International Conference on

Diabetes and Its Complications

November 2-4, 2017

Venue

The DoubleTree Baltimore-BWI Airport
890 Elkridge Landing Road
Linthicum, MD 21090
USA
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A Unified Pathophysiologic Approach to the Complications of Diabetes in the Context of the B-cell–Classification of Diabetes

Stanley Schwartz
Emeritus Associate Professor CE of Medicine, University of Pennsylvania, PA, USA

Abstract

We have previously presented a proposal for a new, beta-cell centric classification of diabetes based on a consilience of genetic, metabolic, and clinical research that have accrued since the current classification was instituted. It recognizes that the beta-cell is THE core defect in all patients with diabetes. Differences in the genetics, insulin resistance, environment and inflammation/immune characteristics of the damage to the beta-cell in each individual will determine the phenotypic presentation of hyperglycemia and allow for a patient-centric, precision-medicine therapeutic approach, part of which we labeled 'the Egregious Eleven'.

We now recognize the same pathophysiologic mechanisms that account for damage to the beta-cells govern the susceptibility of the cells involved in the complications of diabetes to damage by the now well-defined abnormal metabolic environment that typifies beta-cell dysfunction. This abnormal metabolic environment is typified by oxidative stress which alters metabolic pathways a la Brownlee’s Hypothesis model, alterations in gene expression, epigenetics, and inflammation. This unified pathophysiologic approach to the complications of diabetes in the context of the B-cell–classification of diabetes allows us to understand the varied risk of developing complications of diabetes with similar levels of glycemic control, how non-glycemic effects of some medications for diabetes result in marked complication risk modification and the value treating co-morbidities of diabetes in effecting complication risk.

Principles we outlined in using 'the Egregious Eleven' model—use agents that preserve beta-cell function, treat with least number of agents that treat most number of mechanisms of hyperglycemia—can be extended to use those agents, in combination, that also engender weight loss, and decrease CV outcomes. This approach allows for a more accurate assessment of each patient’s disease and effecting true precision medicine.

Biography

Dr. Stanley Schwartz specializes in the diagnosis and treatment of the cardio-metabolic syndrome, Impaired Glucose Tolerance, diabetes, hypoglycemia disorders, and general endocrinologic problems. Dr. Schwartz predominantly cares for patients with type 1 and type 2 diabetes, and their micro and macrovascular complications and is particularly interested in use of incretins in the care of patients with diabetes. He is also involved in designing the Diabetes Population Care for Health Systems by application of computer technology. Dr. Schwartz has been awarded the honor of being a TOP DOC by Philadelphia Magazine many times over the years, including 2009, 2010 and 2011 for the treatment of diabetes and metabolic syndrome. For over 32 years, Dr. Schwartz was an Associate Professor at the University of Pennsylvania, most recently directing the Diabetes Program at the Philadelphia Heart Institute, becoming Emeritus Associate Professor in 2011.
Vascular Complications in Diabetic Retinopathy

Sayon Roy
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Abstract

Worldwide increase in diabetic population predicts a significant rise in the number of individuals with diabetes-related retinal diseases. An overwhelming cause of vision loss in diabetic individuals is related to excess permeability and the development of macular edema, a prominent clinical manifestation of diabetic retinopathy. Despite the use of laser photocoagulation, and available therapeutics, majority of the patients do not fully recover vision loss. Research into areas involving vascular structural alterations and blood retinal barrier characteristics has uncovered a significant underlying factor that contributes to these changes. Our studies indicate that abnormal thickening of the vascular basement membrane (BM) contributes to excess vascular permeability, breakdown in cell-cell communication, and retinal vascular cell loss. It has long been established that vascular BM thickening is a characteristic hallmark of diabetic microangiopathy, however, it is unclear how vascular BM thickening promotes the characteristic lesions seen in diabetic retinopathy. Recent studies have begun to shed light on this subject suggesting vascular BM thickening as a key player that not only compromises the BRB characteristics but also affects vascular homeostasis and promotes cell loss associated with the development and progression of diabetic retinopathy. Importantly, our research has identified several BM genes, fibronectin, collagen IV, and laminin that are abnormally expressed under hyperglycemic condition and contribute to abnormal cell-cell communication and retinal vascular leakage. The topic of this presentation focuses on understanding how vascular leakage develops in diabetes and a strategy for decreasing BM thickening and subsequently preventing excess permeability in the diabetic retina.

Biography

Dr. Sayon Roy received his Ph.D from Boston University and completed his postdoctoral training at Harvard Medical School, Harvard University. Dr. Roy is currently a professor of Medicine, Section of Diabetes, Endocrinology and Nutrition, and a professor of Ophthalmology at Boston University School of Medicine. Recognized as an expert in retinal vascular biology, Dr. Roy’s seminal work has led to the identification of several genes in the retina that are abnormally expressed in diabetic retinopathy. His pioneering work has led to novel gene modulatory techniques using antisense oligonucleotides and siRNA via intravitreal injection. Dr. Roy has received numerous awards including the American Diabetes Association Research Award for the commitment and dedication towards the fight against diabetes, Mentor of the Year Award from Boston University, and the Innovative Award from the Juvenile Diabetes Research Foundation. Research in Dr. Roy’s laboratory has been funded by several organizations including the National Eye Institute, NIH, National Medical Technology Testbed, American Diabetes Association, Juvenile Diabetes Research Foundation International, Fight for Sight, Research to Prevent Blindness, and the Lions Organization. Dr. Roy currently serves as a member of the NEI Study Section of the National Institutes of Health.
Agonist G-Protein Coupled Receptor Autoantibodies and Diabetic Neurovascular Complications

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Rutgers–Robert Wood Johnson Medical School, NJ, USA

Abstract

Obesity and inflammation are risk factors for certain diabetic neurovascular complications including diabetic depression. Endothelial cell (EC) inhibitory autoantibodies were significantly increased in subsets of older adult type 2 diabetes patient having renal, retinal and neuropathic complications from the Veterans Affairs Diabetes Trial. Strikingly, baseline EC autoantibody activity interacted significantly with baseline albuminuria level in predicting a 60-fold difference in the hazard rate for the occurrence of declining renal function, end-stage-renal disease or death (the composite study endpoint) in 305 participants from the VA NEPHRON D. The EC inhibitory autoantibodies had pleiotropic effects in endothelial cells (apoptosis, RhoA/Rho kinase activation, increased intracellular Ca\(^{2+}\)) and in neurons (suppressed neurite outgrowth, prolonged depolarization) suggesting role(s) in increased vascular permeability and neurotoxicity underlying neurovascular complications.

In the present study we tested for involvement of a specific subclass of heterotrimeric G-protein coupled receptor in mediating RhoA/Rho kinase activation, and increased intracellular Ca\(^{2+}\) evoked by a subset of diabetic neurovascular diseases autoantibodies. We now report that diabetic autoantibody-induced acute neurite retraction in mouse N2a mouse neuroblastoma cells was completely prevented by co-incubation with 200 nM concentrations of M100907, a highly selective antagonist of the 5-hydroxytryptamine (serotonin) 2A receptor. Co-incubation with 200 nM concentrations of the selective 5-HT2A R antagonist M100907 completely protected N2a neuroblastoma cells against diabetic autoantibodies-induced accelerated cell death (n= 4 different diabetic patients). M100907 at (200–2000 nM) concentrations significantly protected endothelial cells from cell death induced by diabetic depression autoantibodies. Specific antagonists of the alpha-1-adrenergic, endothelin A, angiotensin II, type 1 or metabotropic glutamate-5 receptor (1-10 µM) concentrations each had much less or no significant protective effect on autoantibody-induced EC cell death. These data suggest that certain neurotoxic and endothelial cell inhibitory effects in subsets of diabetic neurovascular pathologies are likely mediated via heterotrimeric G-protein coupled, 5-hydroxytryptamine-2A, receptor agonist autoantibodies.

Biography

Dr. Mark B. Zimering is the chief endocrinology at the Veterans affairs New Jersey healthcare system in East Orange, New Jersey. His research interests include: biology of fibroblast growth factors and the role of autoantibodies in diabetic vascular complications. He has long-standing collaborations with Dr. Smita Thakker-Varia and Dr. Janet Alder, outstanding neuroscientists at Rutgers- Robert Wood Johnson medical school as well as study investigators in the veterans affairs diabetes cooperative studies program.
Low-calorie Sweeteners in Weight Management and Diabetes

Allison C. Sylvetsky
Department of Exercise and Nutrition Sciences, The George Washington University, DC, USA

Abstract
With increased public health emphasis on reducing added sugar intake, the use of low-calorie sweeteners, such as aspartame, saccharin, and sucralose, has increased markedly over the past several decades. However, whether and how low-calorie sweeteners influence weight management and diabetes prevention is controversial. Dr. Sylvetsky will review findings from recent studies evaluating effects of low-calorie sweeteners on metabolism, weight, and chronic disease. Biologic mechanisms that may explain these effects will also be discussed. While most cross-sectional and prospective cohort studies report positive associations between low-calorie sweetener consumption, higher body weight, and diabetes onset, recent randomized controlled trials demonstrate that low-calorie sweetener use may support adherence to weight loss regimens, particularly when used as part of intentional weight loss and calorie restriction. However, there is little human data available on other metabolic outcomes (e.g., glycemia). Additional long-term, well-controlled intervention studies in humans are needed to determine the role of low-calorie sweeteners in weight management and chronic disease.

Biography
Dr. Allison C. Sylvetsky is an Assistant Professor in the Department of Exercise and Nutrition Sciences at the George Washington University. She obtained her Ph.D. from Emory University in Nutrition and Health Sciences and then completed a post-doctoral fellowship in the Diabetes, Endocrinology, and Obesity Branch of the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health. She joined the faculty at the George Washington University in 2014. Her primary research interests include studying consumption trends and metabolic effects of low-calorie sweeteners and investigating their potential role in dietary patterns, weight, and metabolic disease.

How to Reset your Body Clock with Nutrition

Hana Kahleova
Physicians Committee for Responsible Medicine, DC, USA

Abstract
Accumulating evidence suggests that circadian de-synchrony may be an important contributing factor in the development of chronic disease, including obesity, type 2 diabetes, cardiovascular disease and cancer. While our central body clock in the hypothalamus is entrained by the light and dark cycle, the peripheral body clock found in each cell of our body needs to be synchronized with the central clock, mainly through nutritional stimuli. More specifically, this can be achieved through the fasting and feeding cycle, with a plant-based nutrition, and through proper meal frequency and timing. As the insulin action is the most effective in the morning, eating breakfast enables us to use the energy from the meal more efficiently than from the same meal eaten later in the day. While snacks seem to disrupt our body clock, eating 2-3 meals a day, with breakfast being the largest meal, and dinner being the lightest meal of the day, is a great way how to synchronize our body clock. This brings us back to the ancient proverb: Eat breakfast like a king, lunch like a prince, and dinner like a pauper.

Biography
Dr. Hana Kahleova is director of clinical research for the Physicians Committee for Responsible Medicine. She has conducted several clinical trials, using a plant-based diet in the treatment of obesity, diabetes and metabolic disease. She completed her postdoctoral research fellowship at Loma Linda University in California, analyzing data from more than 50,000 people, who were followed up for more than 7 years, on meal frequency and timing in relationship to body weight regulation. The study showed that eating less frequently, no snacking, consuming breakfast, and eating the largest meal in the morning may be effective methods for preventing long-term weight gain.
Is Vitamin D Deficiency an Indicator of Insulin Resistance and Dysfunctional Adipose Tissue in Obesity?

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Abstract

In recent years, there has been an increased interest in the other roles of vitamin D, in addition to those on the skeletal system and calcium homeostasis. Studies have suggested that vitamin D deficiency is associated with insulin resistance, type 2 diabetes and cardiovascular diseases. Adipocytokines derived from adipose tissue are involved in the pathogenesis of the cardiometabolic disturbances of obesity, and their activity is especially expressed in visceral fat depots. Additionally, in obese patients, there is a suggestion that insulin resistance improves after vitamin D supplementation.

Our study was carried out in a group of 50 obese patients (BMI: 43.5 + 9.2 kg/m²) and 36 normal weight participants (BMI: 22.6 + 1.9 kg/m²). We excluded patients with recent weight changes and those who had been treated with vitamin D within 3 months prior. There was a negative correlation between vitamin D level and anthropometric indicators of obesity: BMI (r = −0.64; P < .001), waist circumference (WC) (r = −0.59; P < .001), and body fat percentage (r = −0.64; P < .001) as well as with fasting plasma insulin (r = −0.35; P < .001) and homeostasis model assessment of insulin resistance (r = −0.35; P < .001). There was a negative correlation between vitamin D level and leptin and resistin (r = 0.61, P < .01), while a positive association with adiponectin concentrations was found (r = 0.7, P < .001). Trend estimation showed that increase in vitamin D level is accompanied by intensive increase in adiponectin concentration.

Finally, vitamin D deficiency can be an indicator of insulin resistance and dysfunctional adipose tissue in obesity. In the view of present findings, we suggest that vitamin D supplementation may have a beneficial effect on insulin resistance via modulation of adipocytokine secretions. Since the dysfunctional adipose tissue is a trigger for insulin resistance and cardiometabolic disturbances in obese patients, interventional trials are required to establish whether vitamin D supplementation could be a therapeutic option for improving adipose tissue function and insulin resistance.

Biography

Prof. Edita Stokic M.D. Ph.D, endocrinologist, Head of Department of Metabolic diseases, at Clinic for Endocrinology, Diabetes and Metabolic Diseases. She is a vice president of Serbian association for the Study of Obesity. Her professional education was conducted in several European centers for endocrinology. In 2004 she was granted National Fellowship for vocational training from The Specialist Certification of Obesity Professional Education (SCOPE) under the International and European Associations for the Study of Obesity project. She is also member of Editorial board for Serbian Archive of Medicine, Medical Review, as well as SM Journal of Food and Nutritional Disorders and Journal of Obesity and Chronic Diseases. She is author and co-author of 439 published scientific articles.

Impaired Capacity for Weight Loss in Type 2 Diabetes

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4Ottawa Hospital Weight Management Clinic, ON, Canada

Abstract

Aims/Hypothesis: Type 2 diabetes (T2D) and obesity are intricately linked epidemics. In both, weight loss is considered part of the first line of treatment. The goal of this study was to evaluate the effect of T2D on weight loss in response to dietary intervention and lifestyle modification.

Methods: Patients were enrolled in a weight loss program and individuals with T2D were compared to those with impaired fasting glucose (IFG) and those with normoglycemia. Rate of weight loss (ROWL) was calculated using the slope of the weights measured during the first 6 weeks of weight loss and percentage of weight loss (PWL) was analyzed at 26 weeks.

Results: 4173 patients entered the program and 2231 remained after exclusions for conditions that affect weight loss. There were significant differences in age, weight, BMI, and HbA1C between patients without T2D, those with IFG and...
those with T2D (p < 0.01 for all). At 26 weeks, adjusted PWL was lower in the group of patients with T2D (0.118 +/- 0.33) when compared to patients without T2D (0.205 +/- 0.31) and patients with impaired fasting glucose (0.195 +/- 0.31, p<0.05). Medications used by patients with T2D did not affect the adjusted ROWL at 6 or PWL at 26 weeks.

**Conclusions:** Patients with T2D have impaired weight loss at 26 weeks when undergoing a defined meal replacement and lifestyle modification program. While the magnitude of this effect is small in comparison to the contribution of sex, and initial weight, this is an important consideration in the treatment of obesity and T2D.

**Biography**

Dr. Ghadi Antoun completed his B.Sc. with Honors in Biomedical Sciences with a Minor in Business Administration at the University of Ottawa and subsequently joined the inaugural class of the MD/Ph.D program at the same university. His doctoral research interests were centered on obesity and diabetes and more specifically on molecular mechanisms involved in disease development and progression. He was the recipient of numerous awards including the prestigious Vanier Canada Graduate Scholarship offered by the Canadian Institutes of Health Research. Having completed both his MD and Ph.D, Dr. Antoun is now pursuing surgical residency training at the University of Montreal.

**Regulatory Role of Exercise-Induced Myokine in Metabolic Diseases**

Ning Chen

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**Abstract**

As we well known Exercise is Medicine. Indeed, exercise is an effective, green and environmentally-friendly intervention strategy for metabolic diseases such as obesity and diabetes. Irisin, as a newly discovered myokine with 112 amino acid residues after exercise training, is firstly up-regulated by exercise or corresponding drug-induced PGC-1α and plays an important regulatory role in a series of metabolic diseases through targeting different tissues or organs, especially for its functions of switching white fat cells to brown fat cells, thus resulting in the prevention and recovery of obesity through exercise intervention. In addition, exercise or drug-induced irisin also can regulate UCP1 generation, improve insulin sensitivity and enhancing β-cell regeneration, which can function as the modulator for the prevention and treatments of a series of metabolic diseases including diabetes and obesity. Moreover, exercise-induced irisin can improve cognition capacity during neuro-degradative diseases. These investigations will provide a clear target for the prevention and treatment of metabolic diseases. Furthermore, this exploration will provide a new strategy for developing a novel and effective candidate drug or supplementary dietary as well as mimic exercise pills for the prevention and treatment of metabolic diseases.

**Treatment of Diabetes and Obesity with Engineered Skin Stem Cells**

Xiaoyang Wu*, Jiping Yue, Xuewen Gou and Barton Wicksteed

The University of Chicago, IL, USA

**Abstract**

Somatic gene therapy with epidermal stem cells of skin can serve as a promising therapeutic approach for both inherited and acquired disorders, owing to several unique features of skin: (1) easy procedure for collection of epidermal stem cells from rodent models and human patients; (2) epidermal stem cells can be cultured long term in vitro, allowing efficient genetic modifications without viral vectors; and (3) the technique to graft human keratinocytes to the patients has been well established. However, engraftment of cultured mouse keratinocytes to immunocompetent host has been technically challenging, hampering our ability to efficiently examine skin stem cell-based therapy with rodent models in a preclinical setting.

