggestions and comments are most welcome (at my email id) in creating a better Newsletter than the one you are taking a glimpse now.

Best regards,

Kaushik Pandit

Joint Secretary,

Convener, ESI Newsletter Committee

Email: kpandit3@gmail.com.

REPORT OF THE CONFERENCE - ESICON 2016

Total Recall (ESICON 2016)

The 46th annual conference of the Endocrine Society of India took place from 20-23rd October 2016 at Hotel Pullman, Aerocity, New Delhi. With more than 1300 delegates registered, this was the largest ever gathering of Endocrinologists in the country. A significant number of physicians, pediatricians and gynecologists also attended the conference on different days, highlighting the increased awareness of Endocrinology & Metabolism among the medical fraternity. There was also an active participation by endocrinologists from the neighboring countries of Nepal, Bangladesh and Sri Lanka.

Prologue

The story of ESICON 2016 started nearly 2 years back when the Department of Endocrinology, All India Institute of Medical Sciences (AIIMS) was awarded the responsibility of holding the conference at New Delhi. Under the able guidance of Prof. Nikhil Tandon and Prof. Rajesh Khadgawat, the entire team of Endocrinologists at AIIMS as well as endocrinologists working at different centers across the city of Delhi put in hundreds of hours behind the scenes, to make this event a grand success.

The selection of Aerocity as the venue was a master-stroke as it removed the "time lost in travel/commuting" factor out of the equation. Delegates from across the country and the globe could land at the New Delhi International Airport and reach the venue within 15 minutes. Hence for the first time the academic session went on till Sunday (23rd October) evening, instead of wrapping up the meet at the noon.

The making of ESICON

The organizing committee had several long brainstorming meeting for nearly a year building up to the ESICON. Every minute details from the size of the halls, the poster area, the industry exhibition area, fooding, accommodation for the faculty and the delegates was attended to. Special emphasis was given to improve the scientific content of the program, focusing on the problem areas and newer developments in endocrinology in the last one-year. On the eve of ESICON, the members of the organizing committee, lodged themselves at the venue, in spite of the day being "Karva Chauth", a popular festival, when the spouses keep fast for the well being of their husbands. Only endocrinologists can do such a balancing act! In spite of all the planning and preparation, the tension was very visible and palpable

Day-1: Pre-conference work shops

Workshop for Endocrinology trainees

For the first time a special whole day preconference workshop was organized for endocrine trainees (DM/DNB) in different institutes from across the countries, focusing on the clinical methods and approach to common endocrine disorders. The highlight of the program was the sessions being taken by senior endocrinologist from different institutes of the country, who are frequently involved in the organization of exit examinations for DNB and DM courses. This provided

a golden opportunity to the current endocrine residents to have one-to-one interaction with the top endocrine faculty from across the country. The residents hugely appreciated the program.

Workshop on Gynecology Endocrinology

This workshop was attended by a large number of gynecologists. This provided a platform to synergize patient management approaches among the endocrinologists and the gynecologists. Controversial aspects in the management of polycystic ovarian syndrome (PCOS), thyroid disorders and infertility was deliberated on in detail.

Workshop on Neonatal Endocrinology

Neonatal endocrinology is perhaps one of the most neglected aspects of endocrinology. This workshop was a huge hit among the local pediatricians and neonatologists in Delhi. Some of the important topics covered in this workshop were pitfalls and fallacies in interpretation of hormonal reports in the neonates, approach to neonatal hypocalcemia, hypoglycemia and failure to thrive. An in depth discussion took place to approach to disorders of sexual differentiation in neonates.

Day-2: Main conference day-1

The main conference began with the plenary session. Renowned endocrinologists from across the globe presented their original and latest work, which was well appreciated by the audience. Highlights of this day included presentation on novel metabolic effects of testosterone replacement in hypogonadotrophic hypogonadism (Dandona P), diagnosis of GH deficiency and related disorders (Dattani M), genetic disorders of the pituitary axis (Chatterjee VK) and advances on insulin pumps in type-1 diabetes (Heller S). The Endocrine Society of India (ESI) awarded the PN Shah Oration Dr. Ramesh J. Subsequent session throughout the day took place in 3 halls (MMS Ahuja Hall, N Kochupillai Hall, and AC Ammini Hall till 6.30 pm in the evening.

Day-3: Main conference day-2

The plenary sessions were again the highlights of the day, which included presentations on nutritional rickets (Thacher T), maternal vitamin D supplementation pregnancy and offspring skeletal health (Cooper C), recent advances in the management of acromegaly (Khardori R), and the role of endocrine disrupting chemicals in thyroid disorders (Demeneix B). The Presidential Oration of the ESI was presented by Joshi SR, which was followed by Shah P being awarded the MMS Ahuja Oration. The rest of the day was full of interesting deliberation of different aspects of endocrinology; meet the professor session during the lunchtime and debates. For the first time, an android application (App) based endocrinology quiz was organized (put together by Nagesh S) which was a huge hit among the delegates.