In this study, we devised a new platform for mouse skin keratinocyte manipulation and grafting by combining genome editing technology using CRISPR_Cas9 system with skin 3D-organotypic culture and engraftment of cultured skin substitute to immunocompetent host animals. Our model creates a novel system to effectively assess the outcome of skin-based gene therapy in mouse models. As a proof-of-principal study, our results demonstrate that engineered skin stem cells can be used to secrete therapeutic hormones, such as glucagon-like peptide 1 (GLP-1) in an inducible manner, and engraftment of the cells to mice can significantly attenuate glycemic excursions in diet-induced obese and diabetic mice. Together, our study revealed great therapeutic potential for somatic gene therapy using skin epidermal stem cells.
Biography
Dr. Xiaoyang Wu is an Assistant Professor at Ben May Department for Cancer Research, University of Chicago. Wu was the first author for a number of publications, including “Focal Adhesion Kinase Regulation of N-WASP Subcellular Localization and Function” and “ACF7 Regulates Cytoskeletal–Focal Adhesion Dynamics and Cell Migration and Has ATPase Activity.” Most recently, he received the Cancer Research Foundation Young Investigator Award and an American Cancer Society Institutional Research Grant.

Intriguing Relationship between Low Density Lipoprotein Cholesterol and Type 2 Diabetes
Huichun Xu

University of Maryland School of Medicine, MD, USA

Abstract
The recent observation that treatment of hypercholesterolemia with statins to reduce LDL-C (low density lipoprotein cholesterol) levels leads to increased risk of type 2 diabetes (T2D) has sparked a heated investigation of the relation between LDL-C lowering and the risk of T2D. Recent studies have tested the association of LDL-lowering alleles and diabetes to evaluate the causal relationship of LDL-lowering on diabetes risk. For example, LDL-C-lowering variants in the molecular target of statins, \textit{HMGCR} (HMG-CoA reductase) have been associated with increased risk of T2D, suggesting that the increased T2D risk observed in stain users is due to on target rather than off target effects of statins. In this presentation, we summarize the current evidence supporting or against the causal relation between LDL-C perturbing and T2D risk, including data from our own large Amish population enriched for a LDL-C-increasing \textit{APOB} R3527Q variant.

Biography
Dr. Huichun Xu is a genetic epidemiologist with a focus on common human complex diseases, particularly cardio- and cerebro-vascular diseases and their risk factors, using both genomics and functional genomics technologies. Currently, Dr. Xu actively involves in genetic study of ischemic stroke under International Stroke Genetics Consortium, and genetic study of metabolic diseases in the Old Order Amish population. Besides DNA level genetic study, Dr. Xu has been heavily involved in methylomics and transcriptomics study of the etiology of metabolic diseases and post-stroke motor function recovery.

Psychological Outcomes and Related Correlations among Family Members of Persons with Diabetes in the Second Diabetes Attitudes, Wishes and Needs (DAWN2) Study

Katharina Kovacs Burns\textsuperscript{1}, Richard Holt\textsuperscript{2}, Antonio Nicolucci\textsuperscript{3}, Giuseppe Lucisano\textsuperscript{3}, Soren Skovlund\textsuperscript{4}, Marco Comaschi\textsuperscript{5}, Michael Vallis\textsuperscript{6} and Mark Peyrot\textsuperscript{7}

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\textsuperscript{3}Center for Outcomes Research and Clinical Epidemiology, Italy
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\textsuperscript{6}Dalhousie University, Canada
\textsuperscript{7}Loyola University Maryland, MD, USA

Abstract
The second Diabetes Attitudes, Wishes and Needs (DAWN2\textsuperscript{TM}) study explored the perceptions and experiences of family members (FMs) caring for adult persons with diabetes (PWD), in relation to psychosocial indicators. The study examined these findings for specific correlates of psychological outcomes among family members (generic psychological well-being and perceived quality of life; and diabetes-related burden, impact and distress), and particularly potential risk factors for poor outcomes. 2057 FMs (about 120 FMs recruited in each of 17 participating countries) living with and involved in the care of PWD, participated in online, telephone or in-person surveys exploring various psychosocial indicators. Multi-level multiple regression analysis identified significant ($P < 0.05$) correlates of psychological outcomes. For FMs not
working due to diabetes or who had other competing obligations, outcomes were worse. They were also worse if PWD were not partners or parents, used injected diabetes medication, had more severe diabetes or had more frequent hypoglycaemia. Outcomes were worse for FMs who had conflicts or were frustrated with PWD regarding their diabetes care or helping them, but were more involved in the PWD care. Outcomes were better for those who received diabetes education, had greater support from others, and found ways to help the PWD. There were significant differences in psychological outcomes and their correlations among countries before and after adjustment for individual characteristics. Several modifiable risk and protective factors for psychological outcomes were also identified. The outcomes for FMs improved with diabetes education and social support, especially if they were helpful in supporting the PWD.

Biography

Dr. Katharina Kovacs Burns, MSc, MHSA, Ph.D, is with the University of Alberta (School of Public Health) and Alberta Health Services (Quality Healthcare and Improvement). She is interested in conducting applied participatory health and social research with interdisciplinary and cross-sector community and patient groups, government, health system, industry and others. Her interests are specific to Patient and Family-Centred Care including patient/family, public and stakeholder engagement and measuring their experiences as part of health system and program decision-making processes. This includes determining patient and family psychosocial burdens and costs associated with self-care, healthcare services access and utilization, and related policies.

Managing Diabetes in Pregnancy Using Cell Phone/Internet Technology

Marguerite Lisa Bartholomew1*, Ivica Zalud1, Janet Burlingame1, Karen Soules2, Kacy Church3, Steve Shaha4, George Graham5 and Lynnae Sauvage6

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3Oregon Health and Science University, OR, USA
4Tufts University School of Medicine, Department of Obstetrics and Gynecology, MA, USA
5First Physician’s Group, FL, USA

Abstract

Objective: To compare compliance and satisfaction between a traditional method of home blood glucose reporting using voicemail (control) and a novel method using cell phone- internet technology (CIT) for the management of pregnant women with diabetes.

Study Design: In a prospective randomized crossover study, 100 women with gestational diabetes or type 2 diabetes were recruited. Women were randomized to the control system or the CIT system to report home blood glucose results for the first three weeks. They switched to the alternate system for the second three weeks. Compliance was determined by the number of blood glucose results reported / expected number of blood glucose results (%). Satisfaction surveys were completed after the six week comparison period.

Results: 74 women completed the study. Overall compliance was 89.3% using CIT and 87.6% using control (p<0.001). The highest compliance was noted for CIT when CIT was used first 91.7% (p=0.049). CIT was superior to control in all areas of satisfaction surveyed.

Conclusion: CIT improved blood glucose reporting compliance over telephone and voicemail (control) reporting. Satisfaction with CIT was superior to control.

Biography

Dr. Marguerite Lisa Bartholomew is an obstetrician-gynecologist in Honolulu, Hawaii. She received her medical degree from University of Miami Miller School of Medicine and has been in practice for more than 20 years. She has received Honolulu Magazine Best Doctors, Hawai’i for four consecutive years between 2011 and 2014.
Multidisciplinary Team Care of Patients with Diabetes in an Outpatient VA Setting

Izabela A. Collier and Alice Abbott

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2Western New England University, College of Pharmacy, MA, USA

Abstract

A multidisciplinary diabetes management team composed of an endocrinologist, a registered nurse, registered dietitians, pharmacists, and a psychologist manage patients with diabetes at VACWM. More complex patients are managed initially in pharmacy or in endocrinology clinic. Patients with better-controlled diabetes are seen by nutrition and diabetes education. The clinical psychologist may work with patients on behavioral modifications. The team has full access to several resources at the VACWM such as home-telehealth. Part of organizing a team was development of the diabetes committee consisting of diabetes team members, a primary care provider, Health Promotion and Disease Prevention Coordinator, the Women's Health Director, other disciplines, and patient representative. The team developed a multidisciplinary diabetes self-management group curriculum for patients with poorly controlled diabetes and overweight/obesity, helping the team to achieve high level of cohesiveness and consistent messaging. Multiple benefits were noted to multidisciplinary team care. Team referral may lead to the most appropriate referral for diabetes care. This may avoid under-referral or multiple referrals leading to patients feeling overwhelmed. Team care facilitated standardization of care and quality improvement. Students receive training in inter-professional collaboration. We noted a high level of cohesiveness among team members, and consistent messaging to patients. Salary costs and time devoted by team members to collaboration were significant. Coordination of schedules was often difficult. The diabetes team is a “working group” which developed initiatives through focused effort. Our experience is available to anyone within the VA nationally.

Biography

Dr. Alice Abbott is an Endocrinologist practicing at the VA of Central Western Massachusetts. She has graduated from internal medicine from St. Luke’s Medical Center in Chicago and completed her fellowship from Joslin Diabetes Center in Boston. She is board certified nationally by both American Board of Internal Medicine and Endocrinology.

Dr. Izabela A. Collier is a Clinical Pharmacist and a Certified Diabetes Educator. She received her B.S. degree in Pharmacy and Ph.D. from the Massachusetts College of Pharmacy and Health Sciences. She is affiliated with Western New England University as an Associate Professor at the College of Pharmacy.

The Phantom of Metformin-Induced Lactic Acidosis in End-stage Renal Disease Patients: Time to Reconsider with Peritoneal Dialysis Treatment

Mohamed Ahmed Nasreldeen, Abdullah K. Al-Hwiesh, Abdul-Salam Noor, Mohammed A. Nasr-El-Deen and Ibrahimi Saeed Abdul-Rahman

1Department of Internal Medicine, Nephrology Division, King Fahd Hospital of the University, University of Dammam, Saudi Arabia
2Department of Electrical Engineering, Queens University, ON, Canada

Abstract

Metformin continues to be the safest and most widely used antidiabetic drug. In spite of its well-known benefits; metformin use in end-stage renal disease (ESRD) patients is still restricted. Little is reported about the effect of peritoneal dialysis (PD) on metformin clearance and the phantom of lactic acidosis deprives ESRD patients from metformin therapeutic advantages. PD is probably a safe guard against lactic acidosis and it is likely that the use of this drug would be feasible in this group of patients.

Material and Methods: The study was conducted on 83 PD patients with type-2 diabetes mellitus. All patients were on automated peritoneal dialysis (APD). Metformin was administered in a dose of 500 mg-1000 mg daily. Patients were monitored for glycemic control. Plasma lactic acid and plasma metformin levels were monitored on a scheduled basis. Peritoneal fluid metformin levels were measured. In addition, the relation between plasma metformin and plasma lactate was studied.

Results: Mean fasting blood sugar (FBS) was 10.9 ± 0.5 and 7.8 ± 0.7, and the mean HgA1C was 8.2 ± 0.8 and 6.4 ± 1.1 at beginning and end of the study, respectively (p < 0.001). The mean body mass index (BMI) was 29.1 ± 4.1 and 27.3 ± 4.5 at the beginning and at the end of the study respectively (p < 0.001). The overall mean plasma lactate level across all
blood samples was 1.44 ± 0.6 and plasma samples > 2 mmol/L but < 3 mmol/L was found in 11.8% and levels of 3-3.6 mmol/L in 2.4% plasma samples. Hyperlactemia (level > 2 & ≤ 5 mmol/L) was not associated with overt acedemia. None of our patients had lactic acidosis (levels > 5 mmol/L). Age ≥ 60 was a predictor for hyperlactemia. No relationship between plasma metformin and lactate levels.

**Conclusion:** Metformin may be used with caution in a particular group of ESRD who are on APD. Metformin allows better diabetic control with significant reduction of BMI. The relationship between metformin and plasma lactate levels is lacking. Peritoneal dialysis appears to be a safeguard against the development of lactic acidosis in this group of patients.

**Biography**

Mohamed Ahmed Nasreldin has been working in the nephrology service at King Fahad teaching hospital in Dammam, Saudi Arabia since 2010, taking care of CKD patients and ESRD patients on hemodialysis and peritoneal dialysis, critical patients in the ICU with acute kidney injury who require either CRRT (contineous renal replacement therapy) or acute PD (peritoneal dialysis) and also taking care of nephrology outpatient clinic, post-transplant patients and teach 4th year medical students, internal medicine residents rotating in nephrology and junior nephrology fellows. Currently he is a Ph.D candidate in clinical nephrology.

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**Modified Social Learning Theory Re-examined: Correlates of Self-management Behaviors of Persons with Type 2 Diabetes**

**Linda Elizabeth Nugent**1 and **Kenneth A. Wallston**2

1* RCSI School of Nursing & Midwifery, Royal College of Surgeons in Ireland, Ireland
2 School of Nursing, Vanderbilt University, TN, USA

**Abstract**

Modified social learning theory (MSLT) applied to health predicts that health behavior is a multiplicative function of health value and perceptions of control over health. The self-management behaviors of persons with Type 2 diabetes mellitus, internal diabetes locus of control (IDLC), diabetes self-efficacy (DSE), and health value (HV) were assessed with an index of diabetes self-care activities in 107 patients receiving insulin. Multiple regression analysis showed DSE as the only MSLT construct that correlated with the index of diabetes self-care behaviors (b = .21, p < .05). While the predicted three-way interaction of IDLC x DSE x HV was significant (DR2 = 4.5 %, p < .05) in the final step of the hierarchical model, the pattern of the findings only partially supported MSLT. Instead of finding that patients who were simultaneously high on all three predictors scored highest on the behavioral index, we found that patients who were low on all three constructs reported the least amount of diabetes self-care behavior. Implications for further modification of MSLT and its applications to clinical practice are discussed.

**Biography**

Dr. Linda Nugent, Ph.D, M.Sc., RGN, B.Sc. is Lecturer and Programme Director at the Royal College of Surgeons in Ireland (RCSI), School of Nursing & Midwifery. She lectures in Advanced Research Methods, Leadership, Change Management and Advanced Strategy Management. She is supervisor to MSc and Ph.D students. She obtained her Ph.D from the University of Edinburgh and then took up post of Research Fellow in RCSI where she developed and implemented (REACH) a research capacity building programme for CNSs and ANPs. Her doctoral research examined the interaction of the constructs of perceived control and health value in relation to Type 2 Diabetes self-management behaviors. This research contributes to knowledge on how diabetes-specific control beliefs explain diabetes self-management behaviors.
The Level of Comorbidity and Compensation of Diabetes Mellitus

Irina Kurnikova
RUDN–university, Russia

Abstract

Statement of the Problem: The “complexity category” of patient management increases many times, if the somatic disease had combined with multi-organ systemic disease, such as diabetes mellitus (type 1 diabetes - DT1 and type 2 diabetes - DT2). Simultaneous formation of several diseases in a patient: arterial hypertension, atherosclerosis, ischemic heart disease and diabetes mellitus, creates not only significant difficulties in diagnosis, but affects the quality of care and worsens the prognosis. The purpose of this study is to study the influence of somatic pathology on the level of glycemic control indices of patients with diabetes mellitus from the viewpoint of cause–effect relationships and mechanisms of polymorphic formation. Methodology & Theoretical Orientation: A special complex examination of patients was conducted. The control of carbohydrate metabolism was provided in accordance with the recommendations of WHO by repeatedly examining the glycemic profile and glycated hemoglobin (HbA1c). The comorbidity was assessed according to the CIRS - Cumulative Illness Rating Scale.

Findings: In our study, the risk of developing concomitant cardiovascular disease had a positive association with DT2 (RR = 3.4, p < 0.001), and the chances of developing a cardiovascular pathology in DT2 were significantly higher (OR = 15.7; X² = 151.6). The multiplicity of complications was significant in patients with DT1 (RR = 1.96, p = 0.095) and 3 times increased the risk of cardiovascular disease (OR = 3.47, p = 0.008), but for DT2 this criterion had a weak negative association for RR (RR = 0.86, p < 0.001) and influenced the increase in odds (OR = 0.39; p = 0.03). The duration of the course of DT1 for more than 10 years contributed to an increase in the relative risk and odds ratio (RR = 3.43, p < 0.001, OR = 8.29, CI 95% 4.36–15.76) for pathology formation. Almost 3 times increased risk of cardiovascular disease in of patients.

Conclusion & Significance: Somatogenic pathomorphological disturbances have a fundamental effect on the course of diabetes, which patients with DT2 with a BMI more than 30 (RR = 2.95, p = 0.063). The risk of cardiovascular disease in case of unsatisfactory compensation of CD1 (RR = 1.16, p = 0.021, OR = 1.27), DT2 (RR = 1.39, p < 0.001, OR = 2.28). However, to assert that the risk of developing concomitant cardiovascular pathology increases the fluctuations in the level of glycemia in patients with diabetes (OR DT1 = 2.19, CI 95% 0.46–10.45, ORSD2 = 5.93 CI 95% 0.75–46, 91) with the obtained CI level of 95% is not possible. The significance of lipid metabolism disorders (atherogenicity index) in the development and progression of coronary pathology in diabetic patients was confirmed, and this factor was much more significant in patients with DT1 (OR DT1 = 11.4; OR DT2 = 30.9). Compensation of diabetes by glycemic values depended on the duration of the disease of DT 2 (r = 0.42, p < 0.05), the severity of comorbidity, and corresponded to the degree of comorbidity (r = 0.67, p < 0.05) in Cumulative Illness Rating Scale (CIRS). For basal glycemia, at the beginning and after treatment, the correlation coefficient (r) is 0.56 and 0.67, respectively. For postprandial glycemia - 0.45 and 0.35, respectively (p < 0.05). The relationship between the values of basal glycemia and the indicators of comorbidity after the completion of the course of treatment is strengthened, and postprandial - decreases. Rates of basal glycemia reached normal values only in patients with low CIRS. At high values of CIRS (14 or more points), it was not possible to normalize the parameters of carbohydrate metabolism in the majority in take is a risk factor for the development and progression of somatic pathology.

Biography

Dr. Irina Kurnikova MD, Ph.D, now is a Professor of Medicine of RUDN University (Peoples Friendship University of Russia), Moscow, Russia. Dealing with Problems of Endocrinology for over 20 years. She had led a course of Endocrinology at the Medical Academy (Izhevsk, Russia), was the Head of Endocrinology department at the Russian Scientific Center of Medical Rehabilitation and Health Resort (Moscow, Russia). Currently she teaches at Peoples’ Friendship University of Russia, curator of the Scientific Direction Endocrinology. She has published more than 30 articles in well-known journals, the author of 25 books and tutorials in Russian language. Author of 9 patents for inventions. She has extensive experience in the field of scientific and practical endocrinology. The main areas of research are the optimization of the system approach to the treatment and rehabilitation of patients with diabetes mellitus, diseases of the thyroid gland. The main directions of scientific research are the influence of disturbances in the system of regulation of the organism and other endogenous factors (comorbidity, disruption of the mechanisms of interstitial humoral transport) on the effectiveness of treatment and the quality of compensation for diabetes and other endocrine diseases.
Aerobic Exercises Like Cycling is Associated with Significant Improvement in Glycemic Control in Patients with T2 DM

AK Jhingan* and RM Jhingan

Delhi Diabetes Research Center, India

Abstract

Aim: To assess effect of cycling on HbA1c, blood pressure (BP) and weight over six months in young individuals with T2DM.

Methods: In this retrospective, observational study, young (18 to <40 years) T2DM patients on upto two Oral DM agents were identified from a cycling group in Delhi. These individuals were involved in a regular exercise program (cycling 25 km/day for at least five days/week). Participants with consecutive six months of cycling were selected. From their medical records-weight, BP, and HbA1c levels were noted at baseline and at six months of cycling program.

Results: From 26 cases identified with T2DM, 20 were included in analysis. Mean age was 35.6 ± 2.6 years, five were <35 years and all of them were males. Cycling resulted in significant reduction in HbA1c (mean change from baseline at six-month: -1.18, 95% Confidence Interval (CI) 1.12, 1.24; p < 0.001). Besides, SBP (-5.2, 95% CI -3.7, -6.6; p < 0.001) and DBP (-3.1, 95% CI -1.7, -4.5; p < 0.001) and weight (kg) (-5.0, 95% CI -4.41, -5.58; p < 0.001) showed significant reduction. Among two age groups (Age < 35 and ≥ 35 years), except for reduction of diastolic BP in age < 35 years, significant reduction in all other parameters was evident in both age groups.

Conclusion: Regular aerobic exercise like cycling results in significant reduction in HbA1c, BP and weight. It should be promoted as a preferred exercise in T2DM to achieve weight loss and glycemic improvement.

Biography

Dr. AK Jhingan is president of Delhi diabetes research center which he set up in 1982 in Delhi, India with the aim of spreading awareness about diabetes and providing medical management as well as financial and social support to patient suffering from type 1 and type 2 diabetes. He completed MBBS from G B Pant Hospital / Moulana Azad Medical College, New Delhi in 1974, FICA from All India Institute of Medical Sciences, New Delhi in 1975 and MD - General Medicine from All India Institute of Medical Sciences, New Delhi in 1997.
Prediction of 10-Year Vascular Risk in Patients with Diabetes: The AD-ON Risk Score

Mark Woodward
The George Institute for Global Health, University of Oxford, UK

Abstract

Cardiovascular risk scores in diabetes are common; renal risk scores less so. Rarely has a combined risk score been formulated, yet this should be more useful to physicians than applying two scores requiring similar risk factor evaluations and, often, similar treatments.

Data were derived from the ADVANCE-ON study amongst 11,140 high-risk diabetic patients. The outcome event was combined macrovascular or renal disease. A Cox regression model was used to determine weightings in the risk score. The resultant score was recalibrated to each of three major global regions, as covered by the ADVANCE-ON study, Asia, Eastern Europe and Emerging Market Economies (including Australia and the UK). Over a median of 9.9 years, 1145 patients experienced the combined outcome event. The resultant, AD-ON risk score, incorporated 13 demographic or clinical variables. Its discrimination was modest (c-statistic=0.668; 95% confidence interval (0.651, 0.685)) but its calibration was excellent (predicted and observed risks coincided well, within the disparate global regions). In terms of the integrated discrimination improvement, its performance was superior to existing risk scores in clinical use, from a restricted version of the same data, for macrovascular and renal disease separately, over a 10-year risk horizon.

The AD-ON risk score has advantages over existing vascular risk scores in diabetes which treat macrovascular and renal diseases separately, including its simplicity of use and global application.

Biography

Dr. Mark Woodward is Professor of Statistics and Epidemiology at the University of Oxford, Professor of Biostatistics at the University of Sydney and Adjunct Professor of Epidemiology at Johns Hopkins University. At Sydney and Oxford, he works for the George Institute for Global Health. He has published two text-books on medical statistics and well over 500 peer-reviewed research papers. In each of the last two years, Professor Woodward was named by Thomson Reuters as one of ‘The World’s Most Influential Scientific Minds’. He has a Ph.D in Applied Statistics and MSc in Operational Research from the University of Reading.
Inpatient Diabetes Management: An Update

Robert J. Tanenberg
East Carolina University and Vidant Medical Center Greenville, NC, USA

Abstract

More than 9% of U.S. residents, have diagnosed or undiagnosed diabetes. A disproportionate number of hospitalized patients experience hyperglycemia. Substantial risk is associated with inpatient hyper- and hypoglycemia due to diabetes. This has led to ongoing efforts to maintain glucose control in hospitalized patients.

Three typical hyperglycemic patterns exist in hospitalized patients: known, previously diagnosed diabetes; undiagnosed diabetes identified during hospitalization; and hospital-related hyperglycemia (“stress hyperglycemia”). Hyperglycemia is an independent predictor of morbidity and mortality in the hospital setting. In one study, patients with hyperglycemia (on admission or in-hospital diagnosis) were 29% more likely to be admitted to the intensive care unit (ICU), and experienced 16% mortality rates.

Glucose management using protocol-driven insulin administration leads to improved outcomes. Oral hypoglycemic agents should be discontinued. The consensus inpatient glucose target is 140–180 mg/dl. In the ICU setting, IV insulin infusion is preferred. Until recently, hospitals have been limited to paper-based insulin protocol management. In the last decade, however, computerized approaches have become available. These systems can be integrated into electronic health records, eliminating the need for paper protocols and resulting in reduced rates of hyper/ hypoglycemia and reduced length of stay.

Hypoglycemia is a major problem in the hospital setting. The most common cause of hypoglycemia is excessive insulin – typically use of the home dose. Other causes are concomitant renal disease, reduced oral intake, tapering of steroids and insulin–food mismatches because of logistical issues. A multidisciplinary approach including collaboration of nurses, pharmacists and physicians emphasizing weight/GFR based dosing reduces hypoglycemia.

Biography

Dr. Robert J. Tanenberg, MD, MACP, is Professor of Medicine, Division of Endocrinology, Brody School of Medicine, East Carolina University in Greenville, North Carolina. Dr. Tanenberg is the medical director of the Inpatient Diabetes Program at the Vidant Medical Center, a 900-bed teaching and tertiary referral medical center in Greenville, NC. Dr. Tanenberg directs the East Carolina University-Diabetes Research Center for Clinical Trials where has been a principal investigator for over 60 diabetes research studies. He is board certified in internal medicine, and in endocrinology and metabolism. Dr. Tanenberg is a Master of the American College of Physicians.
Aging and Type 2 Diabetes: From Telomeres to Epigenetics

Dennis Bruemmer
Vascular Medicine Institute and the UPMC Heart and Vascular Institute, University of Pittsburgh, PA, USA

Abstract

While the relationship between obesity and type 2 diabetes has been extensively investigated, the processes linking aging and type 2 diabetes are less well studied. Currently, an estimated half of the individuals with type 2 diabetes in the United States is above 60 years of age, a number expected to increase to 40 million by 2050. Aging constitutes an important risk factor for type 2 diabetes and is associated with a decline in tissue insulin sensitivity. One of the key mechanisms implicated in cellular aging processes is the shortening of telomeres at the ends of chromosomes. These protective nucleoprotein complexes are maintained by telomerase and prevent replicative senescence during regenerative tissue remodeling. Although telomere shortening is associated with an increased risk for type 2 diabetes, a mechanistic relationship between age-induced telomere attrition and insulin resistance has never been shown. Our recent research provides evidence for a previously unrecognized causal role of telomere attrition in the pathogenesis of insulin resistance. We demonstrate that organismal aging is associated with telomere attrition in adipose tissue and insulin resistance. Experiments in genetically engineered mice establish that telomere attrition induces adipose tissue senescence and activates inflammatory pathways, which ultimately alters adipose tissue insulin signaling. Mechanistically, telomere-depleted cells display increased heterochromatin at mitogenic gene promoters and histone marks associated with a silenced nucleosome, which ultimately establishes a senescent phenotype. The results of these studies characterize telomere attrition as a chromatin modifier of cellular senescence and provide novel insights into the mechanistic basis for the association between aging and type 2 diabetes.

Biography

Dr. Dennis Bruemmer obtained his combined MD and Ph.D degrees from the University of Hamburg, Germany in 1998. Following his clinical residency training in Internal Medicine/Cardiology at the Charité/German Heart Institute in Berlin, Germany, he completed a Research Fellowship in Molecular Biology at the University of California, Los Angeles. In 2004, he was recruited as faculty to the University of Kentucky where he completed additional clinical subspecialty fellowship training in Endocrinology in 2009 and in Cardiovascular Medicine in 2015. Since January 2016, Dr. Bruemmer is a tenured Associate Professor at the Pittsburgh Heart, Lung, Blood, and Vascular Medicine Institute and the UPMC Heart and Vascular Institute.

Dr. Bruemmer’s research program has been supported by the National Institute of Health, the American Heart Association, and the American Diabetes Association. He has published over 80 peer-reviewed manuscripts. This research work has been cited in excess of 2300 times and published in Nature Chemical Biology, Science Translational Medicine, Nature Reviews in Cardiology, The Journal of Clinical Investigation, Circulation, Circulation Research, Journal of the American College of Cardiology, Diabetes and others. Dr. Bruemmer has been the recipient of multiple national and international investigator awards, including the Young Scholars Award of the American Society of Hypertension, the Young Investigator Award in Basic Sciences of the European Society of Cardiology, the Endocrine Society Young Investigator Award, the Merit Award for Young Investigators of the American Heart Association’s Council on Arteriosclerosis, Thrombosis, and Vascular Biology, a Career Development Award from the American Diabetes Association, and the Irvine H. Page Award from the American Heart Association.

Fluoroquinolone Antibiotics and Type 2 Diabetes Mellitus

Stephen J. Telfer
E Ink Corporation, MA, USA

Abstract

Exposure to fluoroquinolone antibiotics is postulated as a risk factor for subsequent development of type 2 diabetes. It is hypothesized that fluoroquinolones induce an intracellular magnesium deficit that can lead to insulin resistance. A temporal correlation is reported between the rate of outpatient prescription of quinolones and the incidence of diabetes during the period 1980–2011 (R^2 = 0.86, P < 10^{-9}). The increase in incidence of diabetes after 1990 and the recent decrease in the number of new cases are both reflected in the fluoroquinolone prescription rates. A geographical correlation was observed (adj. R^2 = 0.7, P < 0.0001) between rates of increase in prevalence of type 2 diabetes in each U.S. state and a model using only local rates of outpatient fluoroquinolone prescription, local rates of increase in the prevalence of obesity, and local rates
of population growth as predictor variables. Prescription rates of non-quinolone antibiotics correlated less well with the local rates of increase in prevalence of type 2 diabetes. The data are consistent with fluoroquinolone exposure predisposing an individual to develop diabetes with a probability that strongly depends upon factors that also lead to an increase in obesity.

Biography

Dr. Stephen J. Telfer is currently a Research Fellow at E Ink Corporation (originator of electrophoretic displays for e-books and other applications). Previously Vice President at Zink Corporation (developed of novel color printing technology), Research Fellow and Divisional Vice President at Polaroid Corporation. Educated at Cambridge University (MA, Ph.D. in organic chemistry). Post-doctoral studies at Stanford University (organic chemistry) and University of California, Berkeley (computer-assisted design of peptide mimetic molecules). Holder of 82 U.S. patents and numerous foreign equivalents.

Despite his original training in chemistry and drug design Dr. Telfer have not worked in this area for many years. Nevertheless, after having suffered a severe adverse reaction to a fluoroquinolone antibiotic, Dr. Telfer researched the likely etiology of this event and discovered correlations between fluoroquinolone prescription rates and the incidence of diabetes in the US. He published in Medical Hypotheses in order to bring this matter to the attention of the medical community, and it is his hope to spur further investigation by giving an oral presentation at the conference.

Inhibition of Cholinergic Potentiation of Insulin Secretion from Pancreatic Islets by Chronic Elevation of Glucose and Fatty Acids: Protection by Casein Kinase 2 Inhibitor

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2Department of Surgery, University of Pennsylvania School of Medicine, PA, USA
3Institute for Diabetes, Obesity and Metabolism, University of Pennsylvania School of Medicine, PA, USA
4Department of Pediatrics, Children’s Hospital of Philadelphia, PA, USA

Abstract

Objectives: Chronic hyperlipidemia and hyperglycemia are characteristic features of type 2 diabetes (T2DM) that are thought to cause or contribute to β-cell dysfunction by “glucolipotoxicity”. Previously we have shown that acute treatment of pancreatic islets with fatty acids (FA) decreases acetylcholine-potentiated insulin secretion. This acetylcholine response is mediated by M3 muscarinic receptors which play a key role in regulating β-cell function. Here we examine whether chronic FA exposure also inhibits acetylcholine-potentiated insulin secretion using mouse and human islets.

Methods: Islets were cultured for 3 or 4 days at different glucose concentration with 0.5 mM palmitic acid (PA) or a 2:1 mixture of PA and oleic acid (OA) at 1% albumin (PA/BSA molar ratio 3.3). Afterwards, the response to glucose and acetylcholine were studied in perifusion experiments.

Results: FA-induced impairment of insulin secretion and Ca2+ signaling depended strongly on the glucose concentrations of the culture medium. PA and OA in combination reduced acetylcholine potentiation of insulin secretion more than PA alone, both in mouse and human islets, with no evidence of a protective role of OA. In contrast, lipotoxicity was not observed with islets cultured for 3 days in medium containing less than 1 mM glucose and a mixture of glutamine and leucine (7 mM each). High glucose and FAs reduced endoplasmic reticulum (ER) Ca2+ storage capacity, however, preserving ER Ca2+ by blocking the IP3 receptor with xestospongin C did not protect islets from glucolipotoxic effects on insulin secretion. In contrast, an inhibitor of casein kinase 2 (CK2) protected the glucose dependent acetylcholine potentiation of insulin secretion in mouse and human islets against glucolipotoxicity.

Conclusions: These results show that chronic FA treatment decreases acetylcholine potentiation of insulin secretion and that this effect is strictly glucose dependent and might involve CK2 phosphorylation of β-cell M3 muscarinic receptors.

Biography

Dr. Nicolai M. Doliba, Ph.D., D.SC. is a Research Assistant Professor of Biochemistry and Biophysics, University of Pennsylvania. His research has focused on the role of bioenergetics, ion transport and metabolic coupling factors in nutrient- and drug-stimulated insulin release at normal conditions and during diabetes mellitus. Using combinations of different methods and approaches, including 31P, 13C, and 1H Nuclear Magnetic Resonance Spectroscopy techniques, polarographic and phosphorescence methods of measuring O2 consumption, Ca2+ imaging and others, Dr. Doliba attempt to directly address the essential mechanisms of stimulus-secretion coupling in pancreatic islets.
Bone and Joint Fungal Infections in Diabetic Patients

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Abstract

Fungal osteomyelitis and arthritis are uncommon diseases that generally present in an indolent manner. Being one of the most challenging complications in orthopedic and trauma surgery, fungal bone and joint infections often require complex treatments in specialized centers. Filamentous fungi belong to the groups of Mucormycosis, *Aspergillus*, and non-*Aspergillus* (e.g., *Hyalohyphomycosis* and *Phaeohyphomycosis*), and yeasts species such as *Candida* are the etiologic agents involved in osteoarticular infections in immunocompromised and immunocompetent individuals. Type of infection may be by direct inoculation, hematogenous, or contiguous depends on the site of infection and portal of entry. The patients at risk for bone and joint fungal infections are those with diabetes mellitus, trauma, corticosteroid therapy, prior surgery, solid organ transplant, solid cancer, hematological malignancy, and neutropenia. Diabetes is one of the important underlying conditions render patients vulnerable to develop secondary complications through bone and joint infections. The estimated osteoarticular infections in diabetic patients reaching 16% with *Aspergillus*, 15.5% with non-*Aspergillus* fungi, 18% with mucormycetes, and 10% with *Candida* arthritis. The organisms are ubiquitously found in soil and decaying matter, as well as on the surfaces of plants. Although these fungi show minimal intrinsic pathogenicity to normal persons, they can initiate aggressive and fulminant infections under certain clinical conditions. Infections of bone and joints by fungi in diabetes patients are usually hematogenous disseminated or contiguous in diabetic foot infections. Bone and joint fungal infections constitute a serious diagnostic and therapeutic challenge. The treatment of choice is amphotericin B, voriconazole or itraconazole but some patients had an unfavorable outcome. Bone and joint infections is a highly destructive infection with a poor prognosis if not diagnosed early. Control of underlying conditions and surgical debridement of infected tissue is critical.

GLP-1 Receptor Expressed in Pancreatic α-Cells Plays a Direct Role in Regulating Glucagon Secretion

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1Department of Medicine, Section of Endocrinology, Tulane University, LA, USA
2Endocrine Discovery, Lilly Research Laboratories, IN, USA

Abstract

GLP-1 receptor (GLP-1R) is a G-protein coupled receptor responsible for GLP-1 action in target cells such as insulin-producing β-cells in pancreatic islets. GLP-1 inhibits glucagon secretion from pancreatic α-cells, but it is unclear whether the inhibition occurs directly through interactions with GLP-1R on α-cells, or indirectly through insulin. To investigate this matter, we first confirmed that GLP-1R was expressed by α-cells in both mouse and human pancreas. Then, we generated α-cell specific GLP-1R knockout (αGLP1R KO) mice, and examined whether it affected glucagon secretion and glucose metabolism. We found that αGLP1R KO mice developed mild glucose intolerance. Interestingly, non-fasting glucagon concentration in blood of the αGLP1R KO mice was significantly higher than that of wildtype (wt) control mice, whereas insulin levels were similar among different groups. In addition, glucose stimulated insulin secretion was maintained in the αGLP1R KO mice, and they responded to the GLP1R agonist, exendin-4, during glucose tolerance test in the same manner as wt mice did, indicating that deletion of GLP1R from α-cells had no effect on β-cell function. Taken together, these data suggested that glucose intolerance of αGLP1R KO mice was due to interference with glucagon suppression. Knockout of GLP-1R from α-cells disrupted GLP-1-mediated glucagon inhibition, which led to elevated glucagon level in circulation and impaired glucose tolerance, whereas insulin secretion was not affected. We thus concluded that GLP-1 suppresses glucagon secretion by directly acting on α-cell expressed GLP-1R.