The highlight of the evening was the colors of India, a cultural program put together by the different endocrinologists from across the country. With 29 states and 7 union territories, India is one of the most ethnically and culturally diverse countries in the world. A brainchild of Kalra S, over a period of 5 hours, it was amazing to enjoy the ethnic fashion walk and dances by senior and junior endocrinologist in the traditional attires of their state. The quality of the program highlighted the amount of hard work and effort put in by the participants. The Kuchupudi dance by Ramesh J, the sword-swashing catwalk, with bright lively turbans and kurtas and dances by team Haryana, Rajasthan and Punjab, the "Bajirao Mastani" and "Shivaji" mash-up by team Maharashtra and invoking the patriotic fervor by rendition of the song "Bharat Bhagya Vidhata" (from which our national anthem is derived) by Team Bengal were a few highlights of the show. The success of the event can be gauged from the fact that the hall was full even at midnight.

Day-4: Main conference day-3

The plenary sessions consisted of new insulin delivery recommendations (Hirsch L), assessment of insulin resistance in clinical practice (Matsuda M), managing Graves' Orbitopathy (Wiersinga W), and modern approach to adrenal adenoma (Stratakis C). The Subhash Mukherjee Oration was awarded to Bhadada S for his work on primary hyperparathyroidism. After another exhaustive day of intense deliberations in the 3 different simultaneously running halls, overwhelmed with the amount of knowledge and information shared, the conference finally drew to its conclusion at 5.30 in the Sunday evening.

Epilogue

As the sun set over the smoggy western horizon of the city of Delhi, with trains of cars and cabs trailing out from the venue to the departure terminal of the Delhi airport, I must say, like all good things in life, come to an end too soon! This ESICON did indeed stood out for the quality of the scientific program, the excellent time management of the sessions, and the diversity among both the faculty and the delegates. The baton has now been handed over to Kochi for ESICON 2017, and Bhubaneswar was awarded the responsibility for organizing ESICON 2018.

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FROM THE DESK OF THE ORGANISING SECRETARY, ESICON 2017

The 47th Annual Conference of the Endocrine Society of India, ESICON 2017, is scheduled to be held on October 13, 14 and 15 at Thiruvananthapuram, Kerala, India. The conference is set to deliver a high-quality scientific program covering various endocrine sub-specialties and also poses itself as a platform for knowledge exchange and building new professional relationships. The meeting is held at Kovalam one of the most picturesque beaches in the country and favorite tourist spot. The venue, Uday Samudra Leisure Beach Hotel and the KTDC Samudra is located right beside the beach.

The pre-conference activities include a CME program for physicians and gynecologists, an Endocrine Radiology Workshop and a post graduate training program. The conference has 6 meet the professor sessions, 6 plenary lectures, 3 debates and 12 thematic symposia. In addition we have 6 corporate symposium spread over 2 days. The abstract submission is through the conference website (www.esicon2017.com). As of date, we have confirmed the presence of eminent international faculty like Prof. William F Young Jr (USA), Prof. Shalender Bhasin (USA), Prof. Susan J Mandel (USA), Prof. Helen L. Baron (USA), Prof. John Newell-Price (UK), Prof. Roy Taylor (UK), Prof. Kris Chatterjee (UK), Prof. Thozhukat Sathyapalan (UK), Prof. Ambika P. Ashraf (UK), Prof. Hans de Vries (Netherlands), Prof. Vlado Perkovic (Australia) and Dr. Manju Chandran (Singapore). Spread over 3 days, the conference is sure to interest both the endocrinologist and physician alike. Most of the accommodation is arranged in and around the venue. Thiruvananthapuram is pleasant in October with average temperature around 27 C with light drizzles. It is the start of tourist season at Kovalam. Thiruvananthapuram is well connected to all metros in India, Maldives, Sri Lanka, Middle East and Far East countries. Kerala is well known for its rich traditional hospitality and cuisine. The organizing committee is pleased to welcome you to Thiruvananthapuram to enjoy the rich academic feast, cuisine and hospitality.

Dr. Mathew John,
Organising Secretary, ESICON 2017
Indian Institute of Diabetes
Pulyanarkotta, Trivandrum 695031, Kerala, India

NOTABLE RECENT PUBLICATIONS IN ENDOCRINOLOGY

Mitochondrial Dynamics and Metabolic Regulation

Trends in Endocrinology & Metabolism, 2016 Feb: Vol. 27, No. 2, Page 105-117.