Biography

Dr. Yanqing Zhang is a Post-Doctoral Fellow at the Tulane University Health Science Center since 2012. She obtained her M. D. from Shandong Mountain Tai Medical College (China) in 1998 and received her Ph.D in Histology and Embryology from Sun Yat-sen University (China) in 2008. She has over 20 publications dealing with therapeutic perspective for diabetes and injured spinal cord. Her research interests are in the areas of gene therapy in diabetes and GLP-1R action in glucagon-producing alpha cells.
Diabetes Mellitus - Perspective of an Oral Pathologist

Deepika Gopal
Penang International Dental College, Malaysia

Abstract

Introduction: Diabetes Mellitus (DM) has become a global problem. The dentist and oral pathologist also have a key role in the early detection of DM because of the various oral alterations and oral complications. This presentation provides an insight about the emerging trends in relation to DM including oral cytological diagnostics and salivary diagnostics from the perspective of an Oral pathologist.

Material & Methods: This presentation discusses an oral cytological study carried out in 100 Type 2 DM patients. The study sample was grouped based on their recent Fasting Plasma Glucose (FPG) levels as: Group I:FPG 110-150 mg/dl; Group II:FPG 150-200 mg/dl; Group III:FPG >200 mg/dl; Control:FPG<110 mg/dl. Smears were taken from the right buccal mucosa and stained by the Papanicolaou technique. The cytomorphometry was evaluated using IMAGE PRO PLUS 5.5 software with Evolution L.C Camera. Smears were viewed with confocal laser scanning microscope (LSM-510 Meta) to view qualitative changes. The alterations in cytomorphometry and cytromorphology of buccal epithelial cells were noted. All findings were statistically analyzed.

Results: The results showed that with increase in FPG levels, there was significant increase in nuclear area, decrease in cytoplasmic area and increase in nuclear-cytoplasmic ratio (P < 0.05) when compared to the control group. Various qualitative changes were also noted.

Conclusion: This study supports and extends the view that these cellular changes can alert the clinician to the possibility of diabetes and also aid in monitoring of diabetes throughout the lifetime of the patient. This paper also provides a review of the various stomatological changes and oral complications seen in a diabetic patient.

Biography

Dr. Deepika Gopal is an Oral Pathologist working as Assistant Professor at Penang International Dental College, Malaysia. She received the ‘Sakunthala Kalyana Sundaram’ Gold medal from Sri Ramachandra University during her post-graduation. She has presented a number of scientific papers and posters in National and International conferences. She received the Dr. R.V Mehta Award for Best Scientific Paper for her research on Diabetic patients at the XIX National & First International conference of Indian Association of Oral Maxillofacial Pathologist. Her research interests include oral manifestations & cytological studies in Diabetics and advanced diagnostic methods in Oral cancer.

Predictors for the Treatment Efficacy of Sodium Glucose Co-transporter 2 Inhibitors in Patients with Type 2 Diabetes Mellitus

Shusuke Yagi* and Masataka Sata
Department of Cardiovascular Medicine, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan

Abstract

Background: Predictors for the efficacy of sodium glucose co-transporter 2 (SGLT2) inhibitors at lowering hemoglobin A1c (HbA1c) levels in type 2 diabetes mellitus patients remain unclear. We therefore aimed to elucidate these predictors in type 2 diabetes patients after 3 months of SGLT2 treatment.

Methods: A total of 302 consecutive type 2 diabetes patients who had been treated with SGLT2 inhibitors as monotherapy or add-on/combination therapy to/with existing antidiabetic treatments were enrolled retrospectively. After excluding 27 patients whose HbA1c levels could not be evaluated 3 months after treatment, the glucose-lowering effects of SGLT2 inhibitors were assessed in 275 patients by measuring HbA1c levels before and 3 months after treatment and predictors for changes in HbA1c levels after 3 months of treatment were evaluated.

Results: SGLT2 inhibitor treatment for 3 months decreased HbA1c levels from 7.8 ± 1.2 to 7.4 ± 1.0% (p < 0.0001) without severe treatment side effects. A multiple regression analysis showed that the independent determinants for SGLT2 inhibitor treatment efficacy included decreased HbA1c levels after 1 month of treatment, high baseline HbA1c levels, and a high estimated glomerular filtration rate (eGFR).

Conclusion: We identified the best candidates for SGLT2 inhibitor treatment are type 2 diabetic patients with preserved renal function with high baseline eGFR, and high baseline HbA1c, and they can be predicted by the initial response to the treatment.
Biography

Dr. Shusuke Yagi is a designated Associate Professor at Tokushima University, Japan. His research work is focused on cardiovascular medicines. He has published over 70 articles and is the author of three books based on cardiology.

Short and Long-Term Repercussions of the Maternal Diabetes in Rat Preimplantation Embryo

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²Basic Sciences Department, Animal Husbandry and Food Engineering School, USP-Univ Estado de São Paulo, Brazil
³Islet Cell and Regenerative Biology, Joslin Diabetes Center, Harvard Medical School, MA, USA
⁴Center of Natural and Human Sciences (CCNH), Federal University of ABC (UFABC), Brazil

Abstract

Early embryos recovered from diabetic rats show increased number of blastomeres undergoing apoptosis and decreased total number of blastomeres, suggesting impaired litter size and newborn weight. This might increase the chances of metabolic disorders in adulthood of these animals. Since diabetes-induced hyperglycemia impairs the redox balance, the aim was at evaluating the embryonic oxidative stress status before the implantation in order to identify whether there are differences in levels of oxidative stress in early embryos from diabetic dams. Thus, we hypothesized the decreased cell number found in early embryos recovered from diabetic rats is due to the low embryonic ability to maintain their own redox balance. Our study shows that rats with streptozotocin-induced mild (abnormal oral glucose tolerance test at adulthood) and severe (glycemia ≥ 300mg/dL at adulthood) diabetes present impaired redox status in early pregnancy. This maternal unbalance directly influences the embryonic redox status, reflecting the increased reactive oxygen species in the morula stage. We also showed that regardless of hyperglycemic level the embryos trigger defense mechanisms involved in the excessive free radical scavenging as an attempt to survive. Nevertheless, the success of this defense mechanism seems to depend on maternal hyperglycemia, highlighting the importance of the programmed pregnancy as well as appropriate medical care starting in early stages of human diabetic pregnancy.

Biography

Dr. Débora Damasceno joined the Obstetrics, Gynecology & Mastology Doctorate in March 1998. Her main research interests are in the area of diabetes and pregnancy and oxidative stress. Dr. Damasceno has worked in the field of pregnant rat biology and physiology for over 20 years. She has developed translational research exploring the cellular and molecular mechanisms of the hyperglycemic damages on preimplantation embryos and has investigated the role of oxidative stress and gender on embryofetal defense, growth and long-term health. Currently, the focus of Dr. Damasceno’s research is to better understand how the abnormal glycaemia impairs pancreas development in different life age and in successive generation.

Cognitive Function and Insulin Resistance

Lina Ma*, Yaxin Zhang, Rong Wang and Yun Li
Xuanwu Hospital, Capital Medical University, China

Abstract

Purpose: To explore the relationship between cognitive impairment and insulin resistance (IR) in elderly patients with type-2 diabetes mellitus.

Materials and methods: Two hundred and twelve elderly patients with type-2 diabetes were enrolled in this study and assigned into either the cognitive impairment group or the normal cognitive group. Gender, age, education, body mass index (BMI), total cholesterol, triglyceride, low-density lipoprotein cholesterol, creatinine (Cr), fasting plasma glucose, fasting insulin (FINS) and homeostasis model of assessment for IR index (HOMA-IR) were compared between the two groups. Multifactorial logistic regression analysis was performed.

Results: In cognitive impairment group, education level was lower, the level of BMI, FINS, HOMA-IR were higher than the control group. In the logistic regression, education level, FINS and HOMA-IR were independent factors.

Conclusions: Our study demonstrates that the education level, FINS and HOMA-IR were independent factors of cognitive impairment in elderly patients with type-2 diabetes. IR is an important risk factor and higher education level in a protective factor for the cognitive impairment in elderly patients with type-2 diabetes.
Hyperbaric Oxygen Therapy in the Treatment of Ischemic Leg Ulcers in Diabetic Patients: A Multicenter Trial

Dirk Ubbink*, Katrien Santema, Robert Stoekenbroek and Mark Koelemay
Department of Surgery, Academic Medical Center, The Netherlands

Abstract

Background: Conflicting evidence exists about the effects of hyperbaric oxygen therapy (HBOT) in the treatment of chronic ischemic leg ulcers. We investigated whether additional HBOT would benefit patients with diabetes and ischemic leg ulcers.

Methods: 120 patients were randomized to standard care without (SC) or with HBOT (SC+HBOT). Eligible patients had a Wagner grade 2-4 ulcer for at least 4 weeks and limb ischemia with or without revascularization options. Primary outcomes were limb salvage and complete wound healing after 12 months. Other endpoints were amputation-free survival (AFS) and mortality.

Findings: Limb salvage was achieved in 47 patients (78%) in the SC group vs. 53 (88%) patients in the SC+HBOT group (risk difference [RD] 0.10, 95%CI -0.04 to 0.23). After 12 months, 28 index wounds were healed in the SC group vs. 30 in the SC+HBOT group (RD 0.03, 95%CI -0.14 to 0.21). AFS was achieved in 41 patients in the SC group and 49 patients in the SC+HBOT group (RD 0.13, 95%CI -0.02 to 0.28). In the SC+HBOT group 21 patients (35%) were unable to complete the HBOT-protocol as initially planned. Those who did had significantly fewer major amputations and a higher AFS (RD 0.26, 95%CI 0.10–0.38).

Interpretation: Additional HBOT did not significantly improve complete wound healing and limb salvage in patients with diabetes and lower limb ischemia. However, a trend was seen towards a better amputation-free survival among HBOT-treated patients. The potential efficacy of HBOT may not be realized because some patients are unable to complete a full HBOT-regimen.

Biography

Dr. Dirk Ubbink has a background in medicine and clinical epidemiology and is currently one of the principal investigators of the Department of Surgery at the Academic Medical Center at the University of Amsterdam. His professional interest focuses on evidence-based medicine and shared decision-making, particularly in surgery. In this area, he coaches several Ph.D students. He also coordinates the ‘academic knowledge and skills’ educational line in the bachelor phase of the medical curriculum.

Spatial Learning and Memory, Transcriptional and Proteomic Analysis of Growth Hormone Action in bGH and GHA Mice Brain

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2Department of Neuroscience, Kenyon College, OH, USA
3HCOM-Biomedical Sciences, Ohio University, OH, USA

Abstract

The growth hormone (GH)/ insulin-like growth factor-1 (IGF-1) axis regulates mammalian longitudinal growth and metabolism. Presence of GH, GH receptor (GHR) and IGF-1 in mammalian brain indicates significance of GH/IGF-1 pathway in central nervous system development and function. Bovine GH transgenic (bGH) mice represent the human
condition of acromegaly, are giant, insulin-resistant and short-lived. Decreased GH/IGF-1 signaling in transgenic GHR antagonist (GHA) mice results in reduced body weight, normal insulin signaling and lifespan. To understand the effect of altered GH signaling in mouse brain, we assessed spatial learning and memory in bGH, GHA and wild type (WT) mice in a Barnes Maze (BM). Quantitative estimation of gene and protein expression, relevant to GH/IGF-1/insulin signaling and cognitive processing, was performed in the brain of bGH, GHA and WT mice. In BM, significantly compromised learning and memory retention by bGH mice suggests a negative influence of excess GH action on cognition. Alternatively, better learning and spatial memory retention were observed in GHA mice compared to controls. Significantly decreased gene expression, relevant to GH/IGF-1/insulin pathway, in bGH mice potentially contribute to their cognitive performance in the BM; whereas unaltered/increased transcript abundance for those genes in GHA mice brain points to their improved learning and memory. Proteomic analysis of the mouse brain supports a regulatory role of GH/IGF-1/insulin in cognition. Our study offers a compelling evidence of GH/IGF-1/insulin regulation of learning and memory in mouse brain. Understanding cognitive regulation by GH/IGF-1/insulin will facilitate therapeutic target identification and future application of IGF-1/insulin in neuropathological conditions.

Biography

Dr. Amrita Basu joined Edison Biotechnology Institute at Ohio University in 2010, where she received her Ph.D. in Molecular and Cellular Biology under the guidance of Dr. John Kopchick. Her doctoral research focused on neuroendocrine function of GH/IGF-1 in transgenic mice with increased and suppressed GH signaling. Following Ph.D., Amrita started her postdoctoral career at University of Massachusetts, Amherst, where she worked on bacterial cancer therapy. Currently she is working as a postdoctoral fellow at Moffitt Cancer Center in Tampa, FL, where her research focuses on cancer epigenetics and kinase signaling in prostate and breast cancer.

Diabetes Management: Awareness, Support, Therapy, and Technology & Biomarkers and Therapeutics

Leveraging Digital Health for Population Health Diabetes Education

Malinda Peeples
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Abstract

Diabetes is a chronic disease affecting a rising number of people globally. In the United States, even with all of the resources dedicated to diabetes management, the challenge remains that many patients fail to meet treatment goals and adhere to medication and lifestyle treatments. Of note, 33-49% of people with diabetes still do not meet standard of care targets for glycemic, blood pressure, or cholesterol control, and only 14% meet targets for all three while also avoiding smoking. Costs associated with diabetes also continue to rise. One study found that the total estimated annual costs in the United States have increased 41%, to $245 billion in 2012 from $174 billion in 2007. Type 2 diabetes is a serious condition that must be managed closely to prevent long-term complications and mortality. The mobile phone provides, for the first time ever, a 24/7 platform for providing real-time education and coaching to guide type 2 patients in the self-management activities associated with the daily metabolic and lifestyle activities. The analyzed, patient-generated data that results from these platforms provides may be shared with the care team to inform treatment decisions. This presentation will provide a case study of a digital therapeutic platform for type 2 diabetes that provides individualized coaching for people with diabetes and connects them with their team to support shared decision making for the individual patient and population support for the practice.

Biography

Malinda Peeples, RN, MS, CDE, serves as Vice President for Clinical Services at WellDoc where she oversees the clinical outreach program, grant and research activities, and professional organization activities. WellDoc is a healthcare company leveraging the mobile technology platform to create clinical and behavioral solutions that impact health and economic outcomes for chronic disease management. Peeples also serves as Adjunct Assistant Faculty, Division of Healthcare Informatics, Johns Hopkins School of Medicine. Previously, Peeples served as president of the American Association of Diabetes Educators (AADE), a professional membership organization devoted to advancing the practice of diabetes education.
Hyperglycemic Dividing Monocytes Cannot Tolerate Glucose Uptake and Initiate Aberrant Hyaluronan Synthesis Responses Involved in Diabetic Pathologies

Amina Abbadi\textsuperscript{1}, Minjia Yu\textsuperscript{1}, Nansy Albtoush\textsuperscript{1}, Xiaoxia Li\textsuperscript{2}, Aimin Wang\textsuperscript{1} and Vincent Hascall\textsuperscript{1*}

\textsuperscript{1}Department of Biomedical Engineering, Cleveland Clinic, OH, USA
\textsuperscript{2}Department of Immunology, Cleveland Clinic, OH, USA

Abstract

Our previous studies have shown that glomerular mesangial cells that divide in hyperglycemic glucose initiate hyaluronan synthesis in intracellular compartments that compromises their normal glomerular functions and that low concentrations of heparin prevent this response and allow normal glomerular functions after division. Our ongoing studies show that U937 cells, a human monocytic cell line, and murine bone marrow monocytes that are dividing in hyperglycemic medium also initiate intracellular hyaluronan synthesis and induce M1 pro-inflammatory macrophage phenotypes after completing cell division, and that low concentrations of heparin prevent the intracellular hyaluronan response and promote M2 anti-inflammatory macrophage phenotypes after cell division. We propose that the aberrant intracellular hyaluronan synthesis and the subsequent M1 pro-inflammatory phenotypes of the macrophages are critically involved in promoting most inflammatory responses in diabetic pathologies.

Preventing Diabetes: Evidence and Perspectives

Jocelyne Karam

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SUNY Downstate Medical Center, NY, USA

Abstract

Type 2 diabetes incidence has alarmingly increased over the past decades. The slow pancreatic beta cell function loss that precedes diabetes onset, leads to abnormal carbohydrates metabolism, manifesting by impaired fasting glucose and impaired glucose tolerance, and allowing identification of patients at risk of developing type 2 diabetes.

Several randomized controlled trials across the world proved lifestyle modifications, including dietary changes, moderate weight loss and moderate intensity physical activity, to be a safe and efficient strategy to prevent diabetes in prediabetic patients. Furthermore, follow-up studies revealed this protective effect was sustained many years after the initial intervention.

Other trials demonstrated that pharmacologic agents such as metformin, thiazolidinediones, alphaglucosidase inhibitors, xenical, liraglutide and insulin, can have a similar beneficial effect in prediabetes. However, except for Metformin, associated safety concerns or lack of sustained efficacy limit the use of these agents in diabetes prevention.

Significant reduction in diabetes incidence was observed after bariatric surgery, presenting the latter as an efficient intervention in preventing diabetes in severely obese subjects.

The American Diabetes Association issued guidelines for the diagnosis, evaluation and treatment of patients with prediabetes. Lifestyle changes including intensive diet, physical activity, and behavioral counseling program, targeting a loss of 7% of body weight, are the recommended initial intervention in patients at risk. Metformin therapy should be considered in patients with prediabetes, especially in those with BMI >35 kg/m2, those younger than 60 years of age, women with history of gestational diabetes, and/or those with rapidly rising HbA1C despite lifestyle modifications.