Timothy Wai and Thomas Langer

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Mitochondrial morphology varies tremendously across cell types and tissues, changing rapidly in response to external insults and metabolic cues, such as nutrient status. The many functions of mitochondria have been intimately linked to their morphology, which is shaped by ongoing events of fusion and fission of outer and inner membranes (OM and IM). Unopposed fission causes mitochondrial fragmentation, which is generally associated with metabolic dysfunction and disease. Unopposed fusion results in a hyperfused network and serves to counteract metabolic insults, preserve cellular integrity, and protect against autophagy. Here, we review the ways in which metabolic alterations convey changes in mitochondrial morphology and how disruption of mitochondrial morphology impacts cellular and organismal metabolism.

Trends

Mitochondrial morphology varies widely across different cell types and tissues and results from the opposing and coordinated forces of mitochondrial fission and fusion of OMs and IMs. The regulation of fusion and fission is manifold and responds rapidly to metabolic cues. The fusion and fission machinery is essential for life, and genetic ablation of individual components in adult tissues impairs organ function and whole-body metabolism. Interpreting the relevance of mitochondrial morphology is complicated by the functional redundancy and additional roles that these components have within as well as outside mitochondria.

www.ncbi.nlm.nih.gov/pubmed/26754340

What is new?

- In many ways, mitochondria are mysterious; sausage shaped organelles, convoluted on the inside, they are known as 'power houses' of the cell. Surprising for a structure that merged from the outside into eukaryotic cells evolutionarily two billion years ago, its structure and function took so long to be unravelled. Mitochondria have independent DNA, coding for a small set of genes, which coordinate with nuclear DNA to regulate its function.

- Mitochondrial structure runs true to the axiom of architecture: 'form ever follows function.' Static sausages are seen by electron microscopes. In real life, mitochondria are dynamic, with a name: 'mitochondrial dynamics'
- Mitochondria both fuse and fissure to ensure homeostasis of the cell by influencing cell signaling, metabolism, aging, beside generation of ATP and buffering of calcium. Fission is mediated by dynamin-related protein and fusion by the proteins mitofusin 1,2 and optic atrophy. Changes in their shape - ranging from elongated intercommunicated network to fragmentation, allows quality control.
- Its role in disease pathogenesis is due to alterations in its shape, brought about by disturbances in the fusion and fission of its membranes.
- More excitingly, an understanding of mitochondrial dynamics may pave the way for targeting therapy for an increasing spectrum of diseases that result from mitochondrial dysfunction: unopposed fission leads to fragmentation and metabolic dysfunction; fusion counteracts the metabolic insults.

Comments Courtesy: Prof. G.R. Sridhar, Visakhapatnam

Association Between Long-term Exposure to Air Pollution and Biomarkers Related to Insulin Resistance, Subclinical Inflammation, and Adipokines

Diabetes 2016 Nov; Vol 65, No 11; Page 3314-3326.

Kathrin Wolf, Anita Popp, Alexandra Schneider, Susanne Breitner,
Regina Hampel, Wolfgang Rathmann, Christian Herder, Michael Roden,
Wolfgang Koenig, Christa Meisinger,1 and Annette Peters,

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Insulin resistance (IR) is present long before the onset of type 2 diabetes and results not only from inherited and lifestyle factors but also likely from environmental conditions. We investigated the association between modeled long-term exposure to air pollution at residence and biomarkers related to IR, subclinical inflammation, and adipokines. Data were based on 2,944 participants of the KORA (Cooperative Health Research in the Region Augsburg) F4 study conducted in southern Germany (2006–2008). We analyzed associations between individual air pollution concentration estimated by land use regression and HOMA-IR, glucose, insulin, HbA1c, leptin, and high-sensitivity C-reactive protein levels from fasting samples using multivariable linear regression models. Effect estimates were calculated for the whole study population and subgroups of individuals who did not have diabetes, had prediabetes, or had diabetes. Among all participants, a 7.9 mg/m³ increment in particulate matter of <10 μm was associated with higher HOMA-IR (15.6% [95% CI 4.0; 28.6]) and insulin (14.5% [3.6; 26.5]). Nitrogen dioxide was associated with HOMA-IR, glucose, insulin, and leptin. Effect estimates for individuals with prediabetes were much larger and highly statistically significant, whereas individuals who did not have diabetes or had diabetes showed rather weak associations. No association was seen for HbA1c level. Our results suggested an association between long-term exposure to air pollution and IR in the general population was attributable mainly to individuals with diabetes.

<http://diabetes.diabetesjournals.org/content/early/2016/08/16/db15-1567>

What is new?

- The first study investigating the long-term effects of air pollution and association with biomarkers of insulin resistance and inflammation in the general population.
- A unique study done in the German town of Augsburg to assess the association between residential long-term exposure to air pollutants and biomarkers of insulin resistance, inflammation and adipokines involving a large population.
- Positive association has been demonstrated with various known air pollutants like PM₁₀, PM_{2.5}, PM_{coarse}, NO_x and NO₂ in relation to increased insulin resistance.
- Nitric oxide a common air pollutant is associated with levels of glucose and leptin.

Clinical pearl

Air pollutants is the new entrant in the long list of aetiological factors for insulin resistance and diabetes.

Comments Courtesy: Dr. Kaushik Pandit, Kolkata

Genetic and Clinical Predictive Factors of Sulfonylurea Failure in Patients with Type 2 Diabetes

Diabetes Technology & Therapeutics 2016 ; Vol 18, No 9: Page 586-593.

Qian Ren, MD, Di Xiao, MD, Xueyao Han, MD, Stacey L. Edwards, PhD, Huaiqing Wang, MD, Yong Tang, MD, Simin Zhang, MD, Xi Li, MD, Xiuying Zhang, MD, Xiaoling Cai, MD, Zhaoqian Liu, MD, Sanjoy K. Paul, PhD, and Linong Ji, MD

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Abstract

Background: Sulfonylureas are widely used to treat type 2 diabetes (T2DM). Although genetic variations are associated with sulfonylurea treatment responses in T2DM patients, whether these variations can be used to predict heterogeneous treatment responses is unclear. In this study, we assessed the potential utility of combining information from multiple variants and phenotypes to predict sulfonylurea response.

Methods: Using data from the "Glibenclamide" arm (365 patients) of the Xiaoke Pill Trial that evaluated the safety and efficacy of sulfonylurea, we identified genetic variants associated with sulfonylurea treatment response, and we explored their ability to predict drug response when combined with phenotype information.

Results: The association of 780 single-nucleotide polymorphisms (using Infinium HD iSelect chip) with drug efficacy was evaluated, and four genes identified with drug metabolism (FMO2, FMO3, UGT2B15, and CYP51A1, $P < 0.05$) were found to be associated with changes in HbA1c. In a clinical model, the baseline values of HbA1c and disposition index (DI) were significantly associated with HbA1c and fasting plasma glucose (FPG) target achievements. Compared with clinical models, the inclusion of genetic markers significantly increased the predictive ability for both HbA1c- and FPG-based outcomes.

Conclusions: Our findings suggest that altered protein function in multiple pathways may cooperatively contribute to the increased discrimination by area under receiver operating curve for T2DM patients, and it may explain, in part, the relationship between inter-individual variability and the sulfonylurea response.

<http://online.liebertpub.com/doi/10.1089/dia.2015.0427>

What is new?

- All T2DM patient does not respond equally to SU and even those who responds initially, a substantial number of them loses there glycaemic control over the time.
- A Diabetes Outcome Progression Trial (ADOPT) showed that the incidence of sulfonylurea monotherapy failure (as defined by a fasting plasma glucose > 180 mg/dl) at 5 years was 34% compared with 15% for rosiglitazone and 21% for metformin.
- Various clinical and genetic factors determine the inter-individual variability to SU therapy. Clinical factors include duration of diabetes, higher baseline glucose levels, declining β -cell function and glucose disposition index while genetic factors include single nucleotide polymorphism (SNP) in various genes associated with beta cell function and drug metabolism.
- The polymorphisms in CYP2C9, the drug metabolising enzyme results in variable plasma level and response to SU. The CYP2C9*3 (Ile359Leu) and to a lesser extent CYP2C9*2 (Arg144Cys) influence clearance of tolbutamide, glibenclamide, glipizide and gliclazide. It is reduced in patients carrying a CYP2C9*3 allele, resulting in decreased clearance and increased plasma drug exposure of most of these agents.
- Four genes associated with drug metabolism (FMO2, FMO3, UGT2B15, and CYP51A1, $P < 0.05$) were found to be associated with changes in HbA1c. Compared with clinical models, the inclusion of genetic markers significantly increased the predictive ability for both HbA1c- and FPG-based outcomes and concluded that these genetic variations may explain, in part, the relationship between inter-individual variability and the sulfonylurea response.
- In recent years, the field of sulfonylurea pharmacogenomics has expanded beyond just variation in drug-metabolism genes to polymorphisms in drug target risk genes, which is the focus of many recent studies. Recently, polymorphisms in various drug target genes like ATP-binding cassette, subfamily C, member 8 [ABCC8] and potassium inwardly-rectifying channel, subfamily J, member 11 [KCNJ11]) and diabetes risk genes (e.g., TCF7L2 and insulin receptor substrate [IRS-1]) have been associated with variability in sulfonylurea response in patients with Type 2 diabetes. 5-6 Presently, there are some limitations before we can utilize this SU pharmacogenomics data in routine clinical practice. The various published studies differ considerably in their designs (e.g., prospective vs population-based cohorts), inclusion criteria, choice of sulfonylurea, treatment duration and outcomes of interest and lack of formal definition of SU failure. Also large number of these studies have not excluded patients with maturity-onset diabetes of the young (MODY) as mutation like hepatocyte nuclear factor-1 α have been shown to influence response to sulfonylurea therapy. Also we need studies to elucidate how this genetic information can be used to select therapy and guide SU dosing and particular type of SU.