Biography

Dr. Jocelyne Karam is an endocrinologist in Brooklyn, New York and is affiliated with Maimonides Medical Center and specializes in Endocrinology, Diabetes & Metabolism and Diabetes. She received her medical degree from St Joseph's University Medical School and has been in practice between 11-20 years.
People with Diabetes Using the One Drop iOS and WatchOS Apps Experience Significant A1c Drop

Chandra Y. Osborn**, Jeff Dachis¹, Brian Huddleston¹, David Rodbard² and Mark Heyman¹⁺³

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²Biomedical Informatics Consultants LLC, TX, USA
³University of California, CA, USA

Abstract

Over 175,000 people from all 206 sovereign states use the One Drop diabetes app available on iOS, WatchOS, and Android. Users can manually and passively (via HealthKit and One Drop’s glucose meter) log blood glucose, medications, activity, food, and store and track A1cs. As of April 10th 2017, there were 188 people with T1D or T2D using the iOS and WatchOS apps who had entered two A1cs >60 and ≤365 days apart (154.8±74.0 days). This sample was 23% female, had diabetes for 8.6±9.5 years, and logged an average 1,946.9 ± 2,884.9 times between their first (8.36±2.34) and second (7.10±1.42) A1c. The second A1c was associated with users’ average blood glucose readings 60-90 days beforehand (all Spearman's rho=0.59-0.60, p<.001). Users with T1D (n=50) reduced their A1c by -1.47% (-2.31% to 0.63%), F(1, 49)=12.35, p<.001, Wilk's Λ=.80, partial η²=.20 with 93% power. Users with T2D (n=133) reduced their A1c by -1.18% (-1.58% to -0.78%), unadjusted p<.001 and -1.09% (-1.50% to -0.68%), adjusted p<.001). Those with T2D and two A1cs ≤6 mos apart (n=101) reduced their A1c by -1.55% (-2.04% to -1.07%), unadjusted p<.001). Tracking blood glucose (Spearman’s rho=.17, p=.08) or food (Spearman’s rho=.23, p=.02) with One Drop iOS and WatchOS apps were marginally and significantly associated with A1c reductions, respectively. Using One Drop to track self-care was associated with improved glycaemia. Users reported a clinically meaningful improvement, up to a 1.55% A1c reduction. In the DCCT and UKPDS trials, a 1.0% A1c drop reduced the incidence of all diabetes-related complications.

Biography

Dr. Chandra Osborn is Vice President of Health and Behavioral Informatics at Informed Data Systems Inc. where she leads all scientific activities, data analyses, and uses behavioral science to inform product design and data-driven insights. With over 90 academic publications and 13 years of consecutive NIH funding, Dr. Osborn is considered an expert in health communication, health disparities, health behavior change, medication adherence, and leveraging patient portals, user-centered design, usability testing, and mobile tailoring to improve the health and wellness of people with diabetes.

Coupling of Insulin Secretion and ZnT8 Display on the Surface of Pancreatic Beta-Cells

Qiong Huang*, Chengfeng Merriman, Hao Zhang and Dax Fu
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Abstract

The islet-specific zinc transporter ZnT8 mediates zinc enrichment in the insulin secretory granules of the pancreatic beta cell. This granular zinc transporter is also a major self-antigen found in type-1 diabetes (T1D) patients. A genetic variant of human ZnT8 arising from a single nonsynonymous nucleotide change contributes to increased susceptibility to type-2 diabetes (T2D). It is not clear whether ZnT8 can be displayed on the cell surface and how insulin secretion may regulate the level of ZnT8 exposure to extracellular immune surveillance. We report specific antibody binding to the extracellular surface of rat insulinoma INS-1E cells that stably expressed a tagged human zinc transporter ZnT8. Flow cytometry analysis following fluorescent antibody labeling revealed strong correlations among the levels of ZnT8 expression, its display on the cell surface and glucose stimulated insulin secretion (GSIS). Glucose stimulation increased the surface display of endogenous ZnT8 from a basal level to 32.5% of the housekeeping Na+/K+ ATPase on the cell surface, thereby providing direct evidence for a GSIS-dependent surface exposure of the ZnT8 self-antigen. Moreover, the variation in tagged-ZnT8 expression and surface labeling enabled sorting of heterogeneous beta cells to subpopulations that exhibited marked differences in GSIS with parallel changes in endogenous ZnT8 expression. The abundant surface display of endogenous ZnT8 and its coupling to GSIS demonstrated the potential of ZnT8 as a surface biomarker for tracking and isolating functional beta-cells in mixed cell populations.

Biography

Dr. Qiong Huang now is working as post-doc fellow in physiology department at the Johns Hopkins University School of Medicine. She is an associate professor in Institute of Clinical Pharmacology at Anhui Medical University, China. Her research focuses on anti-diabetes drugs’ pharmacology, with particular emphasis on anti-diabetes drugs’ pharmacogenetics and regulation.
Dr. Huang earned her Ph.D. in pharmacology from Central South University in Changsha, China. Her research supported by several National Natural Science Foundation of China and has published several peer-reviewed articles.

**Identification of Potential Pharmacoperones Capable of Rescuing the Functionality of Misfolded Vasopressin 2 Receptor Involved in Nephrogenic Diabetes Insipidus**

Timothy P. Spicer\(^1\), Emery Smith\(^1\), Thomas D. Bannister\(^1\), Jo Ann Janovick\(^2\), Justin Shumate\(^1\), Louis Scampavia\(^1\) and P. Michael Conn\(^2\)

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\(^2\)Texas Tech University Health and Sciences Center, TX, USA

**Abstract**

Pharmacoperones correct the folding of otherwise misfolded protein mutants, restoring function (i.e. providing “rescue”) by correcting their trafficking. Currently most pharmacoperones possess intrinsic antagonist activity because they were identified using methods initially aimed at discovering such functions. Here, we describe an ultra-high throughput homogeneous cell-based assay with a cAMP detection system, a method specifically designed to identify pharmacoperones of the vasopressin type 2 (V2) receptor (V2R); a GPCR that, when mutated, is associated with nephrogenic diabetes insipidus. Previously developed methods to identify compounds capable of altering cellular trafficking of V2R were modified and used to screen a 645K compound collection by measuring the ability of library compounds to rescue a mutant hV2R [L83Q], using a cell-based luminescent detection system. The campaign initially identified 3,734 positive modulators of cAMP. The confirmation and counterscreen identified only 147 of the active compounds with an EC\(_{50}\) < 5 mM. Of these, 83 were reconfirmed as active through independently-obtained pure samples and were also inactive in a relevant counterscreen. Active and tractable compounds within this set can be categorized into three predominant structural clusters, described here, in the first report detailing the results of a large scale pharmacoperone HTS campaign.

**Biography**

Dr. Tim Spicer, is an Associate Director and Assistant Professor in the Department of Molecular Medicine and joined Scripps Florida in 2005. Tim has more than 28 years of experience in drug discovery, including 10 years at Bristol-Myers Squibb. He is currently the Director of HTS and Discovery Biology. Germane to this talk, he supervises HTS assay development & related efforts including the advanced development of biology systems for use in High Throughput Screening. He has authored >90 drug-discovery related publications and is an inventor on 3 patents, including clinically useful drugs.
TXNIP Activates NLRP3-inflammasome in a High Fat Diet Model: Beyond the Eye

Azza B. El-Remessy and the Retinopathy Lab
Charlie Norwood VA Medical Center, Augusta Biomedical Research Corporation, GA, USA

Abstract

Obesity has been alarming increasing with the increased saturated fat and carbohydrate intake. Pattern recognition receptors act as sensors for metabolic danger stimuli that are known to instigate obesity-induced inflammation. Our previous work demonstrated that high-fat diet (HFD) triggered nucleotide-binding oligomerization domain-like receptor protein 3 (NLRP3) inflammasome activation and expression of its direct activator, thioredoxin-interacting protein (TXNIP) in rat retina. Here, we examine the impact of genetic deletion of TXNIP on HFD-mediated NLRP3-inflammasome and its associated response on development of retinopathy lesions in the retina. In addition, we examined HFD-impact on development of non-alcoholic steatohepatitis (NASH) and impaired vascular recovery using hind limb ischemia model.

Results: By week-8, HFD caused significantly impaired glucose tolerance, increases in weight, cholesterol and triglycerides, in both wild type (WT) and TXNIP knockout (TKO). HFD significantly increased systemic IL-1β, cleaved-caspase-1 and IL-1β, markers for inflammasome activation compared to ND in the WT-retina, liver and skeletal muscle. In the retina, HFD induced expression of adhesion molecules, leukostasis and microvascular permeability in WT but not in TKO mice. In the liver, HFD resulted in massive hepatic steatosis, lobular and portal inflammation that was accompanied by increase in α-SMA and fibrosis in WT but not in TKO mice. For vascular recovery, HFD significantly impaired blood flow and vascular density, increased infiltration of CD68+ cells in skeletal muscle of WT mice compared to ND but not in TKO.

Conclusion: HFD-induced obesity exerted systemic NLRP3-mediated inflammatory response. Targeting TXNIP-NLRP3 inflammasome pathway can provide potential therapeutic target in obesity-induced vascular complication.

Biography

Dr. Azza El-Remessy is a recognized expert in the fields of oxidative stress and retinal neuroinflammation in models of diabetes and neurotoxicity. Her research program has been supported by multiple-year grants from American Heart Association, Juvenile Diabetes Research Foundation and National Eye Institute. She is a leader in the field of neurotrophins and redox signaling with 80 research and review articles and more than 150-abstracts in the national and international meetings. She has been an active reviewer for pertinent journals in the eye and vascular research. She has successfully mentored several students as well as residents and post-doctoral fellows.

Perinatal Impaired Breathing Induced Diabetic Conditions may Result in Fragile Bone

Eung-Kwon Pae
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Abstract

A common medical condition, periodic breathing, often occurs during postnatal infant stage in humans. However, the current understanding and knowledge on adverse effects of perinatal intermittent hypoxia (IH) are very limited. Including the number of hypoxic events occurring in preterm babies, the total incidence of IH episodes during human neonates is high. Disturbed bone quality resulted from perinatal diabetes-like conditions is not well understood yet. Using a rat model, we discuss the cause-effect relationship between perinatal IH incidence, diabetes-like symptoms and the adverse outcome observed in long bones and the mandible. On postnatal day 0 (or P0) ~ P2, rat pups were treated under IH for as short as 1h, and then maintained in normal ambient air. We observed that hardness and elasticity of the tibia and mandible were significantly declined in 3 weeks after IH exposure. Reduced mineralization and alkaline phosphatase were evident in addition to other molecular changes such as a decreased collagen 1 and Runx2 expressions in bone and the cultured osteoblasts treated by IH. All these observations accompanied a significantly decreased insulin and increased glucose in blood serum along with a disturbed glucose sensitivity assessed by glucose tolerance tests (GTT). As for etio-
pathophysiology, a reduced function of pancreatic beta cells along with a decreased level of zinc uptake transporter ZIP8 due to oxidative stress resulted from IH were attributed to the observations.

Biography

Dr. Eung-Kwon Pae is a Professor and Chair, Department of Orthodontics and Pediatric Dentistry, School of Dentistry, University of Maryland, USA. He earned his MSc and Ph.D. degrees from the University of British Columbia in Vancouver, Canada, in 1989 and 1993, respectively. Dr. Pae received a certificate in orthodontics from the University of Connecticut in 1995. He is a member of the International Association of Dental Research and the American Association of Orthodontists.

The Paper Grip Test for the Early Detection of Intrinsic Muscle Weakness of the Foot Caused by Peripheral Neuropathy

Willem J. Theuvenet and Mahieu R

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2University of Groningen, University Medical Center Groningen, The Netherlands

Abstract

In diabetes, peripheral neuropathy is regarded as one of its more serious complications. Nerve function loss may result in intrinsic muscle weakness, and this again is a contributing factor to the development of functional impairment, and ultimately, deformity of the foot. In the prevention of foot ulceration and deformity there is a need for a tool for the early detection of intrinsic muscle weakness. In this interactive presentation the symptoms of a peripheral neuropathy and especially the consequences of intrinsic muscle weakness on the functioning of the foot are demonstrated, while the Paper Grip Test for its early detection is discussed. Therapeutic options are offered for discussion.

Biography

In 1990 Willem J. Theuvenet and P.W. Roche, from the Leprosy Mission in Nepal, gave rise to the development of the Paper Grip Test as a reliable screening test for the detection of intrinsic muscle weakness of the hallux in leprosy patients. In analogy with leprosy, not only loss of sensibility, but also intrinsic muscle weakness of the hallux exists in the diabetic foot. With this in mind, the role of the Paper Grip Test in the early-stage screening of the diabetic foot is currently under further investigation by, among others, R. Mahieu and W.J. Theuvenet.

Detecting Intrinsic Muscle Weakness of the Hallux as an Addition to Early-Stage Screening of the Feet in Patients with Diabetes

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2Department of Orthopedic Surgery, University Medical Center Groningen, The Netherlands
3Department of Epidemiology, Gelre Ziekenhuis, The Netherlands
4Department of Plastic Surgery, Gelre Ziekenhuis, The Netherlands

Abstract

Present-day screening of the diabetic foot involves the Semmes Weinstein Monofilament Test for evaluating loss of sensibility, while testing for intrinsic muscle weakness is not implied. Just as with the early detection of sensibility loss, early detection of intrinsic muscle weakness might have important implications for the prevention of both ulceration and deformity in patients with diabetes. The purpose of this study is to investigate the prevalence of patients with diabetes presenting intrinsic muscle weakness of the hallux, but with a normal sensibility of the sole of the foot.

A cross-sectional study design was applied. Intrinsic muscle function of the hallux was measured with the Paper Grip Test, while sensibility of the sole of the foot was measured with the Semmes Weinstein Monofilament Test 5.07/10-g.

In a period of three months a total of 266 diabetics (mean age 60, 134 females (50%), 177 type 2 diabetes mellitus (67%)) met the inclusion criteria and were examined for both intrinsic muscle weakness of the hallux and sensibility of the soles of the feet. The results did not only show that intrinsic muscle weakness was present more frequent in patients with impaired sensibility (p=0.001), but also showed that 20% of the population had intrinsic muscle weakness in the presence of normal sensibility. Multivariate regression analysis showed that only age is associated with diabetic patients presenting normal sensibility but impaired intrinsic muscle function (p=0.017).
The Paper Grip Test could have added value to current physical examination of the feet in patients with diabetes.

Biography

In 1990 W.J. Theuvenet and P.W. Roche gave rise to the development of the Paper Grip Test as a reliable screening test for the detection of intrinsic muscle weakness of the hallux in leprosy patients. In analogy with leprosy, not only loss of sensibility, but also intrinsic muscle weakness of the hallux exists in the diabetic foot. With this in mind, the role of the Paper Grip Test in the early-stage screening of the diabetic foot is currently under further investigation. Rutger Mahieu is preparing a Ph.D. under the supervision of Prof. Dr. S.K. Bulstra on this subject.

Non-Alcoholic Fatty Liver Disease is Improved by Transplantation of Modified Human Mesenchymal Stromal Cells (MSCs) in Diet Induced Obese Diabetic mice

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Abstract

**Background:** Mesenchymal stromal cells (MSCs) are multipotent cells that can home-in to the sites of inflammation. It was noted that delivery of SOD2 upregulated human MSCs improved glucose tolerance test (GTT) in leptin resistant db/db, obese diabetic mouse model.

**Hypothesis:** SOD2 and Catalase upregulated MSCs may reduce local/systemic inflammation, improve GTT and help improve diabetic complications such as hepatic steatosis in diet-induced obese (DIO) hyperglycemic mouse models.

**Methods:** We used GFP-containing adenoviral constructs to upregulate mitochondrial and cytosolic antioxidants (SOD2 and Catalase, respectively) in human adipose-derived MSCs, ex-vivo and modified MSCs were delivered intra-peritoneal (IP) into 45% and 60% high-fat DIO mice.

**Results:** We noted a reduction in plasma levels of TNFα (an inflammatory marker) in both DIO groups. The modified MSCs delivery also improved glucose tolerance test (GTT) at week 4 in comparison to Null-MSC (control). Omental fat histology showed less hyperplastic fat in mice that received SOD2 and Catalase upregulated MSCs. Interestingly, liver histology clearly showed a reduction in fat accumulation for mice fed with both high-fat diets and receiving either SOD2- or Catalase-MSCs. An increase in mRNA expression of Fgf21 was also observed in liver of those animals.

**Conclusion:** Transplantation of antioxidant upregulated MSCs reduces systemic inflammation, fat hyperplasia and reduced liver fat deposit. Delivery of antioxidant upregulated modified MSCs appears to be a safe yet a powerful therapeutic tool for improving glucose homeostasis and associated complication such as non-alcoholic fatty liver disease in high fat diet fed obese type 2 diabetes mouse models.

Biography

Dr. Sabyasachi Sen, MD, FRCP (UK), FACP, FACE is an Associate Professor in Medicine/Endocrinology AND Anatomy & Regenerative Medicine at The George Washington University School of Medicine & Health Sciences. Dr. Sen’s research interest involves behavior (survival and differentiation) of human adult stem cells in hyperglycemia. His current research projects include: the effect of exercise and diabetes medications on endothelial dysfunction and endothelial progenitor cells in patients with Prediabetes and type 2 diabetes; use of apoptosis-resistant endothelial progenitor cells to treat diabetic complications and use of genetically engineered human mesenchymal stem cells to reduce inflammation and improve glucose homeostasis in diabetes.
Physical Activity, Sedentary Behavior and Diabetes: Findings from a US Hispanic/Latino Cohort

Qibin Qi
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Abstract

Sedentary behavior is recognized as a distinct construct from lack of physical activity and is associated with deleterious health outcomes. Previous studies have primarily relied on self-reported data, while data on the relationship between objectively-measured physical activity and sedentary time and cardiometabolic health are sparse, especially among U.S. Hispanics/Latinos. In this study, we examined associations of objectively-measured sedentary time (via Actical accelerometers for 7 days) and diabetes traits among 12,083 participants, aged 18–74 years, from the Hispanic Community Health Study/Study of Latinos. Hispanics/Latinos of diverse backgrounds (Central American, Cuban, Dominican, Mexican, Puerto Rican, and South American) were recruited from 4 U.S. cities between 2008 and 2011. After adjustment for moderate-vigorous physical activity and confounding variables, prolonged sedentary time was associated with increased triglycerides, 2-hour glucose, fasting insulin and HOMA-IR. These associations were generally consistent across age, sex, Hispanic/Latino backgrounds, and physical activity levels. Even among individuals meeting physical activity guidelines, sedentary time was detrimentally associated with these diabetes traits. In addition, among 1699 participants with diagnosed diabetes, we found that less sedentary time, but not moderate-to-vigorous physical activity, was associated with improved cardiometabolic risk factor control, specifically in reaching hemoglobin A1c and triglyceride control goals. In summary, our large population-based, objectively-derived data showed deleterious associations between sedentary time and cardiometabolic health, independent of physical activity, in U.S. Hispanics/Latinos. Our findings emphasize the importance of reducing sedentary behavior for the prevention of diabetes and its CVD complications, even in those who meet physical activity recommendations.