Comments Courtesy: Dr. Rajesh Rajput, Rohtak, Haryana

PTH(1–34) for the Primary Prevention of Postthyroidectomy Hypocalcemia: The THYPOS Trial

Journal of Clinical Endocrinology and Metabolism 2016 Nov; Vol 101, No 11: Page 4039–4045.

Andrea Palermo, Giuseppe Mangiameli, Gaia Tabacco, Filippo Longo, Claudio Pedone, Silvia Irina Briganti, Daria Maggi, Fabio Vescini, Anda Naciu, Angelo Lauria Pantano, Nicola Napoli, Silvia Angeletti, Paolo Pozzilli, Pierfilippo Crucitti, and Silvia Manfrini

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Context: There are no studies evaluating teriparatide for prevention of post-thyroidectomy hypocalcemia.

Objective: Our objective was to evaluate whether teriparatide can prevent post surgical hypocalcemia and shorten the hospitalization in subjects at high risk of hypocalcemia following thyroid surgery.

Design: This was a prospective phase II randomized open-label trial.

Setting: This trial was set on a surgical ward.

Patients: Twenty-six subjects (six males, 20 females) with intact PTH lower than 10 pg/ml 4 hours after thyroidectomy were included.

Intervention: Subjects were randomized (1:1) to receive SC administration of 20mcg of teriparatide every 12 hours until the discharge (treatment group) or to follow standard clinical care (control group).

Main Outcome Measure: Adjusted serum calcium, duration of hospitalization, and calcium/calcitriol supplementation were measured.

Results: Overall, the incidence of hypocalcemia was 3/13 in treatment group and 11/13 in the control group ($P=.006$). Treated patients had a lower risk of hypocalcemia than controls (relative risk, 0.26 [95% confidence interval, 0.09–0.723]). The median duration of hospitalization was 3 days (interquartile range, 1) in control subjects and 2 days (interquartile range, 0) in treated subjects ($P=.012$). One month after discharge, 10/13 subjects in the treatment group had stopped calcium carbonate supplements, while only 5/13 in the control group had discontinued calcium. The ANOVA for repeated measures showed a significant difference in calcium supplements between groups at 1-month visit ($P=.04$) as well as a significant difference between discharge and 1-month visit in the treatment group (P for interaction time group = .04).

Conclusions: Teriparatide may prevent postsurgical hypocalcemia, shorten the duration of hospitalization, and reduce the need for calcium and vitamin D supplementation after discharge in high risk subjects after thyroid surgery. (J Clin Endocrinol Metab 101: 4039–4045, 2016)

<http://press.endocrine.org/doi/abs/10.1210/jc.2016-2530>

What's known?

- Severe hypocalcemia leads to cardiac arrhythmias and increases the duration of hospitalization.
- The prevalence of post thyroidectomy hypocalcemia varies between 20–40% after thyroidectomy in high risk cases.
- Recombinant parathyroid hormone (PTH) has been used for the treatment of hypoparathyroidism and hypocalcemia.
- Recombinant PTH (1-84) has been approved by the FDA and is not widely available. PTH (1-34) is widely available and has shown similar efficacy.

What's new?

- Palermo et al have conducted a randomized open-label study using PTH for the primary prevention of post surgical hypocalcemia.
- Patients with postoperative PTH value of less than 10pg/ml are at a high risk for the hypocalcemia.
- They have used the recombinant PTH (1-34) in the dose of 20 mcg twice daily.
- The patients were randomized to receive either PTH or standard care therapy.
- The use of PTH reduced the post surgical hypocalcemia, duration of hospitalization and the need for calcium and vitamin D supplements.

Clinical pearl

- High risk patients may be given the PTH therapy if the postoperative PTH level is less than 10 pg/mL.

Comments Courtesy: Dr. K.V.S. Hari Kumar, Panchkula, Haryana

Perilipin 2 and Age-Related Metabolic Diseases: A New Perspective

Trends in Endocrinology & Metabolism, 2016 Dec: Vol. 27, No. 12, Page 893-903.

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Perilipin 2 (Plin2), a protein associated with the metabolism of intracellular lipid droplets (LDs), has long been considered only for its role in lipid storage. However, the manipulation of its expression affects the severity of a variety of metabolic and age-related diseases, such as fatty liver, insulin resistance and type 2 diabetes (T2D), cardiovascular disease, atherosclerosis, sarcopenia, and cancer, suggesting that this protein may play a role in these pathological conditions. In particular, its downregulation in mice prevents or mitigates some of the above mentioned diseases. Conversely, in humans high levels of Plin2 are present in sarcopenia, hepatic steatosis, atherosclerosis, and some types of cancer. We propose that inhibition of Plin2 might be a strategy to counteract several metabolic and age-related diseases.

Trends

Perilipin 2 (Plin2) is linked to lipid deposition in nonadipose tissues and its increased expression is associated with various metabolic diseases (insulin resistance, type 2 diabetes, atherosclerosis, and cardiovascular diseases) in both animals and humans, with the notable exception of endurance athletes.

Downregulation of Plin2 in vivo protects animal models against experimentally induced metabolic diseases, suggesting a broader role for Plin2 beyond lipid storage.

Plin2 expression appears to also be associated with pathological conditions such as sarcopenia and cancer, both age-related diseases.

Experimental data suggest that, at least in [23TD\$DIF] non-alcoholic fatty liver disease, a possible link between Plin2 and liver steatosis could be inflammation. It is possible, but not yet demonstrated, that this link also exists for other pathologies that have been associated with increased Plin2 expression.

<https://www.ncbi.nlm.nih.gov/pubmed/27659144>

What is new?

- Perilipin 2 (Plin2), a novel protein associated with the metabolism of intracellular lipid droplets (LDs), has long been implicated to play an important role in lipid storage.
- Altered expression of Plin2 leading to high levels may affect the severity of various metabolic and age-related conditions such as type 2 diabetes, atherosclerosis, and cardiovascular diseases, hepatic steatosis, sarcopenia, and certain neoplasias, while a lower level seems to mitigate such conditions.
- It has been hypothesized that downregulating Plin2 may be a good strategy to counteract several metabolic and age-related diseases.

Comments Courtesy: Dr. Manash Pratim Baruah, Guwahati

Serum RARRES2 Is a Prognostic Marker in Patients With Adrenocortical Carcinoma

Journal of Clinical Endocrinology and Metabolism 2016 Sep: Vol 101, No 9: Page 3345–3352.

Yi Liu-Chittenden, Dhaval Patel, Kelli Gaskins, Thomas J. Giordano, Guillaume Assie, Jerome Bertherat, and Electron Kebebew

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Context: Retinoic acid receptor responder protein 2 (RARRES2) is a small secreted protein involved in multiple cancers, including adrenocortical carcinoma (ACC). However, discordant tumor and serum RARRES2 levels have been reported in various cancers. The etiology of this discordance is unknown and has not been studied in pair-matched tumor and serum samples.

Objective: To determine tissue and serum RARRES2 levels in patients with adrenocortical neoplasm and to elucidate the prognostic implications of RARRES2 levels. Design, Settings, and Patients: Tissue and serum RARRES2 levels were analyzed. A pair-matched analysis was performed to examine tissue and serum RARRES2 from 51 patients with benign adrenocortical tumors and 18 patients with ACC. Overall survival was analyzed based on RARRES2 expression. A mouse xenograft model was used to determine the source of serum RARRES2.

Results: Patients with ACC had decreased tumor RARRES2 gene expression ($P < .0001$) and increased serum RARRES2 levels ($P < .005$) as compared with patients with benign adrenocortical tumors. Higher serum RARRES2 levels were

associated with improved overall survival ($P=.0227$). A mouse xenograft model demonstrated that higher tissue RARRES2 expression was associated with higher RARRES2 secretion in the serum and that there was an intrinsic mechanism in maintaining serum RARRES2 homeostasis.

Conclusions: Serum and tissue RARRES2 expression levels are paradoxical in patients with ACC. The elevated RARRES2 in patient serum is unlikely to be secreted from tumor cells. Serum RARRES2 may be used as a novel prognostic marker for ACC. (*J Clin Endocrinol Metab* 101: 3345–3352, 2016)

<http://press.endocrine.org/doi/abs/10.1210/jc.2016-1781>

What is new?

- There is a clear gradient of difference between serum RARRES2 level in patients with adrenocortical carcinoma and benign adrenal adenoma or healthy volunteers thereby probably serving as a good marker.
- The study clearly demonstrated that paradoxically the RARRES2 protein is not manufactured in the malignant cell and most likely is a host cell reaction.
- Paradoxically, patients of adrenocortical carcinoma with higher RARRES2 level have better outcome, therefore may indicate a possible prognostic marker function.

Clinical pearl

RARRES2 may be measured in patients with adrenocortical tumor and may serve the useful differentiating factor between benign and malignant types. Moreover, it may be useful as a positive prognostic marker for patients with adrenocortical carcinoma.

Comments Courtesy: Dr. Kaushik Pandit, Kolkata

Diabetic Ketoacidosis Without Diabetes

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Context: Type B insulin resistance syndrome is a rare disease that occurs due to the development of autoantibodies to the insulin receptor and can result in either severe insulin resistance and hyperglycemia or, conversely, hypoglycemia. Diabetes mellitus is often severe, usually transient, and poorly responsive to exogenous insulin. Diabetic ketoacidosis is an unusual consequence of this most severe form of transient diabetes mellitus.