Biography

Dr. Qibin Qi is currently an Assistant Professor at Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York. Dr. Qi’s research has focused on genomics, metabolomics, diet/lifestyle factors, and their interactions in relation to obesity, diabetes and cardiovascular diseases in human populations. He has authored or co-authored >90 original articles and reviews in scientific journals such as NEJM, JAMA, BMJ, Nature, Nature Genetics, Circulation, and Diabetes. Dr. Qi currently serves an Associate Editor of Diabetologia, an official journal of the Study of Diabetes European Association.

In-Hospital Experience with Insulin Degludec (IDEG)

Maria Fernanda Ozorio de Almeida1,2, Maria Gabriela Pedigoni Bulisani2, Paulo Rizzo Genestretti2, Camila Miranda Abdon2, Ana Cláudia Souza Moreno2 and Marília Izar Fonseca3
1Irmandade da Santa Casa de Misericórdia de São Paulo, Brazil
2Hospital Bandeirantes, Brazil
3Novonordisk, Brazil

Abstract

Introduction: Glycemic control is critical for in-patients and dysglycemia is associated with worse prognosis and mortality. Insulin therapy is the best treatment and insulin analogues, such insulin glargine (IGlar) and IDEg, could be useful options; however there are no studies comparing them in hospitalized patients.

Objective: Present a case series describing efficacy and safety of IDEg in-patients with diabetes when compared with IGlar.

Methods: Retrospective analysis of blood glucose obtained with point-of-care testing of diabetic patients admitted at Bandeirantes Hospital between October 2014 and April 2015, previously treated with IGlar for a minimum of 7 days and switched to IDEg for at least 7 more. Parameters studied included GV, standard deviation (SD), coefficient of variation (CV) and mean glucose levels, obtained from software PXP Abbott. Hypoglycemia was defined as blood glucose (BG) <70 mg/dL, severe if BG <40 mg/dL.

Results: 3/10 patients had type 1 diabetes mellitus (T1DM) for over 10 years. Average age was 46 years and mean HbA1c was 9%. 7/10 patients had type 2 diabetes mellitus (T2DM), duration of >10 years, majority had previous insulin
treatment. Mean age was 70 years and mean HbA1c was 9.7%. All T2DM patients, but not T1DM, maintained CV, and 57% had a reduction in SD, improving GV. Basal dose with IDeg was lower at discharge. Severe hypoglycemia events were diminished after switching.

**Conclusions:** GV was lower in T2DM patients treated with IDeg. More studies in this population are needed to confirm this hypothesis. IDeg proved to be effective at hospital and might improve GV.

**Biography**

Dr. Maria Fernanda Ozorio de Almeida, MD in Endocrinology, Irmandade da Santa Casa de Misericórdia de São Paulo, Brazil. She is specialist in Endocrinology and Metabolism, Brazilian Society of Endocrinology and Metabolism. She actively involves in outpatient clinic for internal medicine.

**UV-B Radiations and T1D High Incidence in the Hot Spot of Sardinia: One More Environmental Factor?**

Marco Songini1*, C. Mannu1, Alessandro Sanna2, Salvatore Prettì1, G. Bruno3 and P. Valera1,4

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2Department of Civil–Environmental Engineering and Architecture – University of Cagliari, Italy
3Department of Medical Sciences, University of Turin, Italy
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**Abstract**

A negative association between Type 1 diabetes (T1D) incidence and ultraviolet B (UV-B) solar radiation has been suggested. We performed an ecological analysis to evaluate the possible relationship between levels of UV-B radiation and incidence of T1D in Sardinia. A standardized algorithm based upon the solar constant and the latitude of each municipality was employed to calculate the amount of total solar irradiance. UV-B radiation (W/m²) during the winter solstice for each Sardinian municipality was then calculated, considering that UV-B radiation is around 0.4% of total solar irradiation. This value was adjusted taking into account the annual mean of cloud cover and the percentage of direct solar irradiation of exposed territory, using the formula: UV-B irradiance adjusted for cloudiness = UV-B irradiance* (1 = percentage of cloudy sky) [W/m²]. T1D incidence data were obtained through the Sardinian Diabetes Registry. The relationship between UV-B radiation and T1D incidence in Sardinia was assessed through a simple correlation analysis. A mild negative correlation (r = -0.154; p = 0.002) was obtained between UV-B radiation and T1D incidence. A protective effect of UV-B irradiance in T1D was suggested by many authors, our results are consistent with this hypothesis, even taking into account the effect of cloudiness percentage of each area. This preliminary result confirms that UV-B might have a protective role on aetiopathogenesis of diabetes. Previous studies have hypothesized a role of vitamin D deficiency in T1D risk our results, based on the analysis performed by the high ecological risk in Sardinia, are suggestive with a protective role of sun exposure. The study confirms that ecological analysis of simple correlation is a suitable statistical method to suggest hypotheses and conduct research.

**The Burden of Functional Disability among Patients with Diabetes and Comorbid Conditions: Evidence from Hospital Based Survey from Pakistan**

**Nadia Shah, Sumera Inam and Shehrish Haider**

School of Public Health, Dow University of Health Sciences, Pakistan

**Abstract**

The presence of diabetes and related comorbidities can intensify treatment demands and adversely impact functional capacity. The goal of our study was to estimate the prevalence and association of functional disability in patients with diabetes and related comorbidities attending diabetes clinic in Karachi. A hospital-based cross sectional data of 800 adults were analyzed. Three categories were created including: diabetes and no comorbidity, diabetes with one-comorbidity and diabetes with two or more comorbidities. Prevalence of functional disability was computed and multi-logistic regression was used to determine the odds of functional disability in diabetes patients with and without comorbidities. Of the total, 23.5 % participants with diabetes showed extreme functional disability. Odds of functional disability increased with age (OR= 10.75, 95% CI= 4.39-26.33, p-value <0.001). Females were twice more likely to have functional disability burden (OR= 1.90 95% CI= 1.06-3.42, p-value 0.029) as compared to males. Odds of functional disability by disease category were as follows: no comorbid condition as reference, the odds of functional disability was (OR= 2.03, 95% CI= 1.15-3.60, p-value 0.014) for diabetes with one comorbid and (OR= 10.98, 95% CI= 6.49-18.58, p-value <0.001) for diabetes with...
two or more comorbid conditions. One of the most upsetting features of fast increase is the co-occurrence of diabetes and multimorbidity is the rising burden of functional disability, particularly in women and older adults. There is a greater need for diabetes related functional disability surveillance and research directed at environment and improving lifestyle factors.

Biography

Dr. Nadia Shah is a professional health economist working at the School of Public Health, Dow University of Health Sciences, Pakistan. Earlier, she has worked as project economist for the socio-economic sector. She has been actively involved in the economic evaluation and research design of various projects at the institute. Her research interests include the Socio-economic impact of communicable and non-communicable diseases, adolescent health, child & maternal health.

Diabetes and Cancer

Effect of Insulin and Metformin Combination Treatment on Colon Adenoma and Advanced Adenoma among DM II

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Abstract

Background: The risk for colorectal adenoma and advanced adenoma among Diabetes Mellitus II (DM II) has been debated to differ with the type of anti-diabetic therapy. Insulin increases whereas metformin decreases the risk for colon adenoma (Ad) and advanced Ad (AAD). There have been no studies to evaluate the effect of combination treatment with Insulin and Metformin on colon Ad and A. Ad.

Methods: The retrospective study included DM II patients undergoing screening colonoscopy. Subjects with incomplete colonoscopy, poor bowel preparation, personal history of colorectal cancer (CRC)/ inflammatory bowel disease/ hereditary nonpolyposis colorectal cancer/ Familial adenomatosis polyposis/ colectomy or family history of CRC were excluded. Subjects was categorized into- Group 1 (Insulin only), Group 2 (Metformin only), Group 3 (Combination of Insulin and Metformin) & Group 4 (miscellaneous). Group 4 was excluded from data analysis. Ad detection rate (ADR) and advanced ADR (AADR) was calculated for each group.

Results: 339 subjects composed the study group, with a mean age of 60.0 years and male to female ratio of 1:1.4. Composite ADR and AADR for study population was 35.1% and 15.3% respectively. Group 1, 2, and 3 were composed of 88 (26.0%), 211 (62.2%) and 40 (11.8%) subjects respectively. ADR for Group 1, 2 and 3 was 40.9%, 33.2% and 32.5% respectively (p value= 0.413). AADR for Group 1, 2 and 3 was 18.2%, 15.2% and 10.0% respectively (p value= 0.489).

Conclusion: A decremental trend was observed in ADR and AADR across group 1, group 2 and group 3 (p value > 0.05).

Biography

Dr. Deepanshu Jain is currently a Gastroenterology and Hepatology fellow at Albert Einstein Medical Center. He has a growing interest in determining the impact of insulin, metformin, diabetes on colon cancer and its pre-malignant lesions and also shares a keen interest in outcome research related to colon cancer prevention.

Effect of Dapagliflozin on Colon Cancer Cell

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Abstract

Dapagliflozin is a SGLT2 (Sodium/Glucose Cotransporter 2) inhibitor that reduces circulating glucose levels in type 2 diabetic patients by blocking the SGLT2-dependent reabsorption of glucose in the kidney. Dapagliflozin is metabolized by UGT1A9 (UDP Glucuronosyltransferase 1 family, Polypeptidase A9) suppressing its activity as SGLT2 inhibitor. However there is little information whether dapagliflozin has any additional biologic actions that occur in the absence of dapagliflozin
metabolism. HCT116 cells, which express SGLT2 but not UGT1A9, treated 0.5 mM dapagliflozin resulted in a significant reduction in cell number. This was not a result of SGLT2 inhibition, as the SGLT2 inhibitor phlorizin had no effect. Dapagliflozin enhanced Erk phosphorylation but with no change in uncleaved, cleaved, and uncleaved caspase-3 and PARP suggesting an apoptotic independent cell death. Taken together, these data present a new potential role of dapagliflozin as an anticancer reagent in tumor cell populations that do not express UGT1A9.

Biography
Dr. Junichi Okada has graduated from Tottori University School of Medicine in the year 2014. He completed his Ph.D. from Gunma University graduate school of medicine, Japan.

What Underlies the Inverse Association between Diabetes and Prostate Cancer Risk: An 11-year Historical Population Follow up Study of More Than 1 Million Men
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Abstract
Aims: An inverse association has consistently been observed between diabetes mellitus and prostate cancer (PCa) incidence. We investigated whether lower PCa incidence among men with diabetes may be attributed to lower detection due to PCa screening patterns.

Methods: A population-based historical cohort of 1,034,074 men aged 21-90 years, without a previous history of cancer, was followed from 2002 to 2012, according to diabetes morbidity, for frequency of PSA-testing, mean PSA values, and detection of PCa, after adjustment for age, ethnic origin, socioeconomic status, glucose control, and PSA-testing.

Results: Men with diabetes (n=268,591) performed approximately 10% more PSA screening compared to men without diabetes, but their rate of PSA positivity (>4 µg/l) was 20% lower. PSA values were already significantly lower about 3 years before diabetes diagnosis. Reduced PCa risk was observed among men with incident diabetes only for low-moderate grade tumors (Gleason score 2-6): adjusted hazard ratio (HR)=0.83 (95%CI 0.77, 0.89). No association was observed for high-grade tumors (Gleason score 7-10): HR=0.99 (95%CI 0.88, 1.11). An inverse relationship was observed between glucose control and PCa risk, where for every 1% increment in mean HbA1c over the preceding 2 years there was a 15% decrease in the risk for PCa (HR=0.85, 95%CI: 0.81-0.89).

Conclusions: Our demonstration of reduced incidence of low-moderate-grade, but not high grade PCa among diabetic men supports the possibility that low PSA levels, rather than lower tumor risk, may explain the observed reduced incidence of PCa. Surveillance bias may explain the inverse association between glucose control and PCa risk.

Biography
Dr. Rachel Dankner is a Professor of Public Health in the Department of Epidemiology and Preventive Medicine, Sackler Faculty of Medicine, Tel Aviv University, and a Senior Researcher at The Gertner Institute for Epidemiology and Health Policy Research in Israel. She received her MD from the Hebrew University of Hadassah, Jerusalem, and her MPH from The John's Hopkins School for Hygiene and Public Health, Baltimore, and a Diploma in Sports Medicine from the Tel Aviv University. Professor Dankner has published 90 peer-reviewed articles in leading international journals and has national and international research collaborations. Her present work is supported by a grant from EFSD.
Adherence to Medication for Type 2 Diabetes among Syrian Refugees and Host Communities in Lebanon

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Abstract

Rapid growth in the scale of global displacement in urban contexts, coupled with aging populations and the resulting increase in non-communicable diseases globally pose many new challenges in meeting health needs of displaced populations worldwide. Through baseline data from a longitudinal cohort study implemented in primary care settings in Lebanon, this analysis was undertaken to characterize determinants of interrupted medication use for type 2 diabetes among Syrian refugees in Lebanon.

A two-year longitudinal cohort study sought to develop, implement and evaluate the effectiveness of treatment guidelines and a mHealth application on patient and provider compliance, quality of care, and health outcomes among patients with hypertension and type 2 diabetes in ten clinics in Lebanon. This analysis utilizes baseline data obtained through phone interviews with Syrian refugees enrolled in the study. The main outcome variables to be assessed include interrupted use of medication for type 2 diabetes (having stopped prescribed medication for two weeks or longer in the preceding six months) and the four-item Morsky Medication Adherence Scale (MMAS-4). Associations between background characteristics such as age, gender, medication assistance, and socioecoomic quartile, among others, and interrupted medication use for type 2 diabetes will be assessed using multilevel logistic regression.

The results of this analysis will provide useful evidence of the burden of interrupted medication use in the Lebanese context among Syrian refugees and host community members, as well as characterizing associated factors and reasons for non-adherence among type 2 diabetics, providing insights to inform decision making in this and similar humanitarian contexts.

Diabetes Connect: A Diabetes Self-Management Education and Support Program for Saint Anthony Hospital Community

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Abstract

Problem: Diabetes is increasing at an alarming rate nationwide affecting mostly minorities. In fact, Saint Anthony Hospital (SAH) community in Chicago has a significant increase of diabetes prevalence from 8% in 2009 to 17% in 2015 and predominantly serves Hispanics (49%) followed by African-Americans (26%). Also, population assessment and chart reviews conducted in collaboration with SAH key stakeholders shows a high rate of uncontrolled diabetes (blood glucose of >212 mg/dl) and has led to increased emergency department visits.

Purpose: A diabetic wellness and education program following American Diabetes Association guidelines has been developed to address this issue with a focus on diabetes self-management education and support (DSME/S).

Methods: DSME/S is the delivery of knowledge, skills and capacity needed for diabetes self-care with support for achieving and sustaining behaviors and coping skills needed for self-management after education. Following the PRECEDE-PROCEED planning framework, the program was divided into two phases. Phase one addressed organization change using Lewin's planned change theory. Phase two was implementation of SAH redesigned DSME/S program called ‘Diabetes Connect’ using Bandura’s social cognitive theory for individual change. The program was delivered in English and Spanish in summer and fall 2017. It includes four weekly 90-120 minute sessions using Conversation Maps®. Recruitment site were an SAH satellite primary care clinic and the emergency department. Phase three, an addendum to the initial program, involved using a multimodal community based recruitment plan.

Results: Program is still ongoing and concludes on October 3. Outcomes will be presented at conference.
A Community Outreach Initiative with Favorable Impact on Diabetes Mellitus and Cardio Metabolic Risk

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Abstract

Americans (AA) are more likely to have uncontrolled CMR compared with Whites. Diabetes Mellitus (DM) and Hypertension (HTN), weight and physical activity less at goal and there are more serious comorbidities in this group. Even modest body weight gain and inactivity may be associated with a 3-fold increase in DM development. AAs participate in risk reduction behavior and adherence at lower rates than other racial groups. These differences are due in part to social determinants of health (SDOH) resulting in increased prevalence, morbidity and mortality of Cardiovascular Disease (CVD).

Urban communities can be favorably impacted by sustained outreach efforts which address SDOH such as the Harlem Healthy Hearts (HHH) program. Single annual or quarterly health fairs are not as efficacious. HHH is a culturally sensitive project developed and implemented to impact the entire family. The ongoing series of 12 monthly workshops for the past 5 years with over 2000 encounters focuses on education, screening, diet, exercise and referral, with an aim to controlling DM and other CMR contributors. To impact SDOH, this important program includes input and buy-in from stakeholders (e.g. Community residents, institutions of higher learning, faith based organizations and community medical providers. Indicators such as weight loss, blood glucose and blood pressure control have been noted in the participants. Qualitative data themes, including enhanced quality of life, have been acquired during participant feedback. This type of grassroots approach will undoubtedly result in a reduction in premature morbidity and mortality within this population over the long term.

Relationship between Years of Marijuana use and the Four Main Diagnostic Criteria for Metabolic Syndrome among United States Adults

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Abstract

Research on marijuana use suggests a protective effect on metabolic syndrome. National Cholesterol Education Program, Adult Treatment Panel III, World Health Organization, European Group for the study of Insulin Resistance and International Diabetes Federation have different criteria for metabolic syndrome. We examine the relationship of years of marijuana use with the four common definitions of metabolic syndrome. A Cross-sectional study of 3051 adults aged ≥ 20 years who participated in the National Health and Nutrition Examination Survey 2011-2012 and responded to the question, “Have you ever even once used marijuana or hashish?” Using multivariate logistic regression, we estimated odds ratios for metabolic syndrome and its components with each year of marijuana use. Adjusted odds ratios (AOR) for having metabolic syndrome with each increase in year of marijuana use was 1.05 (95% CI: 1.02, 1.08) using NCEP ATP III criteria. Respective AOR using International Diabetes Federation (IDF) was 1.08 (95% CI: 1.04, 1.13) and 1.05 (95% CI: 1.04, 1.13) using World Health Organization (WHO) or European Group for the study of Insulin Resistance (EGIR) criteria. Using ATP III or IDF criteria, the adjusted odds ratio of having hypertension (AOR Hyp) for each year of marijuana use was 1.07 (95% CI: 1.03, 1.12). Adjusted odds ratio for having high oral glucose tolerance test levels was 1.12 (95% CI: 1.07, 1.18) using WHO and EGIR criteria. Irrespective of the criteria for metabolic syndrome, each year of marijuana use showed increased odds of having metabolic syndrome, hypertension or high oral glucose tolerance test levels.
Identification of Clinical Determinants for Coefficient of Variation of R-R Intervals in Patients with Type 2 Diabetes

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4Tokushima University Fujii Memorial Institute of Medical Sciences, Japan

Abstract

**Background:** Since autonomic neuropathy is a major complication in patients with diabetes and it decreases quality of life and increases mortality, evaluation and clinical assessment of autonomic function is very important issue to treat diabetic complications.