Case Description: A 39-year-old Nigerian woman presented with significant weight loss, severe diabetic ketoacidosis, and severe insulin resistance requiring massive doses of exogenous insulin. She was diagnosed with systemic lupus erythematosus and type B insulin resistance syndrome. She was treated by immunomodulation with rituximab and pulse dose dexamethasone, and she entered euglycemic remission after 4 months of treatment. She remains independent of exogenous insulin 1 year later on maintenance azathioprine therapy.

Conclusion: We report a case of severe type B insulin resistance syndrome complicated by severe diabetic ketoacidosis soon after the initial diagnosis of diabetes, despite large doses of exogenous insulin therapy. Our patient achieved euglycemic remission after combination immunomodulation. This case illustrates the severe catabolic state that may occur with high anti-insulin receptor antibody titers and that combination therapy with rituximab and dexamethasone, followed by maintenance azathioprine therapy for 1 year, is an effective treatment approach for the management of type B insulin resistance syndrome. (*J Clin Endocrinol Metab* 101: 3870–3873, 2016)

<http://press.endocrine.org/doi/10.1210/jc.2016-2146>

What is new?

- Extreme elevation in anti-insulin receptor antibody (AIRA) titers can severely impair insulin signaling to cause of state of functional insulin deficiency (pseudo-insulin deficiency) resulting in manifestation of diabetic ketoacidosis
- Severe Acanthosis, in the setting of cachexia with markedly elevated fasting insulin, hyperadiponectinemia, and low/normal fasting triglyceride concentrations, with blood glucose values ranging from hypoglycemia to hyperglycemia are pointers towards AIRA mediated type-B insulin resistance (TBIR).
- TBIR is most commonly associated with lupus. Can be a paraneoplastic manifestation of myeloma and Hodgkin's disease
- TIBA is associated with 50% mortality at 10 years, even in those achieving remission, either spontaneously or drug induced.
 - Pulse rituximab with pulse high dose glucocorticoids with or without cyclophosphamide followed by maintenance therapy of mycophenolatemofetil or azathioprine is considered to the treatment standard

Comments Courtesy: Dr. Deep Dutta, New Delhi

Factitious Graves' Disease Due to Biotin Immunoassay Interference— A Case and Review of the Literature

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Context: Biotin (vitamin B7) is an essential co-factor for four carboxylases involved in fatty acid metabolism, leucine degradation, and gluconeogenesis. The recommended daily intake (RDI) of biotin is approximately 30 µg per day. Low-moderate dose biotin is a common component of multivitamin preparations, and high-dose biotin (10 000 times RDI) has been reported to improve clinical outcomes and quality of life in patients with progressive multiple sclerosis. Biotin is also a component of immunoassays, and supplementation may cause interference in both thyroid and non-thyroid immunoassays. **Objective:** To assess whether biotin ingestion caused abnormal thyroid function tests (TFTs) in a patient through assay interference. **Design:** We report a patient with biotin-associated abnormal TFTs and a systematic review of the literature.

Setting: A tertiary endocrine service in Hamilton, New Zealand.

Results: The patient had markedly abnormal TFTs that did not match the clinical context. After biotin cessation, TFTs normalized far more rapidly than possible given the half-life of T4, consistent with assay interference by biotin. Multiple other analytes also tested abnormal in the presence of biotin.

Conclusion: Biotin ingested in moderate to high doses can cause immunoassay interference. Depending on the assay format, biotin interference can result in either falsely high or low values. Interference is not limited to thyroid tests and has the potential to affect a wide range of analytes. It is important for clinicians to be aware of this interaction to prevent misdiagnosis and inappropriate treatment. (J Clin Endocrinol Metab 101: 3251–3255, 2016)

<http://press.endocrine.org/doi/abs/10.1210/jc.2016-1971>

What is new?

- A markedly abnormal TFT in the absence of symptoms should arouse the suspicion of biotin-induced alteration of TFT.
- High dose biotin has been found to be effective treatment for multiple sclerosis and is frequently employed.
- Depending on the type of immunoassay (competitive or immunometric), high circulating levels of biotin result in falsely high or low levels of thyroid hormones.

Clinical pearl

Air pollutants is the new entrant in the long list of aetiological factors for insulin resistance and diabetes.

Comments Courtesy: Dr. Kaushik Pandit, Kolkata

Systematic review of treatments for diabetic peripheral neuropathy

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Abstract

Aim To evaluate treatment options for neuropathic pain and sensory symptoms resulting from diabetic peripheral neuropathy of the feet.