**Materials and Methods:** One hundred and twenty-seven adult patients (66 males and 61 females, mean age: 58.1±14.2 years) with type 2 diabetes (T2DM) were retrospectively analyzed. They were hospitalized in the department of Endocrinology and Metabolism at Tokushima University Hospital for glycemic control between April 2013 and September 2015. The coefficient of variation of the R-R intervals (CVR-R) on electrocardiograms at resting and deep breathing were measured in those patients on admission. The relevance of clinical parameters to the CVR-R was statistically evaluated.

**Results:** Multiple regression analysis showed that age (coefficient:-0.025, p < 0.01), duration of diabetes (coefficient:-0.030, p < 0.05) and low-density lipoprotein (LDL) cholesterol (coefficient:-0.006, p < 0.05) were inversely associated with CVR-R at resting. In addition, age (coefficient:-0.063, p<0.01), duration of diabetes (coefficient:-0.061, p < 0.05) and heart rate (coefficient:-0.056, p < 0.05) were inversely associated with CVR-R at deep breathing.

**Conclusions:** Diabetic autonomic disorder represented by CVR-R is associated with age, duration of diabetes, LDL cholesterol and heart rate. These results suggest that in addition to glycemic control, correction of serum lipid profile and circulatory dynamics ameliorate the autonomic neuropathy in patients with T2DM.

Heparin Cofactor II: A Serine Protease Inhibitor is Associated with Albuminuria in Humans and Mice

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Abstract

**Background:** Diabetic nephropathy is a critical problem to promote albuminuria leading to development of chronic kidney disease (CKD). Since accelerated thrombin activation exerts various adverse biological effects, including renal injury and since heparin cofactor II (HCII), a serine protease inhibitor, effectively inactivates thrombin action via complex formation with dermatan sulfate in vivo, we hypothesized that HCII is associated with progression of CKD in patients with lifestyle-related diseases such as diabetes.

**Methods:** Plasma HCII activity and surrogate markers of glucose metabolism, including HbA1c, fasting plasma glucose (FPG) and albuminuria were determined in elderly Japanese individuals. Relationships between plasma HCII activity and those surrogate markers were statistically evaluated. In addition, we treated HCII+/+ mice and HCII+/- mice with angiotensin II-loading (2.0 mg/kg/day) for 2 weeks, and analyzed daily excretion of albuminuria in those mice.

**Results:** There were significant inverse relationships between HCII and HbA1c value (p < 0.005) and between HCII and FPG (p < 0.05). In addition, HCII was inversely associated with log-transformed urinary albumin-to-creatinine ratio (p < 0.05). Angiotensin II infusion prominently increased albuminuria in HCII+/- mice than HCII+/+ mice.

**Conclusions:** These results suggested that HCII is a novel regulating factor for development of CKD represented by albuminuria. Therefore, HCII may be one of the therapeutic target for diabetes and diabetic nephropathy.
Bioenergetic Effects of Mitochondrial KATP Channel Opener Diazoxide in Rat Liver Mitochondria

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Abstract

**Background:** Diazoxide (DZ), mitochondrial K\(_{ATP}\) channel (mtK\(_{ATP}\)-channel) opener, is a promising drug in the correction of hormonal responses to hypoglycemia under diabetes treatment. It is generally supposed that cytoprotective effects of DZ largely result from the activation of K\(^+-\)cycle, but the impact of DZ on mitochondrial bioenergetics varies significantly between cell types. Our aim was the estimation of DZ effects on mtK\(_{ATP}\)-channel activity and resulting bioenergetic effects in rat liver mitochondria.

**Results:** In the absence of Mg and ATP it was found that peak activation of native mtK\(_{ATP}\)-channel by DZ occurred at ≤500 nM with parallel increase in ATP-insensitive K\(^+-\)uptake, state 4 respiration and the activation of K\(^+-\)-cycle. The rise of DZ concentration above ~500 nM did not augment mtK\(_{ATP}\)-channel activity, but enhanced ATP-insensitive K\(^+-\)uptake, which was suppressed by Mg\(^{2+}\) and, unlike mtK\(_{ATP}\)-channel, was not restored by DZ. Bioenergetic effects of DZ at nanomolar concentrations − mitochondrial uncoupling and inhibition of ATP synthesis ensued from the activation of K\(^+-\)-cycle. Meanwhile, suppression of phosphorylation resulted not from uncoupling, but from direct inhibition of ATP synthase activity.

**Conclusions:** High sensitivity of native mtK\(_{ATP}\)-channel to DZ was found with parallel activation of ATP-insensitive potassium transport, which were novel effects of this drug. Despite the lack of selectivity, the estimation of the share of mtK\(_{ATP}\)-channel in potassium transport and state 4 oxygen consumption allowed establish the share of the channel in the modulation of mitochondrial bioenergetics (respiratory uncoupling and suppression of phosphorylation) under DZ treatment.

Simplified Method of Plantigrafia for Assessing the Feet of Diabetic Patients

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Abstract

**Introduction:** The complications in the feet of diabetic patients include high rates of amputations and hospitalizations and leads to reduction of work capacity of people still of working age. High plantar pressure is a proven risk factor for ulceration among individuals with DM. The photopodoscopia is one of the tools used in screening for high plantar pressure among these subjects. However, an examination photopodoscopy is not accurately demonstrates the high pressure area and there is no specific computer program to analyze the image plant.

**Objectives:** Developed a simplified method of plantigrafia for assessing the feet of diabetic patients and a computer program to analyze footprint of diabetic patients.

**Methods:** The method was developed by medical professionals and systems analysts from the University of Vale do Sapucaí, Minas Gerais, and Brazil. It is in registration process with the National Institute of Intellectual Property (INPI). Footprints were taken from 113 subjects using the photopodoscopia and plantigrafia. It was compare high pressure points plant between the two tests. It was analyzed the agreement and intra-rater reliability.

**Results:** All patients were type 2 diabetics and 56, 6% were women. The average age was 62, 8±9, 8. The weighted kappa coefficient was high concordance (Kw>0.79) for the intra-examiner analyses for most of the points studied on both feet.

**Conclusions:** The plantigrafia with a specific computer program to analyze the footprints feature ease of handling and low cost, it may represent an important social impact.
Evaluation of Patient Satisfaction after using Prefilled Insulin Pen SoloSTAR in Real Life in Lithuania

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2Sanofi-Aventis Lietuva UAB, Lithuania

Abstract

Background: This survey was performed to evaluate patients’ satisfaction with the SoloSTAR insulin pen (Sanofi-Aventis) in a real life situation in Lithuania, with special focus on comparison of satisfaction in various patients groups.

Methods: This was a multi-centre, observational survey. Current users of insulin pen SoloSTAR with at least 3 months experience were asked to evaluate their pen. Survey participants completed Patient Questionnaires containing questions about previously used insulin pen, details on current insulin treatment, technical aspects of current SoloSTAR handling, if training on SoloSTAR use was provided.

Results: A total of 393 patients with diabetes completed questionnaires. On a 5-point scale, ranging from 1 (excellent) to 5 (very poor), mean ±SD rating of patient satisfaction with SoloSTAR pen was 1.4±0.5. The proportion of patients, who were satisfied with each feature of the pen (i.e. rated it as good or excellent), ranged from 89.3% to 96.7%. After face-to-face training on the use of SoloSTAR, 94.0% (95% CI 91.6 – 96.38%) of patients were fully confident in the use of the pen. Patients became confident in the use of SoloSTAR on average within two days. Patients were satisfied with SoloSTAR pen irrespectively of prior experience with insulin pens (92.6% - 98.8% of unexperienced patients rated individual pen features as good or excellent) or the presence of impairment (88.1% - 97.8% of patients with any type of impairment were satisfied with pen features).

Conclusions: High satisfaction and confidence in managing SoloSTAR pen has been demonstrated in a wide range of patients with diabetes.

The Renal Threshold for Glucose Re-Absorption Predicts Diabetes Improvement by Sodium Glucose Co-Transporter 2 Inhibitor Therapy

Shuichi Okada* and Masanobu Yamada
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Abstract

In this study we examined the efficacy of the sodium glucose co-transporter 2 (SGLT2) inhibitions on improvement of glycated hemoglobin (HbA1c) in comparison with the renal threshold for glucose re-absorption in patients with type 2 diabetes mellitus. Patients visited the hospital once a month for regular follow-up examination with the determination of blood glucose and HbA1c levels and urinary glucose concentration from spot urine samples. Patient samples were compared before and after ipragliflozin administration. We defined the renal threshold for glucose re-absorption as the lowest blood glucose level that correlated with first detectable appearance of urine glucose. These data revealed a significant negative correlation between improvement of HbA1c level and renal threshold for glucose re-absorption in patients treated with the SGLT2 inhibitor. These findings indicate that patients who have higher renal threshold for glucose re-absorption can be expected to more effectively respond to SGLT2 inhibitor therapy in terms of lowering HbA1c levels.
A Diabetes Education Program Incorporating Supervised Exercises Improves Acute Blood Glucose Management in Individuals with Type 1 Diabetes

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Abstract

Effective management of type 1 diabetes mellitus (T1DM) is frequently achieved through access to an interdisciplinary qualified staff that provide individualized diabetes education aimed at achieving glycemic control. This study aimed to examine acute and long-term improvements in glycemic control in T1DM individuals who undertook supervised exercise in interdisciplinary diabetes education program.

Individuals with T1DM attended 20 program meetings 1-3 times per week during a 4-month period. Subjects (16 males/23 females) ranged from 07 to 58 years (mean age 23 ± 12; mean diabetes diagnosis, 8 ± 7 years). Data included: 1) initial capillary blood glucose (IBG) self-monitoring; 2) nutritional and insulin recalls; 3) 50 minutes of exercise; 4) 30 minutes of educational activities; 5) final self-monitoring of blood glucose (FBG). Blood glucose (BG) values were categorized into strata based on glycemic goals and analyzed for acute and chronic improvements in meeting targets.

IBG averaged 182.38±93.83 mg/dL and FBG values were significantly lower (131.43 ± 68.70 mg/dL, p<0.001). Normoglycemic strata (71-140mg/dL) shifted from 33.3% initial to 47.2% final. Most IBG values were between 141-250 mg/dL and 44.2% of those finished in normoglycemic strata. Among the 27.9% (n=218) with IBG hypoglycemia, only 7.7% (n=60) of FBG values remained into the strata. Long-term effect on BG values were not significant (p>0.11).

Diabetes education program that includes supervised exercise were beneficial to acute blood glucose management in individuals with T1DM and require self-monitoring of blood glucose and a multidisciplinary approach to evaluate and supervise glycemic responses based on diet, insulinization, and physical activity.

Effect of High Fructose Intake on the Development of Hypertension in the Spontaneously Hypertensive Rats: The Role of AT1R/Gp91phox Signaling in the Rostral Ventrolateral Medulla

Kay Lh Wu and Chih-Wei Wu*
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Abstract

Both genetic and dietary factors determine the development of hypertension. Whether dietary factor impacts the development of hereditary hypertension is unknown. Here, we evaluated the effect of daily high fructose diet (HFD) on the development of hypertension in adolescent spontaneously hypertensive rat (SHR). Six-week-old SHR were randomly divided into two groups to receive HFD or normal diet (ND) for 3 weeks. The temporal profile of systolic blood pressure (SBP), alongside the sympathetic vasomotor activity, in the SHR-HFD showed significantly greater increases at 9-12 weeks of age compared with the age-matched SHR-ND group. Immunofluorescence was used to identify the distribution of reactive oxygen species (ROS), oxidants and antioxidants in rostral ventrolateral medulla (RVLM) where sympathetic premotor neurons reside. In RVLM of SHR-HFD, the levels of ROS accumulation and lipid peroxidation were elevated. The changes in protein expression were measured by Western blot. NADPH oxidase subunit, gp91phox and angiotensin II type I receptor were upregulated in RVLM neuron. On the other hand, the expression of extracellular superoxide dismutase was suppressed. Both molecular and hemodynamic changes in the SHR-HFD were rescued by oral pioglitazone treatment from week 7 to 9. Furthermore, central infusion with tempol, a ROS scavenger, effectively ameliorated ROS accumulation in RVLM and diminished the heightened pressor response and enhanced sympathetic activity in the SHR-HFD. Together, these results suggest that HFD intake at adolescent SHR may impact the development of hypertension via increasing oxidative stress in RVLM which could be effectively attenuated by pioglitazone treatment.
A Potential Screening Strategy of Pancreatic Cancer in New-Onset Diabetes Patients Using Serum CA19-9 in Combination with Age and BMI

Xiangyi He* and Yaozong Yuan
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Abstract

**Background and aim:** Type 2 diabetes mellitus is widely considered to be associated with pancreatic cancer. New-onset diabetic mellitus (NODM) is recently recognized as the early symptom of pancreatic cancer (PC). We aimed to establish screening strategy based on NODM for PC using serum CA19-9 and clinic characteristics.

**Methods:** Preoperative serum levels of CA19-9 and clinicopathological characteristics were retrospectively analyzed in consecutive 30 with or 30 without pancreatic ductal adenocarcinoma (PDA) in new-onset diabetes (less than 24 months) patients.

**Results:** Patients studied are described in more detail in Table 1. The gender distribution and Fasting Blood Glucose (FBG) was similar in both groups. The average age of the 2 groups was significantly different (P= 0.01) with the NODM group being younger than the PC with NODM group, the average age (SD) are 62.85(9.86) year and 76(9.94) respectively. The BMI of malignant group was lower than NODM group (they are 21.63±3.03 Kg/M² and 24.77±3.80 Kg/M² respectively), and the duration of DM was also shorter in PC group. The ROC curve based on CA19-9 resulted in an AUC of 0.975 (95% CI, 0.943-1.0), at the cut-off value of 35u/l, the sensitivity and specificity were 82.8% and 100% respectively. Furthermore, in subgroup of patients BMI>22, 11 NODM with PC and 21 NODM were included, AUC of serum CA19-9 was 1, at the cut-off value of 35 u/l, the sensitivity and specificity were both 100% and 100% respectively.

**Conclusions:** The NODM patients with old age and low BMI are more likely to be PC. Screening for pancreatic cancer (PC) based on NO-DM using serum CA19-9 have low sensitivity but high specificity, but in BMI > 22 patients, the diagnostic accuracy of serum ca19-9 is more high. However, our hypothesis needed more data to support.

Effects of Biotin Supplementation During the First Week Post-Weaning

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Abstract

**Introduction:** Pancreatic islet maturation plays an important role in islet function later in life. In rodents, the first week of post-weaning is critical for islet maturation. Multiple studies have documented the detrimental effects of several conditions on pancreatic maturation; however, few studies have addressed the use of pharmacological agents to enhance islet maturation. Biotin might have a potential action on islet maturation. Pharmacological concentrations of biotin can modify different biological functions, such as development or islet function. In a previous study, we found that mice fed a biotin-supplemented diet for eight weeks after weaning increased insulin secretion, enlarged islet size and modified islet morphology. In this study, we investigate the effect of biotin during the first week post-weaning.

**Methods:** Female BALB/cAnN Hsd mice were fed a control or a biotin-supplemented diet (0.8 or 100 mg of biotin/kg diet, respectively) for one week after weaning.

**Results:** Versus the control, biotin-supplemented mice showed increased beta-cell proportion (control=69.4±1.49; biotin-supplemented=78.3±1.04 %) and decreased alpha-cell (control=30.7±1; biotin-supplemented=21.7±1.04 %, p<0.005). The number of islets and the islet area increased 35.1 and 40 %, respectively, compared with the control group (p<0.005). This effect was due to increased proliferation (Ki67 positive beta-cells: control=1.20±0.93; biotin-supplemented=5.59±1.01; p<0.01) but not to neogenesis or apoptosis. No differences were found in insulin secretion, blood glucose concentrations, or serum insulin levels.

**Conclusion:** These results indicate that biotin supplementation is capable of affecting beta-cell proliferation and might be a therapeutic agent for establishing strategies for regenerative medicine.
Nanocurcumin-Chitosan Targets GLUT-4 Translocation and PI3 Kinase Pathway in L6 Skeletal Muscle Cells

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Abstract

Curcumin, a yellow pigment in the Indian spice, turmeric is in general considered its most active constituents, was explored earlier for its therapeutic role in diverse disorders. The major factor limiting its optimum potential is its low bioavailability. The present study was carried out to investigate whether curcumin nanoparticles play any beneficial role against diabetes mellitus. The objectives of the present study included preparation, characterization and exploration of nanocurcumin for improved bioavailability and therapeutic efficacy in experimental diabetes and identification of cellular targets.

Nanocurcumin encapsulated with chitosan (NC-C) were prepared, characterized by biophysical techniques and pharmacokinetics of NC-C was studied. The effects of nanocurcumin were investigated on GLUT-4 translocation and on PI3 Kinase pathway in L6 skeletal muscle cells. The therapeutic efficacy of NC-C was evaluated in experimental diabetes by monitoring appropriate biochemical and cellular markers of diabetes, dyslipidemia, plasma and cellular oxidative stress, liver and kidney functions following dose response studies.

A significant increase in bioavailability was recorded with nanocurcumin encapsulated in chitosan. Biophysical characterization by electron microscopy and other techniques confirmed the nanoparticles. Treatment of L6-GLUT4myc myotubes with nanocurcumin encapsulated in chitosan caused a substantial increase in the GLUT-4 translocation to the cell surface and was associated with the phosphorylation of AKT (Ser-473). Administration of NC-C or nanocurcumin to streptozotocin treated diabetic animals for 30 days, resulted in glucose and lipid homeostasis. The oxidative stress was alleviated significantly by nanocurcumin administration.