Methods The databases Pub Med, Embase and Web-of-Science were searched for randomized controlled trials, published in the period from database inception to 2 July 2015, that evaluated treatments for diabetic peripheral neuropathy of the feet with placebo or standard treatment as comparators. Participants in these trials included people with diabetes mellitus and diabetic peripheral neuropathy who were given any treatment for diabetic peripheral neuropathy. Risk of bias was assessed using the Delphi list of criteria. Data from the trials were extracted using standardized data extraction sheets by two authors independently. All analyses were performed using REVMAN 5.2. In case of clinical homogeneity, statistical pooling was performed using a random effects model.

Results This review included 27 trials on pharmacological, non-pharmacological and alternative treatments. In the meta-analysis of trials of α -lipoic acid versus placebo, total symptom score was reduced by -2.45 (95% CI -4.52; -0.39) with 600 mg i.v. α -lipoic acid (three trials), and was reduced by -1.95 (95% CI -2.89; -1.01) with 600 mg oral α -lipoic acid (two trials). Significant improvements in diabetic peripheral neuropathy symptoms were found with opioids, botulinum toxin A, mexidol, reflexology and Thai foot massage, but not with micronutrients, neurotrophic peptide ORG 2677 and photon stimulation therapy.

Conclusion In this review, we found that α -lipoic acid, opioids, botulinum toxin A, mexidol, reflexology and Thai foot massage had significant beneficial results.

<http://onlinelibrary.wiley.com/doi/10.1111/dme.13083/abstract>

What is new

- Large number of studies was screened for this study using very stringent criteria on bias and randomization.
- Pharmacological, nonpharmacological and alternative treatment regimen were included and compared.
- Meta-analysis of trials involving α -lipoic acid (ALA) at the dosage of 600 mg pre day showed significant beneficial effects.
- Micronutrients, Photon stimulation therapy and neurotropic peptides however were found not to improve the symptoms.

Clinical pearl

ALA turns out to be a new promising agent for the treatment of painful diabetic neuropathy based on the strong pillar of evidence based medicine.

Comments Courtesy: Dr. Kaushik Pandit, Kolkata

Random non-fasting C-peptide: bringing robust assessment of endogenous insulin secretion to the clinic

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Abstract

Background Measuring endogenous insulin secretion using C-peptide can assist diabetes management, but standard stimulation tests are impractical for clinical use. Random non-fasting C-peptide assessment would allow testing when a patient is seen in clinic.

Methods We compared C-peptide at 90 min in the mixed meal tolerance test (sCP) with random non-fasting blood C-peptide (rCP) and random non-fasting urine C-peptide creatinine ratio (rUCPCR) in 41 participants with insulin-treated diabetes [median age 72 (interquartile range 68–78); diabetes duration 21 (14–31) years]. We assessed sensitivity and specificity for previously reported optimal mixed meal test thresholds for severe insulin deficiency (sCP < 200 pmol/l) and Type 1 diabetes/inability to withdraw insulin (< 600 pmol/l), and assessed the impact of concurrent glucose.

Results rCP and sCP levels were similar (median 546 and 487 pmol/l, $P = 0.92$). rCP was highly correlated with sCP, $r = 0.91$, $P < 0.0001$, improving to $r = 0.96$ when excluding samples with concurrent glucose < 8 mmol/l. An rCP cutoff of 200 pmol/l gave 100% sensitivity and 93% specificity for detecting severe insulin deficiency, with area under the receiver operating characteristic curve of 0.99. rCP < 600 pmol/l gave 87% sensitivity and 83% specificity to detect sCP < 600 pmol/l. Specificity improved to 100% when excluding samples with concurrent glucose < 8 mmol/l. rUCPCR (0.52 nmol/mmol) was also well-correlated with sCP, $r = 0.82$, $P < 0.0001$. A rUCPCR cut-off of < 0.2 nmol/mmol gave sensitivity and specificity of 83% and 93% to detect severe insulin deficiency, with area under the receiver operating characteristic curve of 0.98.

Conclusions Random non-fasting C-peptide measures are strongly correlated with mixed meal C-peptide, and have high sensitivity and specificity for identifying clinically relevant thresholds. These tests allow assessment of C-peptide at the point patients are seen for clinical care.

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This article has immense clinical application. As most diabetes centers see patients at all hours of day, and as most laboratory data are valid at any time of the day (a few exceptions are peak serum cortisol and non-fasting serum triglycerides), it is important to validate C-peptide assessment also from the same stand-point.

The authors have looked at non-fasting random C-peptide estimation as well as non-fasting urinary C-peptide/creatinine ratio against the mixed meal stimulated C-peptide which is considered a gold standard and found comparable sensitivity and specificity of the random C-peptide assay. The results were more reliable with the concurrent blood glucose value of > 8 mmol/liter, which is very likely to be present in post-meal random samples.

Comments Courtesy: Dr. Hemraj B. Chandalia