New Treatment of Complications after Drainage Surgery Neovascular Glaucoma in Patients with Diabetes

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Abstract

Actuality: Drainage operations are becoming more widespread in the treatment of neovascular glaucoma in patients with diabetes mellitus. Unfortunately, according to various authors, their effectiveness does not exceed 70-80%. There is a question of finding ways for normalization increased intraocular pressure (IOP) in postoperative period.

Aim: The aim is to estimate efficiency of contact transscleral diode-laser cyclocoagulation drainage after surgery neovascular glaucoma, which did not lead to normalization of IOP.

Materials and Methods: The study included 8 patients observed in the ophthalmic department of Endocrinology Research Centre, Moscow. All of them had previously drainage operation for secondary noncomensated neovascular glaucoma on the background of diabetic retinopathy. It wasn't succeeded to stabilize IOP in the postoperative period. It was performed contact transscleral diode-laser cyclocoagulation by an original method

Results: Intraocular pressure was compensated (within 12-15 mm Hg) at all patients after trans-scleral contact diode-laser cyclocoagulation. Any complications during the period up to half a year haven't been noted.

Conclusion: It is possible to use contact transscleral diode-laser cyclocoagulation after drainage surgery of neovascular glaucoma for normalization of non-compensated intraocular tension at patients with diabetes mellitus.
Accuracy of Capillary Blood Sugar Test When Fasting in Diabetes Patients or General Population, Comparison with Venous Blood Sugar Test: Performance Evaluation of G300 Based on ISO 15197 Standards

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Abstract

Self-monitoring of blood glucose (SMBG) plays an important role in management of diabetes mellitus. Blood sugar measurement is based on using plasma glucose separated from whole blood, but many people with diabetes and health care providers use a portable glucose meter for convenience. However a glucose meter uses whole blood and evaluation method is different from clinical laboratory, performance evaluation of a glucose meter is essential process. The aim of this study was to evaluate the accuracy and agreement of G300 portable glucose meter against standard venous glucose testing methods.

This study is the evaluation of G300 system accuracy following ISO 15197 standards. Fasting capillary and venous glucose samples were collected from 100 adult patients and general population. Capillary blood samples collected by pricking a fingertip with a lancet were immediately analyzed using a Green Cross Medis G300® portable glucose meter, and venous samples were analyzed using machine in a clinical laboratory.

In repeatability precision evaluation of those glucometers, standard deviation is 2.9-3.7 mg/dL at glucose levels under 100mg/dL and coefficient of variation is 1.7-3.2% at glucose levels over 100mg/dL. In accuracy evaluation, 99.5% of difference values between results of G300 portable glucose meter and clinical laboratory were within 95%. In Consensus Error grid analysis, all values (100%) are within zone A. These results were acceptable for the ISO15197 criteria in all glucose concentrations.

This study showed that G300 can provide reliable blood glucose results for patients and health care providers to manage diabetes mellitus, satisfying the ISO15197 criteria.

The Effect of Locally Delivered Vanadyl Acetylacetonate on the Biomechanical Properties of Bone in Diabetes-related Osteoporosis

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Abstract

Type 1 diabetes-related (T1DM-related) osteoporosis is a prominent health concern characterized by impaired bone strength that predisposes patients to increased risk of fracture. With a lack of safe and effective anabolic therapies for over 400,000 people in the United States who suffer from this complication, there is an unequivocal clinical need to identify treatment options. Vanadyl acetylacetonate (VAC) is an effective insulin-mimetic that has been found to accelerate both diabetic and normal fracture healing experimentally. We therefore hypothesized that VAC would enhance bone growth and stability in a BB Wistar T1DM-related osteoporosis rat model. A surgical procedure was performed in which either a 0.1 mL saline solution or 1.5 mg/kg VAC solution was injected into the intramedullary canal of each rat’s right femur. Animals were sacrificed 4 and 8 weeks post-surgery and bone mineral density (BMD) was assessed using micro computed tomography. VAC-treated femora showed a 5.1% increase in BMD at 4 weeks and a 16.8% increase at 8 weeks, compared to controls. The positive effects of VAC will be more clearly revealed through further addition of animals to both treatment and experimental groups of this pilot study. We plan to perform torsional testing that can link the observed increases in BMD following VAC treatment to improvements in biomechanical properties. Although preliminary, the data regarding VAC’s role in improving the diminished osseous properties of TIDM-induced osteoporotic bone indicates a promising starting point to reverse this complication.
Dulce Wireless Tijuana: Adaptation and Impact of the Project Dulce™ Model with and without Mobile and Wireless Technology in Patients with Type 2 Diabetes Mellitus at a Family Medicine Unit in Northern Mexico

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Abstract

Introduction: This study evaluated a model of care for patients with type 2 diabetes with multidisciplinary care, multi-partner participation and the use of Mobile Wireless Technology (MWT).

Objective: To evaluate the effectiveness of the clinical education model Project Dulce™ with and without MWT to achieve improved metabolic control, the practice of healthy lifestyles, knowledge of the disease and quality of life in patient’s w/T2DM.

Material and Methods: Randomized control clinical trial of 301 patients with diabetes type 2 and glycated hemoglobin (HgA1c) ≥ 8 %, receiving care at the clinic UMF No. 27 IMSS in Tijuana, Mexico. 99 patients received the clinical, education model Project Dulce™ (PD); 102 patients received the MWT plus the Project Dulce™ model (PD-TE); and 100 patients received standard medical treatment (CG). Patients were followed for 10 months. Comparisons between groups were performed using one-way ANOVA.

Results: Significant decreases of 3.02 % HgA1c for the PD-TE intervention group and 2.63% for the PD group were observed between baseline and the tenth month (p < 0.001). The CG also showed declines of 1.30% (p < 0.001). Similarly, significant improvements were obtained in knowledge of diabetes in all groups, favoring more the PD-TE intervention group and 2.63% for the PD (p < 0.001). Similarly, significant improvements were obtained in knowledge of diabetes in all groups, favoring more the PD-TE intervention group.

Conclusions: Project Dulce™ model with or without MWT provides an effective method for improving glycemic control and knowledge of diabetes in the management of type 2 diabetes in low income populations. Enhancing clinical and educational interventions with the DWT technology tools has the potential to produce larger reductions in HgA1c.

Cardiometabolic Syndrome and Body Composition of Individuals after Cervical Spinal Cord Injuries Compare to the Healthy Control

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Abstract

Physical activity is widely accepted as a necessary component for individual health. Regular exercise leads to favorable changes in glucose and lipoprotein metabolism. The beneficial effects of exercise training on prevention of cardiometabolic complications include decrease in serum glucose concentrations, increase in serum high density lipoprotein and a reduction in serum triglyceride levels. Impaired motor function may also contribute to limited mobility and increase the risk of metabolic disorders commonly associated with numerous pathological complications. Therefore, the aim of the study was to analyze selected factors of metabolic syndrome in individuals after cervical spinal cord injuries (CSCI), and the potential relationship between these variables and somatic parameters and sports activity. It was hypothesized that, compared to healthy population, enforced sedentary lifestyle and muscle paresis below the level of injury may increase the risk of hyperglycemia and dyslipidemia in men after CSCI.

Material and methods: Thirty-six males with chronic SCI assigned into the physically active “low point” (LP, n = 18) or “high point” (HP, n = 6) WR players groups and the sedentary controls (SED, n = 12), participated in this study. The study group comprised wheelchair rugby competitors and, according to IWRF26. All study participants were in the chronic phase of disability and only moved using the wheelchair.

The following biochemical parameters were measured in order to determine the risk of metabolic syndrome: glucose, total cholesterol, HDL and LDL cholesterol and triglycerides (TG). Body mass was measured using chair scales WE150P3 K (MENSOR, Poland). Visceral fat level and trunk fat percentage were estimated with the Tanita Viscan visceral and trunk fat analyser AB140. Body mass index (BMI), waist circumference (WaC) and body adiposity index (BAI) were all calculated. Body structure and composition of men after CSCI compared to the able-bodied population was analysed with the test for proportion using data from the report of the Central Statistical Office.

Results: Body structure of men after CSCI was compared to that of the able-bodied population based on the BMI. HDL cholesterol levels differed significantly (ie., by 34.9%) between men after CSCI and the able-bodied
population (p<0.05). The difference between glucose levels (17.2%) was also significant (p<0.05). The body adiposity index differed significantly between the wheelchair rugby players and post-CSCI men not engaged in any sporting activities (p<0.05). A significant correlation was noted between sporting activity and visceral adipose tissue mass in the control participants and low-point players (p<0.001 and p<0.05) and between TC/HDL-C ratio (F=3.50, p<0.05) and the LDL/HDL-C ratio (F= 3.51, p< 0.05).

**Conclusion:** Sports activities undertaken by post-CSCI men improve their cardiometabolic status, but not to the level presented by general population. Hyperglycemia has been demonstrated in the SED group and among the low point players below 30 years of age.

**Inflammatory Cytokine, Neurotrophic and Growth Factors Responses to Continuous and Intermittent Exercise in Patients with Type 1 Diabetes and Healthy Controls**

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**Abstract**

**Introduction:** Type 1 diabetes mellitus (T1DM) is commonly associated with pathological complications, such as micro- and macroangiopathy, neuropathy, and nephropathy. According to scientific reports diabetic neuropathy can result in reduced muscle strength due to progressive muscular atrophy. Regular physical exercise has been shown to improve cognitive function by increasing neurotrophins and growth factors in healthy individuals. Nonetheless, data is conflicting on whether exercise augments chronic glycaemic control and hormonal alterations related to muscle atrophy in patients with T1DM. It seems to be important to find an effective method for preventing chronic complications associated with T1DM. Therefore, the aim of the study was to assess the effect of continuous and intermittent exercise on glycaemic control and concentration of inflammatory cytokine, neurotrophic and growth factors in patients with Type 1 diabetes.

**Methods:** Twelve patients (age: 29.2 ± 9.5 years) suffering from T1DM for 12.1 ± 6.0 years, with HbA1c at approximately 56.3 mmol/mol, free of diabetic complications, and twelve adults without diabetes performed the 40 min continuous exercise (ExC of 50% of lactate threshold load) and intermittent exercise (ExInt of 120 % LAT with duration of 4 × 5 minutes, intermittent with 5 minute rest after each bout of exercise). Glycaemia, transforming growth factor beta (TGF-β), tumor necrosis factor alpha (TNF-α), insulin like growth factor -1 (IGF-1), their binding protein (IGFBP-3), and brain-derived neurotrophic factor (BDNF) concentrations were measured at rest, immediately and up to 24 h after exercise.

**Results:** A significant decrease in serum glucose concentration was observed immediately after ExC (p < 0.01) and a tendency to lower fasting glycaemia on day after ExC and ExInt was revealed. Insulin dosage was slightly reduced after each exercise test. A significantly lower baseline serum concentrations of IGF-1 and BDNF were showed in the T1DM in comparison with healthy subjects (p < 0.05). In the T1DM group ExC significantly increased the level of IGF-1 (188.2 ± 34.8 vs. 265.5 ± 80.3 ng/mL; p < 0.05). Significant interaction effects for the type of exercise (p < 0.01) on IGF-1 and BDNF was revealed. Serum concentration of BDNF increased in response to ExInt (p < 0.01). TGF-β increased significantly in response to ExC in T1DM (p < 0.05), and in response to ExInt (p < 0.01) in the control group. The post-exercise level of TNF-α after ExInt was significantly lower compared to TNF-α after ExC (p < 0.05).

**Conclusions:** The study results suggest that the continuous and high-intensity intermittent exercise may be effective in reducing the risk of glycaemic disorders in the T1DM patients. The intermittent exercise could increase the secretion of selected neurotrophic factors and reduce inflammation, potentially leading to improved neuromuscular function. Whether this therapy results in long-term clinical benefits needs further investigation.
Impact of Obesity and Insulin-resistance on Bone Mineral Density in Tunisian Postmenopausal Women

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Abstract

Aim: The association of bone mineral density with obesity and insulin-resistance remains unclear. This study aimed to explore associations of obesity and its related parameters with bone mineral density in Tunisian postmenopausal women. Independently from obesity, we also investigate the effect of insulin-resistance on bone.

Methods: Eighty-one postmenopausal women were recruited. Data were analyzed for obese (N= 57) and non-obese women (N= 24) and for insulin-resistant (N= 43) and non-insulin-resistant women (N=36). Anthropometric and biochemical parameters were recorded. Bone mineral density in different sites and body composition were measured using dual-energy X ray absorptiometry.

Results: Higher bone mineral density was observed in obese women than those non-obese in the left femur (P = 0.0067), right femur (P = 0.0108), total hip (P = 0.0077) and the whole body (P = 0.0276). Also bone mineral density was significantly greater in insulin-resistant women than in non-insulin-resistant women when measured in the left femur and total hip. Positive correlations were recorded between bone mineral density and anthropometric parameters, body composition parameters, and glycemia (r = 0.249, P < 0.05). Multiple linear regression analysis shows that only trunk fat (P < 0.05) and lean mass (P < 0.05) were independently and positively related to bone mineral density, and the waist circumference was the only anthropometric parameter independently and negatively associated to bone mineral density.

Conclusions: Bone mineral density is improved in obese and insulin-resistant women. Also, trunk fat and lean mass are likely to be a key positive independent factor for bone mineral density.

Adjusting Doses of U-500R Insulin: The Importance of Using Continuous Blood Glucose Monitoring

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Abstract

Introduction: A U-500R insulin titration protocol was implemented for patients requiring > 200 units of insulin per day. Similar to U-100 insulins, titration was based on patient BG logs. However, there was concern for nocturnal hypoglycemia, as U-500R is expected to peak while the patient is sleeping and s/he may not realize hypoglycemia is occurring. In this report, we describe how continuous blood glucose monitoring (CGM) may have prevented serious hypoglycemia in a patient receiving U-500R insulin.

Case study: A 61 year-old patient receiving U-500R. BG log demonstrated an average: FBG 220 mg/dL, breakfast PPBG 209 mg/dL, lunch PPBG 181 mg/dL, dinner PPBG 154 mg/dL and bedtime BG 155 mg/dL, with no values < 70 mg/dL. Based on these readings, the evening dose was increased to 0.29 mL (145 units) and the morning dose remained at 0.37 mL (185 units). A CGM was then applied to the patient’s arm for two weeks. Despite the lack of patient reported hypoglycemic episodes per BG logs or symptoms, when the data was reviewed, CGM patterns revealed six events of hypoglycemia where BG was <70 mg/dL and may have been as low as < 40 mg/dL. The majority of these events occurred between midnight at 6am. The bedtime dose was decreased and CGM was repeated to more accurately stabilize his insulin therapy.

Conclusion: If the U-500R dose had continued to be adjusted based on patient recorded BG values alone, we likely would have continued to increase the nighttime dose to reduce FBG values, which may have resulted in severe hypoglycemia or death.
Increased Uptake of Oxidized LDL by Macrophages from Type 2 Diabetics is Inhibited by Polyamines

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Abstract

The aim of this study was to evaluate the effect of polyamines putrescine, spermidine and spermine on human LDL oxidation and to assess the ability of macrophages derived from type 2 diabetic patients to uptake oxLDL. Polyamine effect was compared with α-tocopherol. Four healthy subjects and eight type 2 diabetic patients were included in this study. To characterize type 2 diabetic patients and non-diabetic subjects, laboratory test were carried out. Glucose, glycated haemoglobin (HbA1C), triglycerides, low (LDL) and high density lipoproteins (HDL) and serum lipid peroxidation were measured in blood. The study was performed in three stages. For each stage, ten experimental conditions comparing the effect of polyamines with α-tocopherol (10 mM solutions) on LDL oxidation and the uptake of oxLDL by macrophages were analyzed. MDA concentration was found to be significantly higher in type 2 diabetic patients compared to healthy subjects (5.6 ± 0.58 vs. 2.66 ± 0.31 mM MDA, respectively, (P <0.05)). Percent of macrophages containing oxLDL was determined by means of red oil staining. The uptake of oxLDL by macrophages derived from diabetic patients was clear. The uptake of oxLDL was inhibited when the oxidation was prevented by polyamines or α-tocopherol. Spermine showed high antioxidant capacity (96.67 ± 1.53 % vs. 25.67 ± 2.30 %) compared to α-tocopherol (96.67 ± 1.53 % vs. 47.00 ± 7.20 %) at the concentration tested.

In conclusion, polyamines especially spermine, has a potent antioxidant effect compared to α-tocopherol on human LDL oxidation, followed by spermidine and putrescine. The results have clinical relevance in the diabetic complications and add knowledge on the role of polyamines as natural antioxidants.

Attenuation of STZ-induced Diabetic Neuropathy by Bacopa monnieri via Inhibition of Advanced Glycation End Products and Oxidative/Nitrosative Stress

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Abstract

Objectives: Reactive oxygen species, formation of AGEs and apoptosis are implicated in the pathogenesis of diabetic neuropathy. The aim of the present study was to explore the effect of Bacopa monnieri L. (Family: Scrophulariaceae) on thermal and mechanical hyperalgesia, allodynia, MNCV and oxidative-nitrosative stress in streptozotocin- (STZ) induced experimental diabetes.

Methods: Diabetes neuropathy was induced in Wistar rats by injection of STZ (65 mg/kg, i.p.) 15 min after Nicotinamide (230 mg/kg, i.p.) administration. Hydro-alcohol extract of B. monnieri aerial parts was assessed by oral administration at 100, 200 and 400 mg/kg in STZ-induced diabetic rats. Thermal hyperalgesia (Eddy’s hot plate and tail immersion), mechanical hyperalgesia (Randall-Selitto) and tactile allodynia (Von Frey hair tests) were evaluated in all groups of streptozotocin diabetic rats to assess the extent of neuropathy. Diabetic rats developed neuropathy which was evident from a marked hyperalgesia and allodynia; reduced MNCV associated with increased formation of AGEs and reactive oxygen/nitrogen species.

Results: Chronic treatment with B. monnieri hydro-alcohol extract (100, 200 and 400 mg/kg) for 30 days starting from the 60th day of STZ-induction significantly attenuated behavioral and biochemical changes associated with diabetic neuropathy.

Conclusion: Present study suggested that B. monnieri hydro-alcohol extract corrected the hyperglycemia and partially reversed the pain response in diabetic rats through modulation of oxidative-nitrosative stress and reduction in AGEs formation in the diabetic rats and thus it may find clinical application to treat neuropathic pain in diabetic patients.
Notes
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